DONATION OF HUMAN EGGS FOR RESEARCH

A REPORT BY
THE BIOETHICS ADVISORY COMMITTEE

SINGAPORE

November 2008

FOREWORD

The use of human eggs in biomedical research is not new. For many years researchers have successfully used eggs to investigate the causes and treatment of infertility. However, new directions in research and a growing concern with the ethics of egg donation have prompted the present Report. Research with human eggs is no longer confined to research into infertility. Increasingly, it is part of a much wider inquiry into the properties of stem cells and their potential clinical applications. In addition, the ethics of egg donation have received recent attention and publicity because eggs are also a valuable fertility resource, and are sought after for use in fertility treatment. The demand for eggs for fertility treatment and for research raises the possibility of exploitation of women for their eggs.

The ethical aspects of egg donation also take on an added importance when it is recognised that donation is not without risk to the donor. In general, the ethics of donation of tissue raises issues of safety, informed consent and compensation. The BAC thus views it as timely to review the ethics of egg donation for research, and the regulatory implications that may follow from such a review.

This Report is the outcome of over a year of deliberation, in the course of which consultations were made with civic, religious, medical and scientific bodies, and international guidelines and best practice were reviewed. Local and international experts were consulted, and a public forum was organised. The result is a total of seven recommendations, dealing with consent, compensation and care of donors, the import and use of eggs in research, and the need for regulatory control.

I hope this Report and its recommendations will help support research whilst ensuring that it is done in an ethical way. I would like to thank all who have given the BAC their views. Comments from concerned organisations and individuals were all considered and have helped shape the eventual position the BAC has adopted. I would also like to thank Professor Lee Eng Hin, Chair of the Working Group that produced this report, and the members of the Group, for their time and effort.

Professor Lim Pin
Chairman
Bioethics Advisory Committee
November 2008

BIOETHICS ADVISORY COMMITTEE (2007 – 2008)

Chairman

Professor Lim Pin
University Professor, National University of Singapore

Deputy Chairman

Professor Lee Hin Peng
Department of Community, Occupational and Family Medicine, Yong Loo Lin School of Medicine, National University of Singapore

Members

Professor Alastair Campbell
Director, Centre for Biomedical Ethics, Yong Loo Lin School of Medicine, National University of Singapore

Mr Han Fook Kwang
Editor, The Straits Times

Professor Kandiah Satkunanantham
Director of Medical Services, Ministry of Health

Professor Eddie Kuo Chen-Yu
Professorial Fellow, Division of Communication Research, Wee Kim Wee School of Communication & Information, Nanyang Technological University

Professor Lee Eng Hin
Director, Division of Graduate Medical Studies, Yong Loo Lin School of Medicine, National University of Singapore

Mr Charles Lim Aeng Cheng
Principal Senior State Counsel and Parliamentary Counsel, Legislation and Law Reform Division, Attorney-General's Chambers

Mr Nazirudin bin Mohd Nasir
Head, Office of the Mufti, Majlis Ugama Islam Singapura

Associate Professor Nuyen Anh Tuan
Department of Philosophy, Faculty of Arts and Social Sciences, National University of Singapore

Associate Professor Patrick Tan Boon Ooi
Duke-NUS Graduate Medical School and Group Leader, Genome Institute of Singapore

Professor Yap Hui Kim
Head and Senior Consultant, Paediatric Nephrology, Dialysis and Renal Transplantation, National University Hospital

HUMAN EMBRYO AND CHIMERA RESEARCH WORKING GROUP

Chairman

Professor Lee Eng Hin
Director, Division of Graduate Medical Studies, Yong Loo Lin School of Medicine, National University of Singapore

Members

Professor Eddie Kuo Chen-Yu
Professorial Fellow, Division of Communication Research, Wee Kim Wee School of Communication & Information, Nanyang Technological University

Dr Lim Bing
Senior Group Leader, Biological Investigations, Genome Institute of Singapore

Mr Nazirudin bin Mohd Nasir
Head, Office of the Mufti, Majlis Ugama Islam Singapura

Professor Ng Soon Chye
Director, O & G Partners Fertility Centre, Gleneagles Hospital

Associate Professor Nuyen Anh Tuan
Department of Philosophy, Faculty of Arts and Social Sciences, National University of Singapore

INTERNATIONAL PANEL OF EXPERTS

Professor Martin Bobrow
Emeritus Professor of Medical Genetics, University of Cambridge, United Kingdom

Professor Bartha Maria Knoppers
Professor of Law, University of Montreal, Canada, and Canada Research Chair in Law and Medicine

Professor Bernard Lo
Professor of Medicine and Director, Program in Medical Ethics, University of California, United States of America

Dr Thomas H Murray
President, The Hastings Center, United States of America

SECRETARIAT

Dr Sylvia Lim
Head of Secretariat

Associate Professor John Elliott
Research Fellow

Mr W Calvin Ho
Senior Research Associate

Miss Charmaine Chan
Administrative Officer (from September 2008)

Mr Alvin Chew
Administrative Officer (till July 2008)

Miss Seah May-Ann
Management Assistant Officer (from July 2008)

About the Bioethics Advisory Committee

The Bioethics Advisory Committee (BAC) was established by the Singapore Cabinet in December 2000 to examine the ethical, legal and social issues arising from research in the biomedical sciences and to develop and recommend policies on these issues. It aims to protect the rights and welfare of individuals, while allowing the biomedical sciences to develop and realise their full potential for the benefit of mankind.

The BAC reports to the Steering Committee on Life Sciences (formerly the Life Sciences Ministerial Committee).

11 Biopolis Way
#10-12 Helios
Singapore 138667
www.bioethics-singapore.org

CONTENTS

ANNEX A **Consultation Paper:**
Donation of Human Eggs for Research

ANNEX B **Consultation Paper Distribution List**

ANNEX C **Written Responses to the Consultation Paper**

ANNEX D **Summary of Responses from REACH Online Discussion Forum and e-Consultation**

ANNEX E **Background Papers**

1. Oocyte Donation — Clinical and Scientific Aspects
   - Professor Ng Soon Chye
   Director, O & G Partners Fertility Centre, Gleneagles Hospital, Singapore

2. Oocyte Procurement for Research
   - Dr Benjamin Capps
   Centre for Biomedical Ethics, National University of Singapore; and Centre for Ethics in Medicine, University of Bristol, UK

DONATION OF HUMAN EGGS FOR RESEARCH

EXECUTIVE SUMMARY

1. This Report addresses the ethical, legal and social issues raised when human eggs are donated for research and highlights the importance of ensuring that the eggs are obtained ethically. The Report follows a public consultation conducted by the BAC from 7 November 2007 to 7 January 2008.

2. The procedure by which eggs are obtained is invasive and carries some risk and inconvenience, which are accepted by women seeking fertility treatment, but probably deter altruistic donation by women not undergoing any treatment. Women donating eggs for treatment or research are exposed to this risk as part of the process of obtaining their eggs. The main risk lies in the development of ovarian hyperstimulation syndrome, a condition which may be life-threatening if severe, although such cases are rare.

3. The informed consent of the donor is a fundamental requirement when any human tissues, including eggs, are donated for research purposes. It is important that this requirement is met in the case of women considering donation of eggs for research.

4. In the case of a donor undergoing fertility treatment, it is also important that her consent be taken independently of the treatment team. Consent should be taken only if she has indicated a willingness to donate her surplus eggs for research after discussing the fate of such eggs with her physician. She must be certain that she will not require these eggs for future use and must also have decided that she does not want to donate them for the fertility treatment of others.

5. The Report considers the issue of compensation for egg donation, and the associated risk of exploitation through commercialisation of eggs, either as an explicit policy or as an unintended consequence of substantial compensation amounting to an inducement. Recent developments in relation to compensation of egg donors in Europe and North America highlight continuing concerns over the potential trade of eggs across national boundaries and the exploitation of women.

6. It is the view of the Bioethics Advisory Committee (BAC) that altruism should be the basis of egg donation, as is already reflected in legal prohibitions on commercial transactions in eggs. Women should not be compensated for the donation of eggs for research when these are surplus to fertility treatment or obtained as a result of other medical treatments. It does, however, consider that women not undergoing any treatment, who donate eggs specifically for research, should be compensated for loss of time and earnings in addition to reimbursement of expenses directly incurred in donating. Such compensation must not amount to an inducement, and should not be tied to the actual number or quality of eggs provided.

7. The BAC is of the view that all research with human eggs should be regulated, and that the standards applicable to the donation of eggs for research in Singapore should also apply to eggs obtained abroad and used in Singapore.

LIST OF RECOMMENDATIONS

Recommendation 1
The procurement and use of human eggs for research should be regulated.

Recommendation 2
Consent for the donation of human eggs for research should be obtained without any coercion or inducement. Potential donors must be provided with sufficient information in an understandable form, and given adequate time to make an informed decision.

Recommendation 3
Donors should be informed that they have the right to withdraw consent or vary the terms of consent any time before their eggs are actually used in research.

Recommendation 4
Consent for the donation of eggs for research from women undergoing fertility treatment should be taken independently of the treatment team. The donors should confirm in writing that they do not require these eggs for future reproductive use.

Recommendation 5
Women undergoing ovarian stimulation specifically for research should be provided with prompt and full medical care when complications occur as a direct and proximate result of the donation. Responsibility for this provision should rest with the researchers and their institutions.

Recommendation 6
Egg donors should be compensated only for loss of time and earnings as a result of the procedures required to obtain the eggs, and only if the eggs were obtained specifically for research purposes, and not as a result of clinical treatment. Such compensation should be in addition to any reimbursement of expenses incurred. The relevant regulatory authority should determine the appropriate amount of such compensation.

Recommendation 7
The procurement or use of human eggs from any source by procedures not consistent with the recommendations in this Report should be prohibited.

DONATION OF HUMAN EGGS FOR RESEARCH

I. Introduction

1.1 The Bioethics Advisory Committee (BAC) was established in December 2000, to examine the ethical, legal and social issues arising from biomedical research and development in Singapore, and to recommend policies to the Steering Committee on Life Sciences (formerly called the Life Sciences Ministerial Committee).

1.2 Donating eggs for fertility treatment has been practiced for more than two decades and is considered a well-established method for helping women who have problems conceiving. In contrast, the donation of eggs for research is more recent, and mainly follows from advances in embryonic stem cell research. Such research is important in contributing to our basic knowledge of the nature and potential of stem cells. This understanding is generally viewed as the key to unlocking the potential of stem cell therapy for serious and currently untreatable diseases, such as diabetes, Alzheimer's disease and Parkinson's disease.

1.3 However, the availability of human eggs for research is limited as donors are almost invariably women undergoing fertility treatment, which naturally takes priority over any donation of eggs for research. Moreover, the invasiveness of the medical procedures involved in obtaining the eggs entails some risk to the donors. Thus safety and ethical concerns arise, the most important being the possibility that vulnerable women may be exploited, through various forms of inducement to provide eggs for research. Associated with this is also the risk of commercialisation of the body.

1.4 At a practical level, the difficulty lies in determining whether any payment or compensation should be given to egg donors, and if so, the appropriate form or amount, and how to regulate it. It is also necessary to consider if it is ethically acceptable for researchers to obtain eggs from women who are not undergoing fertility treatment, in which case similar concerns arise.

1.5 The need for guidance on the donation of eggs for research, and ethical issues of equity, compensation and the welfare of donors, formed the basis of a public consultation conducted by the BAC from 7 November 2007 to 7 January 2008. A Consultation Paper,[1] set out in Annex A, was sent to 94 research, governmental and healthcare institutions (including 21 fertility clinics), and professional and religious organisations for comment. A list of these institutions

1 Bioethics Advisory Committee, Singapore, *Donation of Human Eggs for Research: A Consultation Paper,* 7 November 2007.

and organisations is given in Annex B. Feedback was also received from members of the public through various means including email, and an online discussion forum and e-consultation managed by REACH.[2] A public talk on the subject was held on 22 November 2007.

1.6 Opinion on the following issues was solicited:

(a) Whether healthy women not undergoing fertility treatment should be allowed to donate eggs for research, and if so, under what conditions;

(b) Whether egg donors for research should be compensated for time, inconvenience and risk, and if so, what type of compensation or monetary amount would be acceptable, and not amount to an inducement;

(c) Whether there are circumstances in which the compensation for eggs could amount to a sale, and if so, whether such a sale should ever be contemplated; and

(d) Any prohibitions, limits or regulatory mechanisms that should govern the supply and use of human eggs for research in Singapore.

Respondents were also invited to raise any other matters of concern related to the donation of human eggs for research.

1.7 Written responses from 23 organisations, institutions and individuals were received and are set out in Annex C. A summary of the views received through the online discussion forum and e-consultation is provided in Annex D. This Report was finalised after careful consideration of the feedback and suggestions from the various organisations as well as the public. The recommendations take into account advice, comments and suggestions from local experts and the members of the BAC's International Panel of Experts. The BAC also considered two background papers on this subject prepared by experts in this area. Annex E consists of these two papers.

2 REACH (Reaching Everyone for Active Citizenry @ Home) is an agency set up by the Singapore Government to engage and connect with its citizens. http://www.reach.gov.sg/

II. Human Eggs in Research

2.1 Human eggs are required for embryonic stem cell research, and research into human fertility. The eggs can be used without being fertilised, for example, in studies into methods of egg maturation and preservation, or they can be used to create embryos.

2.2 An embryo can be created from an egg through *in vitro* fertilisation (IVF) by a sperm or through technologies such as somatic cell nuclear transfer (SCNT)[3] and parthenogenesis.[4] Stem cells can be derived from embryos thus created, and are useful for research that has the potential of understanding disease processes and finding cures for them. SCNT has the advantage of producing patient-specific cells that would not be rejected, when used for treatment.

2.3 Recently, several research groups have demonstrated that human skin cells can be transformed into cells with properties similar to those of embryonic stem cells through the introduction of specific genes into the cells.[5] Such cells are called induced pluripotent stem cells or iPS cells. This could lead to the creation of disease-specific or patient-specific cells, which are useful for further research into understanding the disease process or for clinical applications. However, it is still too early to decide whether this technology can replace the derivation of stem cells from embryos through IVF or cloning technology.

2.4 Human eggs are not readily available, and currently, most eggs for research are from women who have undergone fertility treatment. These could be surplus eggs which were not used for treatment, eggs that had failed to fertilise, or they could be immature eggs that were unsuitable for fertilisation. Other sources of eggs for research include cadavers, aborted foetuses and women undergoing medical procedures such as the removal of their ovaries.

2.5 Theoretically, it might also be possible to create eggs from embryonic stem cells, and eggs created this way could then be used in research. In 2005, researchers in the UK demonstrated that human embryonic stem cells displayed a capacity to generate immature gametes.[6] However, while it has been possible

---

3 Also sometimes referred to as research cloning or therapeutic cloning. SCNT involves the transfer of the nucleus of a somatic (differentiated) cell into an egg cell, the nucleus of which has been removed.

4 The process whereby the development of an organism starts in an egg that has not been fertilised.

5 Takahashi K et al, Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors, *Cell*, 131 (2007): 1-12; and Yu J et al, Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells, *Science*, 318 (2007): 1917-1920.

6 Aflatoonian B and Moore H, Germ cells from mouse and human embryo embryonic stem cells, *Reproduction*, 132 (2006): 669-707.

to create mouse eggs from mouse embryonic stem cells,[7] research on creating human eggs from human embryonic stem cells is still in the preliminary stages.

2.6 As eggs from fertility treatment are often all fertilised *in vitro* to ensure sufficient embryos for implantation, or are retained for future use by the woman herself or donated to other couples undergoing fertility treatment, insufficient eggs are available for research. Indeed, scientists have indicated that the scarcity of human eggs is a major limiting factor in stem cell research. In some leading scientific nations, the possibility of obtaining eggs from women not undergoing any form of medical treatment (i.e. healthy women) has been considered. There are however significant ethical questions to be considered if this is done. These questions are discussed in Part IV below.

7 Hubner K et al, Derivation of oocytes from mouse embryonic stem cells, *Science*, 300 (2003): 1251-1256.

III. Procedures and Risks Involved in Egg Donation

3.1 The procedures which a woman has to undergo in order to obtain eggs for fertility treatment or for research are essentially the same, and it is important that she understands the procedures and risks involved.

3.2 Donating eggs is a time-consuming process, associated with a certain degree of discomfort and possible health risks. A woman has to undergo stimulation of her ovaries through multiple hormone injections, followed by close monitoring of the development of her eggs through ultrasound scans and blood tests. Thereafter, the eggs are collected under mild anaesthesia via a special needle attached to an ultrasound vaginal probe. One can expect an average of between 20 to 40 injections under the usual regimes of ovarian stimulation.

3.3 Ovarian stimulation carries some health risks, because it can lead to a condition called ovarian hyperstimulation syndrome (OHSS). In addition, egg retrieval may cause excessive bleeding or infection. As the procedure of egg retrieval is done under mild anaesthesia, there are also risks associated with the type of anaesthesia administered. However, the risks in egg retrieval are relatively low. In a review of more than 4000 cases in an egg donation programme over a period of about seven years, it was found that the incidence of moderate to severe OHSS was 0.54% and that of complications related to egg retrieval was 0.4%.[8]

3.4 Mild OHSS is relatively common, affecting up to 10% of women undergoing ovarian stimulation, usually between five to nine days after egg retrieval. The condition can be easily managed without hospitalisation and usually resolves spontaneously within several days. Severe OHSS is rare but will require urgent medical attention. It is of late-onset (occurring between ten days to three weeks after egg retrieval) and is often associated with pregnancy. Women undergoing ovarian stimulation specifically for the purpose of donating eggs for research are unlikely to develop severe OHSS, as pregnancy is not expected to follow the retrieval of eggs. More details on the clinical aspects of ovarian stimulation are provided in the background paper (1) in Annex E.

3.5 There is some documented evidence that ovarian stimulation, which exposes women to increased concentrations of hormones, may lead to an increased risk of future cancers of the breast, ovary and uterus, although the risk appears low.[9] While the possibility of long term effects still needs further study, and current findings are not consistent or conclusive, it is not possible to rule out such effects. In view of possible health risks, the American Society for Reproductive

8 Bodri D, Complications related to ovarian stimulation and oocyte retrieval in 4052 oocyte donor cycles, *Reproductive Biomedicine Online,* 17, no. 2 (2008): 237-243.

9 Brinton L, Long-term effects of ovulation-stimulating drugs on cancer risk, *Reproductive Biomedicine Online*, 15, no. 1 (2007): 38-44.

Medicine has recommended limiting the number of stimulated cycles that a donor should undergo to about six.[10]

3.6 Women who are less than 30 years of age, with low body weight, irregular menstrual cycles, or polycystic ovaries are at increased risk of developing OHSS. OHSS can be prevented by careful exclusion of such less suitable egg donors, judiciously minimised use of the drugs given for ovarian stimulation, and close monitoring of the individual's response to the drugs. It is the responsibility of the attending physician to advise on whether a woman should undergo ovarian stimulation and to ensure that the risk of OHSS is reduced as much as possible in every case.

10 American Society for Reproductive Medicine, Practice Committee Opinion, Repetitive oocyte donation, *Fertility and Sterility*, 86 Suppl 4 (2006): S216-217.

IV. Ethical, Legal and Social Considerations

General Ethical Principles

4.1 Certain ethical principles have formed the basis of the BAC's recommendations in its various reports. These can be summarised as follows:

(a) *Respect for individuals*. The autonomy of individuals is to be respected, and their welfare and interests are to be protected, especially when their ability to exercise their autonomy is impaired or lacking. This principle underscores the importance of informed consent, respect for privacy, safeguarding confidentiality, and it also entails a proper regard for religious and cultural diversity;

(b) *Reciprocity*. The BAC has interpreted the idea of reciprocity between the individual and the wider society as an expression of the well established idea that there is some implicit recognition of mutual obligation that regulates the relationship between the individual and society. In biomedical research, agreed social benefits – as a public good – carry an implication that, if accepted, they inherently reflect an in-principle willingness to consider participation in research of the kind yielding the accepted benefits. This means that there is a balance to be struck between the interests of the public and the rights of individual participants, and that incompatible and irreconcilable ethical perspectives should be resolved with regards to the public interest;

(c) *Proportionality*. The regulation of research should be in proportion to the possible threats to autonomy, welfare or public good;

(d) *Justice*. The idea of justice as applied to research includes the general principle of fairness and equality under the law. This implies that access to the benefits of publicly funded research, and the burden of supporting it, should be equitably shared in society. It also implies that researchers incur a responsibility for the welfare of participants and their possible compensation or treatment in the event of adverse outcomes arising directly from their participation; and

(e) *Sustainability*. The research process should be sustainable, in the sense that it should not jeopardise or prejudice the welfare of later generations. For example, research leading to permanent change to the human genome would not be considered ethical, on the grounds that the long term implications are unforeseeable and might not be beneficial.

Ethical Governance of Research Involving Human Eggs

4.2 It is important to ensure that human eggs for research are obtained in a manner based on internationally accepted ethical principles and practices. The general principles for research involving human participants will ordinarily apply, although there are certain issues, such as informed consent and compensation, that need special consideration. In addition, caution must be taken to ensure that no one is exploited, especially vulnerable individuals who are financially disadvantaged or in dependent relationships.

4.3 The BAC notes that the International Society for Stem Cell Research (ISSCR)[11] and the California Institute for Regenerative Medicine (CIRM)[12] have provided details on the informed consent process, which includes information to be provided to prospective donors, monitoring of recruitment practices, rigorous review to ensure that reimbursements or financial considerations of any kind do not constitute an inducement, and the requirement that egg procurement procedures be done by medically qualified and experienced physicians, using carefully controlled ovarian stimulation to reduce the risk of OHSS and ensure that women do not undergo excessive ovarian stimulation for research.

4.4 These requirements are consistent with the framework for ethical governance recommended by the BAC, whereby any biomedical research in Singapore that involves a human subject, personal information or human tissue will need to undergo a process of ethics review by an institutional review board (IRB) prior to the commencement of the research. Ethics review ensures, among other things, that participation in research, whether in person or through the contribution of biological tissue or information, presents minimal harm, is voluntary and on an informed basis.

4.5 In addition, research that involves human eggs and embryos is subject to legal regulation and scrutiny by the Ministry of Health (MOH). The MOH regulates hospitals and clinics that provide assisted reproduction services under the Private Hospitals and Medical Clinics Act. The Assisted Reproduction (AR) Directives promulgated under the Act require all research on human eggs (including those obtained from excised ovarian tissue) or on human embryos to be subject to prior written approval from the MOH.[13] While it is already a requirement for the procurement of eggs for research to be performed by medically qualified physicians in licensed institutions, the BAC is of the view that all research with eggs, and all procurement of eggs, in any premises whatsoever, should be regulated.

---

11 International Society for Stem Cell Research, *Guidelines for the Conduct of Human Embryonic Stem Cell Research*, December 2006.

12 California Institute for Regenerative Medicine, *The CIRM Medical and Ethical Standards Regulations*, 2007, chapter 2.

13 Ministry of Health, Singapore, Licensing & Accreditation Branch, *Directives for Private Healthcare Institutions Providing Assisted Reproductive Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations* (Cap 248, Reg 1), March 2006, paragraph 8.1.

Recommendation 1
The procurement and use of human eggs for research should be regulated.

Privacy

4.6 A number of respondents to the BAC's public consultation emphasised that researchers should respect the privacy concerns of donors and safeguard any confidential information that has been entrusted to them. The BAC is in agreement and reiterates its view that personal information that is used in research should be de-identified as far and as early as possible, and should be stored or transferred as de-identified information.[14]

Informed Consent

4.7 Intrinsic to the principle of respect for individuals is the requirement that potential egg donors should freely decide whether or not to contribute eggs for research. Their consent must be given without coercion or inducement, and on the basis of information that is sufficient and appropriately presented. Potential donors should also be provided with adequate time to make an informed decision. In addition, they should be informed that they have the right to withdraw consent or vary the terms of consent at any time before their eggs are actually used in research.

4.8 To ensure that a potential donor is fully informed before making a decision to donate eggs for research, the consent taking process should include the following information, insofar as applicable:

(a) the purpose and nature of the research;

(b) the procedures and possible health risks;

(c) the possibility of a reduced chance of achieving pregnancy;

(d) that the research may not have any direct benefit to her, as any potential benefit can only be realised in the future and is for the public good;

(e) the ways in which her privacy and the confidentiality of her personal information will be safeguarded;

(f) whether the donated eggs may be used to create embryos for research, which will thus be destroyed during the process;

(g) whether the derived cells will be kept for future research that is not predictable at the present time;

14 Bioethics Advisory Committee, Singapore, *Personal Information in Biomedical Research,* 2007, Recommendation 2, page 20.

(h) whether she may be re-contacted regarding the future use of her eggs, eg. for the creation of gametes, or for research into therapeutic applications where the personal information of the donor needs to be retained;

(i) whether the eggs or derived cells may be used for research involving genetic manipulation;

(j) that eggs used for stem cell research will not be used to produce a pregnancy, and will not be allowed to develop *in vitro* for more than 14 days;

(k) whether the results of the research will be conveyed to her;

(l) the disclosure of any expected possible commercial benefit;

(m) that she has the right to withdraw consent or vary the terms of her consent at any time before her eggs are actually used in research, how she may withdraw consent and the implications of any withdrawal; and

(n) whether and how she will be compensated for her donation.

4.9 A potential donor needs to be reassured that any current or prospective benefit, or medical care will not be affected if she decides not to consent. This is especially true if she is in a dependent relationship, where caution may be necessary. In a situation where the risk of coercion, inducement or undue influence cannot be avoided, the donation should not be accepted. For instance, it would be ethically inappropriate for principal investigators to accept the donation of eggs by members of their research team, due to a serious risk of undue influence.

4.10 The voluntary nature of contributing tissue for research mandates that there should be no pressure on women undergoing IVF treatment to donate eggs out of a sense of obligation to their attending physicians. The free and informed nature of consent should be ensured, and this entails avoiding any conflicts of interest in the process of taking consent. In this regard, the ISSCR has indicated that, "wherever possible, the treating physician should not also be the investigator who is proposing to perform research on the donated materials."[15] The BAC is of the view that consent from women undergoing fertility treatment should be taken independently of the treatment team. In addition, donors should be sure that they do not require the eggs for future reproductive use and confirm this in writing.

15 International Society for Stem Cell Research, *Guidelines for the Conduct of Human Embryonic Stem Cell Research*, December 2006, paragraph 11.4.

4.11 In research involving eggs from fertility treatment, the time of consent taking is an important consideration in ensuring that reproductive choice remains free of any influence by researchers. Referring to embryos, a number of organisations have made ethical recommendations on this point. The American Society for Reproductive Medicine (ASRM)[16] and the Australian National Health and Medical Research Council (NHMRC)[17] have recommended that consent for the use of embryos in research should be taken only after the couple have decided not to continue storing their embryos, or have confirmed that the embryos are truly surplus embryos.

4.12 Certain policy bodies have also considered the need to allow donors the opportunity to reconsider whether their gametes or embryos should be used in research if consent was taken prior to the treatment. This is to ensure that they are given the opportunity to change their minds if they so wish. For instance, the Canadian Institutes of Health Research (CIHR) indicates that consent should be re-taken at the time when the embryos are to be used in research, even if consent has been given before the collection of the gametes, unless appropriate consent has been given for unrestricted research use.[18] Similarly, the Indian Council of Medical Research (ICMR)[19] and the ISSCR[20] have indicated that consent should only be given near or at the point that surplus embryos are to be transferred for research use. Given the gravity of the decision for donors, the HFEA requires that they be "given sufficient time to consider the implications of their donation" before their embryos or gametes may be used for research.[21] The NHMRC has specified an interval of at least two weeks before donated embryos may be used for research.[22]

4.13 The BAC does not consider there to be a material distinction between consent taking for the donation of embryos and that for the donation of eggs by women undergoing fertility treatment. As a matter of good practice, the disposal of surplus eggs should be discussed with the woman at the start of her fertility treatment, including the option of contribution for research. Provided that the woman at this stage indicates of her own accord an interest in donating eggs for

16 American Society for Reproductive Medicine, Ethics Committee, Donating spare embryos for embryonic stem cell research, *Fertility and* Sterility, 78 (2002): 957-960, page 959.

17 National Health and Medical Research Council, Australia, *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*, June 2007, paragraph 17.13.

18 Canadian Institutes of Health Research, *Updated Guidelines for Human Pluripotent Stem Cell Research,* June 2007, paragraph 8.3.2.

19 Indian Council of Medical Research, *National Guidelines for Stem Cell Research and Therapy,* 2006, paragraph 11.2.

20 International Society for Stem Cell Research, *Guidelines for the Conduct of Human Embryonic Stem Cell Research,* December 2006, paragraph 11.2.

21 Human Fertilisation and Embryology Authority, UK, *Code of Practice*, 7th Edition, revised September 2008, Section S.8.4.2 (c).

22 National Health and Medical Research Council, Australia, *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*, June 2007, paragraph 17.19.

research, confirms in writing that she does not require these eggs for future reproductive use and conflicts of interest are avoided, the BAC sees no objection to the woman giving specific informed consent for the use of her eggs for research, and this consent, because it is informed, can be given before the start of treatment.

Recommendation 2
Consent for the donation of human eggs for research should be obtained without any coercion or inducement. Potential donors must be provided with sufficient information in an understandable form, and given adequate time to make an informed decision.

Recommendation 3
Donors should be informed that they have the right to withdraw consent or vary the terms of consent any time before their eggs are actually used in research.

Recommendation 4
Consent for the donation of eggs for research from women undergoing fertility treatment should be taken independently of the treatment team. The donors should confirm in writing that they do not require these eggs for future reproductive use.

Egg Donation by Healthy Women

4.14 It is ethically acceptable for informed and consenting healthy women not undergoing fertility treatment to donate eggs for research. The principle of respect for individuals (and their autonomy in decision-making) supports this, and it is already the legal position in Singapore. The public consultation that was recently conducted by the BAC indicated that the general public is mostly supportive of this position, provided that donors are counselled to ensure their donation is genuinely informed and voluntary, and that there are effective safeguards against exploitation.

4.15 One safeguard against exploitation is the requirement by the MOH for all prospective egg donors for research to be provided with comprehensive information and be interviewed by a three-member panel before ovarian stimulation begins. The panel, which may be from the hospital's ethics committee, consists of a lay person and 2 medical practitioners, one of whom must be an authorised assisted reproduction practitioner. The panel must be satisfied that the prospective donor is of sound mind, clearly understands the nature and consequences of the donation, and has freely given explicit consent, without any inducement, coercion or undue influence.[23] Even with this process,

23 Ministry of Health, Singapore, Licensing & Accreditation Branch, *Directives for Private Healthcare Institutions Providing Assisted Reproductive Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations* (Cap 248, Reg 1), March 2006, paragraphs 8.5 and 8.6.

much vigilance is required as there is no perfect safeguard against the threat of exploitation. Members of the public have raised a number of considerations during the public consultation which may be helpful. These include giving due regard to the donors' residential and financial status, and their age and educational level. It was proposed that the number of times that donation may be made should be set by the regulating authority. The BAC is of the view that safeguards in the consent taking process should be reviewed from time to time to ensure that they remain effective.

Non-Commercialisation of the Human Body

4.16 A central ethical concern arising from obtaining human eggs for research relates to the possible commercialisation of the human body. The current view in research and clinical practice alike, is that the commercialisation of human tissues is not desirable, as it conflicts with a principle of respect for individuals. It is for this reason that blood donors, for example, are not paid but make a voluntary contribution to the public good. An egg donor, on this view, should not be motivated by any financial incentive in making the donation, although reasonable reimbursement of expenses incurred may be given.

4.17 The Human Cloning and Other Prohibited Practices Act of 2005[24] gives legal effect to this ethical principle, specifying that a person is prohibited from giving or receiving valuable consideration for the supply of human eggs, or to otherwise make an offer to that effect. "Valuable consideration" includes "any inducement, discount or priority in the provision of a service to the person, but does not include the payment of reasonable expenses incurred by the person in connection with the supply."

4.18 The BAC maintains that when tissue is donated for research, it should be an outright gift. This implies that the donor does not retain rights over the donated tissue (including eggs) or the results of research done using it. However, a donor can express a view as to the type of research that may or may not be done with the donated material. Donors can always decline to donate if any restrictions they wish to place on the research are not acceded to, and this matter should be addressed during the process of consent taking.[25]

4.19 Respect for the human body has always been seen as fundamental to ethical thinking and conduct in both medical practice and biomedical research. Commercialisation of the human body, by treating it, or part of it, as a disposable economic asset is generally taken to be inconsistent with this principle. This view is not unchallenged, but insofar as it underpins current ethical thinking in Singapore, it supports a view that financial inducement to

24 *Human Cloning and Other Prohibited Practices Act* (Cap 131B), revised 2005, Singapore, section 13.

25 Bioethics Advisory Committee, Singapore, *Human Tissue Research,* 2002, paragraphs 13.1.8 to 13.1.10.

provide an organ or tissue, would amount to a form of commercialisation and is not acceptable. Furthermore, this view found strong public support during BAC's public consultation on the donation of human eggs for research. There is thus no compelling force in reason or public sentiment to depart from this view.

4.20 There are other social and cultural reasons for safeguarding against potential commercialisation of not only the human body, but also the entire process of procreation. The BAC notes that many countries have adopted a variety of legislative and regulatory policies to this effect. In Japan[26] and Norway[27] for instance, egg donation for reproductive purposes is prohibited. This would prevent a couple undergoing fertility treatment from seeking 'egg donors' with certain preferred characteristics (such as physical appearance or academic accomplishment). In Denmark,[28] egg donation for reproductive purposes is restricted to women receiving treatment themselves, so that while 'egg sharing' among these women is permissible, a woman is not allowed to undergo ovarian stimulation specifically to donate eggs for the infertility treatment of another woman. Table 1 provides a summary of the laws and guidelines of various countries on whether egg donation is allowed, and if so, whether compensation may be provided.

4.21 The BAC, similarly, is interested in ensuring that neither the human body, nor any aspect of the reproductive process, becomes the subject of commercialisation. It is sensitive to the great importance attributed to the institution of the family in Singaporean society, and reproduction is a key element of this institution. Reproductive choice should remain the prerogative of the couple and it should be free from undue influence from third parties such as researchers. For this reason, the BAC does not support the implementation of schemes whereby individuals may be financially induced to provide eggs for research. However, it considers ethically acceptable for women undergoing fertility treatment to donate eggs for research, provided that these are freely donated as gifts, without compensation, and if they are not required for future reproductive use.

---

26 International Federation of Fertility Societies, IFFS Surveillance 07*, Fertility and Sterility*, April 2007, 87 Suppl 1 (2007): S1-67, page S31.

27 *Act on the Medical Use of Biotechnology*, Norway, 2003, sections 2-18.

28 *Order No 728 of 17 September 1997 on Artificial Fertilization,* Denmark, chapter 1, paragraph 9.

Table 1: Regulatory Approaches of Selected Countries to Human Egg Donation[1]

Country[2]	Egg Donation for Assisted Reproduction (AR)	Payment[3] (Egg donation for AR)	Egg Donation for research[4]	Payment[3] (Egg donation for research)
Austria	✗	na	✗	na
Australia (Commonwealth)	✓	R	✓	R
Belgium	✓	C	✓	NI
Brazil	✓	NI	✓	R
Canada	✓	R	✓	R
China	✗	na	✓	R
Czech Republic	✓	R	✓	R
Denmark	✓	C	✓	NI
Estonia	✓	R	✓	R
Finland	✓	R	✓	R
France	✓	R	✓	R
Germany	✗	na	NI	NI
Greece	✓	✗	✓	✗
Hong Kong	✓	C	✓	C
Hungary	✓	C	✓	C
India	✓	C	✓	R
Israel	✓	NI	NI	NI
Italy	✗	na	NI	NI
Japan	✗	na	✓	R
Korea (South)	✓	R	✓	R
Netherlands	✓	R	✓	R
New Zealand	✓	R	✓	R
Norway	✗	na	✗	na
Singapore	✓	R	✓	R
Slovenia	✓	R	NI	NI
South Africa	✓	R	✓	R
Spain	✓	C	✓	C
Sweden	✓	R	✓	R
Switzerland	✗	na	NI	NI
Taiwan	✓	C	NI	NI
Turkey	✗	na	NI	NI
United Kingdom	✓	C	✓	C
USA (Federal)	✓	C	✓	C

Legend:

✕	Prohibited
✓	Allowed
C	Compensation allowed
R	Reimbursement of expenses allowed
na	Not applicable
NI	No information that directly addressed the issue was found or the position on the issue was unclear

(1) The information set out in the table is indicative and not necessarily a complete representation of the regulatory approach of the specified country. In particular, the regulatory approach of each country presented has been interpreted in relation to that of Singapore and for the purposes of this Report.

(2) Countries are selected based on several factors including availability of information (in English), availability of legislation and guidelines (both legally binding and non-binding) on the issues considered, and the extent that these issues have been deliberated on and debated in those countries.

(3) In this Report, compensation is considered distinct from reimbursement. Reimbursement is defined as payment for incurred expenses. In contrast, compensation includes recompense for loss of time and earnings as a result of the procedures required to obtain the eggs. It is not intended to include any transaction for monetary gain.

(4) Many countries have specific provisions for certain types of research involving eggs, such as the creation of an embryo, and therapeutic or research cloning. These specific types of research are not considered here. Rather, this column indicates whether eggs may be contributed for research in general. Countries with legislation or guidelines on egg donation for assisted reproduction may not have made similar (or explicit) provisions for egg donation for research. However, many countries that allow egg donation for assisted reproduction would generally allow a similar donation to research that is concerned with reproduction.

Compensation for Donating Eggs for Research

4.22 Concerning the issue of compensation, it is instructive to consider the position in major jurisdictions elsewhere. In the UK, the Human Fertilisation and Embryology Authority (HFEA) allows donors providing eggs for fertility treatment to be compensated for loss of earnings (but not for other costs or inconveniences) up to a daily maximum of £55.19 (about S$168) and an overall limit of £250 (about S$760) for each cycle of egg donation. These sums are in addition to reimbursement of reasonable expenses incurred.[29] In February 2007, when the HFEA announced that women will be allowed to donate eggs for research whether or not in conjunction with their own fertility treatment, it stated that this system of compensation was to be adopted by researchers as well.[30] Similarly, the Ethics Committee of the American Society for Reproductive Medicine is of the view that egg donors, whether for fertility treatment or for research, should be compensated for their time, inconvenience and discomfort and decided that "at this time sums of $5,000 or more require justification and sums above $10,000 are not appropriate."[31] These sums seem considerable, and might easily amount to an inducement for less well to do (or actually impoverished) potential donors.

4.23 In addition, the HFEA indicates that other benefits in the form of treatment services, which are of unrestricted value, should be provided in the course of the donation cycle unless medical considerations dictate otherwise.[32] Some cost of fertility treatment might be offset, as compensation, in return for the provision of eggs for research, an arrangement known as 'compensated egg sharing'. The Medical Research Council has expressed support for compensated egg sharing by providing funds for subsidising the IVF treatment of women who choose to donate some of their eggs for a research project undertaken by the North East England Stem Cell Institute.[33] This scheme is the first of its kind in the world.[34]

---

29 Human Fertilisation and Embryology Authority, UK, *Directions given under the Human Fertilisation and Embryology Act 1990: Giving and Receiving Money or Other Benefits in Respect of Any Supply of Gametes or Embryos*, 2006, paragraphs 3 and 4. http://www.hfea.gov.uk/docs/D2006_1_Directions_on_giving_and_receiving_money.pdf (accessed 30 October 2008).

30 Human Fertility and Embryology Authority, UK, HFEA Statement on Donating Eggs for Research, 21 February 2007. http://www.hfea.gov.uk/en/1491.html (accessed 30 October 2008).

31 Ethics Committee of the American Society for Reproductive Medicine, Financial compensation of oocyte donors, *Fertility and Sterility*, 88 (2007): 305-309.

32 Human Fertilisation and Embryology Authority, UK, *Directions given under the Human Fertilisation and Embryology Act 1990: Giving and Receiving Money or Other Benefits in Respect of Any Supply of Gametes or Embryos*, 2006, paragraph 5. http://www.hfea.gov.uk/docs/D2006_1_Directions_on_giving_and_receiving_money.pdf (accessed 30 October 2008).

33 Medical Research Council, UK, *Women undergoing IVF to donate eggs for stem cell research in return for reduced treatment costs*, 13 September 2007. http://www.mrc.ac.uk/consumption/groups/public/documents/content/mrc003971.pdf (accessed 30 October 2008).

4.24 The BAC remains doubtful about the acceptability of compensated egg sharing schemes for research, as it appears to amount to a financial inducement to have eggs for research, and such external pressure seems inappropriate. It is contrary to the principle of respect for individuals, and the BAC is seriously concerned with the possibility of exploitation of women, especially those of limited economic means. Furthermore, with research rapidly expanding beyond the borders of Singapore, the effectiveness of regulating any such scheme in ways that could avoid financial inducement and unnecessary risk to women is questionable.

4.25 Similarly, in a situation where eggs have been obtained from a woman who has specifically undergone ovarian stimulation for the fertility treatment of another woman, the donor will not be eligible for compensation if eggs that are surplus to the treatment are contributed for research. This is because the original giving of the eggs was directed at therapeutic use, and if compensation is allowed, there is a real risk that the commercialisation of eggs may result.

Compensation in the Case of Healthy Donors

4.26 If commercialisation of the body is unacceptable, and altruistic donation of tissue is to be the basis of research participation, it follows that inducement is unacceptable. The BAC is of the view that to induce an otherwise reluctant woman to donate eggs by offering money or services amounts to commercialisation. On the other hand, if a woman's reluctance arises from a hesitation to actually suffer financial or other loss, a case can be made for compensation in respect of such loss under the principle of justice. There are three general approaches to paying women for providing eggs for research:

(a) *No payment beyond reimbursement* of expenses incurred. This clearly implements a philosophy of altruistic donation that is free of any risk of inducement;

(b) *Payment as compensation* for loss of time and earnings, which loss may or may not be precisely quantifiable, in addition to reimbursement of incurred expenses. This is not inconsistent with a philosophy of altruistic donation provided the quantum of compensation is not disproportionate, and neither the quantity nor the quality of the donor's eggs affects the compensation; and

(c) *Substantial payment* for eggs as a commodity. In this case, the provider is in effect a vendor making a profit, and not a donor, especially if the

34 North East England Stem Cell Research Institute, *Egg sharing: Women to get help with IVF treatment costs for donating eggs to research*, 13 September 2007. http://www.nesci.ac.uk/news/item/egg-sharing-women-to-get-help-with-ivf-treatment-costs-for-donating-eggs-to-research (accessed 30 October 2008).

price paid is contingent on the quantity or presumed genetic quality of the eggs. The BAC is opposed to this option.

4.27 Only the first approach – no payment beyond reimbursement of expenses – is not affected by ethical concerns about inducement. Once the possibility of compensation is raised, it becomes much harder to compute a quantum that represents a fair compensation but does not amount to an inducement.

4.28 The procedures for obtaining eggs are invasive with certain health risks entailed. However, the risk, discomfort and lost time are an inherent part of fertility treatment. Thus women who donate eggs from their fertility treatment are at no increased risk and they do not undergo additional discomfort or inconvenience to donate these eggs for research. These women will undergo voluntary ovarian stimulation and retrieval of eggs anyway. It can therefore be argued that they are not appropriate candidates for compensation, following a general principle that does not compensate individuals for doing what they would do in any event.

4.29 On the other hand, in the case of healthy women who volunteer to donate specifically for research, loss of time and earnings are a real cost incurred by any decision to donate. In such cases, however, it is difficult to determine a level of compensation that will not amount to undue influence or inducement, as this would depend on a number of factors including the financial status of the women concerned. This is made even more difficult as biomedical research assumes an increasingly global character. Owing to differences in payment or compensation schemes among countries, women from a country that does not allow compensation for the donation of eggs for research may be induced to make the donation in another country that allows a large payout to be made. Furthermore, there is concern that researchers from wealthy countries may attempt to obtain eggs from women in poor countries, where the compensation, if required, would be financially less burdensome for these researchers. Even within the same country, instituting payment schemes that appeal only to the poorer members of society may be socially divisive and thus run counter to the ideal that medicine, as far as possible, should not do harm. There is no simple response to this concern, but many countries are mindful that globalisation has a bearing on what might be considered as reasonable compensation for egg provision.

4.30 The issue of compensation has been considered in a number of major jurisdictions. In the US and the UK, while compensatory payment beyond reimbursement of expenses incurred could be made to the donors of eggs for research, there is a general recognition of the need to guard against such payment becoming an inducement. As mentioned in paragraph 4.22 above, total compensation that may be paid to a donor in these countries is capped at a particular amount that is considered fair and not amounting to an inducement. The European Society on Human Reproduction and Embryology (ESHRE)

Task Force on Ethics and Law indicated that vulnerable groups such as illiterate and poor women, as well as women from abroad, may have to be excluded from donating in order to prevent them from being exploited.[35]

4.31 In the Hong Kong SAR, donors are not paid for the supply of eggs (whether for research or clinical use), but may be compensated for loss of earnings and expenses incurred.[36]

4.32 Based on the principle of justice, the BAC is of the view that compensation for loss of time and earnings should be provided to women not undergoing fertility treatment who donate eggs specifically for research. Such compensation should not be dependent on the quantity or the quality of the eggs obtained, as it is not payment for the eggs. The relevant governmental authority may wish to consider setting a limit on the amount of compensation in order to avoid any inducement. In the case of donors who are not employed, the relevant regulatory authority should determine an appropriate compensatory amount for these donors based on the time spent as a result of the procedures required to obtain the eggs for research. The authority may need to review current legislation to determine whether legislative amendments are required to implement any proposal for compensation.

4.33 As the process of ovarian stimulation needed to yield eggs is invasive, and carries a health risk, a number of respondents[37] have emphasised the need to provide egg donors with medical care should an adverse event occur as a consequence of the donation. The BAC agrees that such provisions should be made. Donors should be provided with prompt and full medical care when complications occur as a direct and proximate result of donating eggs specifically for research. If the supply of eggs was a commercial matter, one might expect the vendors to shoulder the risk, but since it is not a commercial proposition, as explained above, it is the responsibility of researchers and their institutions to provide the medical care when required.

Recommendation 5

Women undergoing ovarian stimulation specifically for research should be provided with prompt and full medical care when complications occur as a

35 European Society for Human Reproduction & Embryology, Task Force on Ethics and Law, Oocyte donation for non-reproductive purpose, *Human Reproduction*, 22 (2007): 1210–1213, page 1213.

36 The three categories of expenses that an egg donor in Hong Kong may claim are loss of earnings, specified accountable expenses (such as travel expenses and minding services), and medical expenses. There is no limit for claimable medical expenses but the maximum daily payment in respect of loss of earnings and specified accountable expenses cannot exceed HK$1,060 (S$184), and HK$1,360 (S$236) on the day of egg collection for each donation (i.e. the sum of loss of earnings and specified accountable expenses, but excluding medical expenses, which do not have a limit). Council on Human Reproductive Technology, Hong Kong SAR, *Code of Practice on Reproductive Technology & Embryo Research*, December 2002, Section 4.14 and Appendix II.

37 Such as the Graduates' Christian Fellowship and the Law Society of Singapore.

direct and proximate result of the donation. Responsibility for this provision should rest with the researchers and their institutions.

Recommendation 6
Egg donors should be compensated only for loss of time and earnings as a result of the procedures required to obtain the eggs, and only if the eggs were obtained specifically for research purposes, and not as a result of clinical treatment. Such compensation should be in addition to any reimbursement of expenses incurred. The relevant regulatory authority should determine the appropriate amount of such compensation.

Importation of Human Eggs

4.34 The BAC notes that importation of human eggs is not subject to regulatory control. This notwithstanding, the BAC is of the view that any research use of human eggs in Singapore, whether imported or not, should be confined to eggs that have been obtained in accordance with the recommendations in this Report. They should also conform to all earlier relevant recommendations, such as those mandating ethics review. Furthermore, in cross-border research collaborations, the requirements specified in this Report should be met if the project is to receive approval by any IRB in Singapore.

Recommendation 7
The procurement or use of human eggs from any source by procedures not consistent with the recommendations in this Report should be prohibited.

V. Conclusion

5.1 The BAC has considered international practices and guidelines on the donation of human eggs for research purposes, together with expert views on the subject. It has also carefully considered the feedback received from the public and the written responses from various organisations. It has reached the following conclusions, which form the basis of seven recommendations:

(a) The general ethical principles of research involving human participants should apply to the procurement and use of human eggs for research;

(b) It is ethically acceptable for fully informed and freely consenting healthy women, not undergoing any medical treatment, to donate eggs for research;

(c) Women who are not undergoing fertility treatment and who donate eggs specifically for research should be compensated for loss of time and earnings as a result of the procedures required to obtain the eggs. In addition, they should receive reimbursement of expenses incurred, and should also receive prompt and full medical care if complications arise as a direct and proximate result of the procedures; and

(d) Women donating surplus eggs from fertility treatment should not be compensated, as they do not incur additional loss of time and earnings to donate their eggs for research.

5.2 **List of Recommendations:**

Recommendation 1
The procurement and use of human eggs for research should be regulated.

Recommendation 2
Consent for the donation of human eggs for research should be obtained without any coercion or inducement. Potential donors must be provided with sufficient information in an understandable form, and given adequate time to make an informed decision.

Recommendation 3
Donors should be informed that they have the right to withdraw consent or vary the terms of consent any time before their eggs are actually used in research.

Recommendation 4
Consent for the donation of eggs for research from women undergoing fertility treatment should be taken independently of the treatment team. The donors should confirm in writing that they do not require these eggs for future reproductive use.

Recommendation 5
Women undergoing ovarian stimulation specifically for research should be provided with prompt and full medical care when complications occur as a direct and proximate result of the donation. Responsibility for this provision should rest with the researchers and their institutions.

Recommendation 6
Egg donors should be compensated only for loss of time and earnings as a result of the procedures required to obtain the eggs, and only if the eggs were obtained specifically for research purposes, and not as a result of clinical treatment. Such compensation should be in addition to any reimbursement of expenses incurred. The relevant regulatory authority should determine the appropriate amount of such compensation.

Recommendation 7
The procurement or use of human eggs from any source by procedures not consistent with the recommendations in this Report should be prohibited.

———————————

BIBLIOGRAPHY

Aflatoonian B and Moore H. Germ cells from mouse and human embryo embryonic stem cells. *Reproduction*. 132 (2006): 669-707.

American Society for Reproductive Medicine, Ethics Committee. Donating spare embryos for embryonic stem cell research. *Fertility and Sterility*. 78 (2002): 957-960.

American Society for Reproductive Medicine, Ethics Committee. Informed consent and the use of gametes and embryos for research. *Fertility and Sterility*. 82 Supp 1 (2004): S251-252.

American Society for Reproductive Medicine, Ethics Committee Report. Financial Compensation of Oocyte Donors. *Fertility and Sterility*. 88 No.2 (2007): 305-309.

American Society for Reproductive Medicine, Practice Committee Opinion. Repetitive oocyte donation. *Fertility and Sterility*. 86 Suppl 4 (2006): S216-217.

Austria. *Reproductive Medicine Act* (as interpreted by the Bioethics Commission at the Federal Chancellery in its decisions of 3 April and 8 May 2002). 1992.

Australia. *Prohibition of Human Cloning for Reproduction and the Regulation of Human Embryo Research Amendment Act*. 2006.

Balen A. *Ovarian Hyperstimulation Syndrome – A Short Report for the HFEA*. UK, 2005.

Belgium. *Law on Research on Embryos In Vitro* (Translation by the European Society for Human Reproduction and Embryology, 11/05/2003). 2002/2003.

Bioethics Advisory Committee. *Donation of Human Eggs for Research: A Consultation Paper*. Singapore, 2007.

Bioethics Advisory Committee. *Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning*. Singapore, 2002.

Bioethics Advisory Committee. *Human Tissue Research*. Singapore, 2002.

Bioethics Advisory Committee. *Personal Information in Biomedical Research*. Singapore, 2007.

Bioethics Advisory Committee. *Research Involving Human Subjects: Guidelines for IRBs*. Singapore, 2004.

Bodri D. Complications related to ovarian stimulation and oocyte retrieval in 4052 oocyte donor cycles. *Reproductive Biomedicine Online*. 17, no. 2 (2008): 237-243.

Brazil. *Biosafety Law*. 2005.

Brinton L. Long-term effects of ovulation-stimulating drugs on cancer risk. *Reproductive Biomedicine Online*. 15, no. 1 (2007): 38-44.

California Institute for Regenerative Medicine. *The CIRM Medical and Ethical Standards Regulations*. US, 2007.

Canada. *Assisted Human Reproduction Act*. 2004.

Canadian Institutes of Health Research. *Updated Guidelines for Human Pluripotent Stem Cell Research*. Canada, 2007.

Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada. *Tri-council Policy Statement: Ethical Conduct for Research Involving Humans*. Ottawa: Interagency Secretariat on Research Ethics, 2005.

Capps B. *Oocyte Procurement for Research*. A background paper for the Bioethics Advisory Committee. Singapore, 2007 (see Annex E(2) of this Report).

China. *Ethical Guiding Principles on Human Embryonic Stem Cell Research*. 2003.

China, Hong Kong SAR. *Human Reproductive Technology Ordinance*. 2000.

Council of Europe. *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*. 1997.

Council on Human Reproductive Technology. *Code of Practice on Reproductive Technology & Embryo Research*. Hong Kong SAR, 2002.

Czech Republic. *Act on Research on Human Embryonic Stem Cells and Related Activities and on Amendment to Some Related Acts*. 2006.

Denmark. *Law No. 427 of 10 June 2003 amending the Law on artificial fertilization in connection with medical treatment, diagnosis, and research*. 2003.

Denmark. *Order No. 728 of 17 September 1997 on Artificial Fertilization.* 1997.

Estonia. *Embryo Protection and Artificial Fertilisation Act*. 1997.

Ethics Committee of the American Society for Reproductive Medicine. Financial Compensation of Oocyte Donors. *Fertility and Sterility*. 88 (2007): 305-309.

European Commission. *Report on the Regulation of Reproductive Cell Donation in the European Union: Results of Survey*. February 2006.

European Parliament and European Council. *Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells*. 2004.

European Society of Human Reproduction & Embryology, Task Force on Ethics and Law. Oocyte donation for Non-Reproductive Purpose. *Human Reproduction*. 22 (2007): 1210-1213.

Finland. *Medical Research Act*. 1999.

France. *Bioethics Law*. 2004.

Germany. *Embryo Protection Act*. 1990.

Greece. *Law 3089 on Medically Assisted Human Reproduction*. 2002.

Heng B C. Taiwan (Republic of China) legitimizes substantial financial remuneration of egg donors: implications for reproductive tourism in East Asia. *Expert Review of Obstetrics & Gynecology.* 2, no. 5 (2007): 545-547.

Human Fertilisation and Embryology Authority. *Directions given under the Human Fertilisation and Embryology Act 1990: Giving and Receiving Money or Other Benefits in Respect of Any Supply of Gametes or Embryos.* UK, 2006.

Hubner K et al. Derivation of oocytes from mouse embryonic stem cells. *Science*. 300 (2003): 1251-1256.

Human Fertilisation and Embryology Authority. *Code of Practice,* 7th Edition. UK, revised September 2008.

Human Fertilisation and Embryology Authority. *Directions on Giving and Receiving Money or Other Benefits in Respect of any Supply of Gametes or Embryos*. UK, 2006.

Human Fertilisation and Embryology Authority. *Donating eggs for research: safeguarding donors*. UK, 2006.

Human Fertilisation and Embryology Authority. *Donating Eggs for Research: Safeguarding Donors, A report on the HFEA consultation*. UK, 2007.

Human Fertilisation and Embryology Authority. *HEFA Statement on Donating Eggs for Research.* UK, 2007.

Hungary. *Parliamentary Act No. CLIV of 1997 on Health*. 1997.

Iceland. *Regulation No. 568 on Artificial Fertilization*. 1997.

Indian Council of Medical Research. *National Guidelines for Stem Cell Research and Therapy*. India, 2006.

International Society for Stem Cell Research. *Guidelines for the Conduct of Human Embryonic Stem Cell Research*. US, 2006.

International Federation of Fertility Societies. IFFS Surveillance 07. *Fertility and Sterility*. 87 Suppl l (2007): S1-67.

International Stem Cell Forum Ethics Working Party. Oocyte Donation for Stem Cell Research. *Science*. 316 (2007): 368-370.

Isasi, R M. and Knoppers B M. Monetary payments for the procurement of oocytes for stem cell research: In search of ethical and political consistency. *Stem Cell Research*. 1 (2007): 37–44.

Italy. *Law No. 40 on Regulation of Medically Assisted Reproduction*. 2004.

Japanese Ministry of Culture, Sports, Science, and Technology. *The Guidelines for Derivation and Utilization of Human Embryonic Stem Cells*. 2001.

Lo B et al. Informed consent in human oocyte, embryo, and embryonic stem cell research. *Fertility and Sterility*. 82 No. 3. (2004): 559-563.

Magnus D and Cho M K. Issues in Oocyte Donation for Stem Cell Research. Science. 308 (2005): 1747-1748.

McLaren A. Free-Range Eggs? *Science*. 316 (2007): 339.

Ministry of Health. *Directives for Private Healthcare Institutions providing Assisted Reproduction Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations* (Cap 248, Reg 1). Singapore, revised 2006.

National Health and Medical Research Council. *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*. Australia, 2004, revised 2007.

National Research Council and Institute of Medicine. *Guidelines for Human Embryonic Stem Cell Research*. US, revised 2008.

National Research Council and Institute of Medicine. *Assessing the Medical Risks of Human Oocyte Donation for Stem Cell Research: Workshop Report*. US, 2007.

The Netherlands. *Embryo Act*. 2002.

New Zealand. *Human Assisted Reproductive Technology Act*. 2004.

Ng SC. *Oocyte Donation – Clinical and Scientific Aspects*. A background paper for the Bioethics Advisory Committee. Singapore, 2007 (see Annex E(1) of this Report).

Norway. *Act on the Medical Use of Biotechnology*. 2003.

Norway. *Act of 5 December 2003 No. 100 relating to the application of biotechnology in human medicine, etc*. 2003.

North East England Stem Cell Research Institute. *Egg sharing: Women to get help with IVF treatment costs for donating eggs to research*. UK, 2007.

Schenker J G. Legal Aspects of ART Practice in Israel. *Journal of Reproduction and Genetics*. 20, no. 7 (2003): 250-258.

Singapore. *Human Cloning and Other Prohibited Practices Act* (Cap 131B). Revised 2005.

Slovenia. *The Law on Treatment of Infertility and Biomedically Assisted Fertilisation*. 2000.

South Africa. *National Health Act*. 2003.

South Korea. *Bioethics and Biosafety Act No. 7150*. 2005.

Spain. *Human Assisted Reproduction Techniques Act*. 2006.

Steinbrook R. Egg Donation and Human Embryonic Stem Cell Research. *New England Journal of Medicine*. 354;4 (2006): 324-326.

Sweden. *The Genetic Integrity Act*. 2006.

Switzerland. *Federal Act on Research on Surplus Embryos and Embryonic Stem Cells*. 2004.

Takahashi K et al. Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors. *Cell.* 131 (2007): 1-12.

The Newcastle Upon Tyne Hospitals. *Information Leaflet for Egg Sharing for Research.* UK, 2007.

Thompson C. Why we should, in fact, pay for egg donation. *Regenerative Medicine.* 2, no. 2 (2007): 203-209.

United Kingdom. *Human Fertilisation and Embryology Act*. 1990.

United Kingdom. *Human Fertilisation and Embryology (Amendment) Bill*. 2007.

Yu J et al. Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells. *Science*. 318 (2007): 1917-1920.

DONATION OF HUMAN EGGS FOR RESEARCH

A CONSULTATION PAPER

BIOETHICS ADVISORY COMMITTEE

SINGAPORE

7 November 2007

DONATION OF HUMAN EGGS FOR RESEARCH

SUMMARY

1. Human eggs have for some time been needed and used for the treatment of infertility, but recently they have also been needed for research, such as embryonic stem cell research. Understanding the nature of stem cells is generally viewed to be the key to unlocking the vast potential of stem cell therapy for serious and currently untreatable diseases, such as diabetes, Alzheimer's disease and Parkinson's disease.

2. Eggs for research are in short supply. Indeed, scientists have indicated that the scarcity of human eggs is a key limiting factor in embryonic stem cell research. Women who themselves are undergoing fertility treatment may sometimes donate suitable eggs for research. Eggs from other sources such as cadavers or foetuses, or women undergoing surgery, for example, the removal of ovaries, are often immature and unsuitable, and are anyway insufficient.

3. The procedures which a woman has to undergo in order to obtain eggs for fertility treatment or for research are essentially the same. The process of obtaining eggs is not straightforward and carries some risk to the donor. It is important that she understands the procedures and risks involved. There is also the question of inducement. Thus ethical concerns arise. The main issues are as follows:

(a) The question of inducement

Women could be induced to provide eggs for research, by offers of money or benefits in kind. Women who are poor would be most susceptible to inducement.

(b) Limiting payment to reimbursement

This avoids inducement, since there is no net gain in income, and reflects the view that altruistic donation free of inducement is the proper basis for contributing to research.

(c) Compensation

The possibility of some additional payment to compensate for time, risk and inconvenience, or for lost earnings does not contradict the idea of altruistic donation, although it is often difficult to clearly demarcate compensation from inducement in every situation. Nevertheless, payment of a large sum of money tends to suggest inducement rather

than compensation. In addition, payment should not be based on the quantity or quality of the donor's eggs.

(d) Foreign donors

Biomedical research is increasingly global. There are differences in payment or compensation schemes in different countries. This means that women from a country that does not allow compensation for the donation of eggs for research may be induced to make the donation in another country that does not prohibit a large payout to be made. Furthermore, researchers from wealthy countries could attempt to obtain eggs from women in poor countries, where any compensation would be financially less burdensome for these researchers.

(e) The freedom to choose to donate

Should healthy women be free to decide whether or not to donate eggs for research? Under Singapore's Ministry of Health (MOH) regulations, healthy women may presently donate eggs for research. The risk being explained, people can freely decide to accept it and support the research. Egg donation is of no benefit to a healthy donor not undergoing fertility treatment, and it can be argued that it is up to them, given the information they need, to decide whether the risk is acceptable. This is what happens with research participants in other areas of clinical research. Nevertheless, some may wonder if a medical risk of donation can be justified when the donor receives no benefit from the process.

4. There is a need to ensure that consent to donate eggs for research is freely given when a woman is undergoing treatment. A woman undergoing fertility treatment should not be subjected to more risks than her treatment requires, and the number of eggs obtained should not be excessive. It follows that her consent to donate eggs for research should be taken by an independent person wherever possible. This is because she may feel under some obligation to the medical team which is providing the treatment.

5. In Singapore, using eggs from women, whether for infertility treatment or for research is regulated by the MOH, and the payment of reasonable expenses, which includes the cost of collecting, storing and transporting the egg, is permitted by law. It is not clear if additional payment to compensate for time, risk and inconvenience is permissible.

6. The number of eggs likely to be obtained from healthy donors will probably remain low. Scientists may have to continue with the current practice of using eggs contributed by women undergoing fertility treatment or look for alternative means to achieve their scientific goals, such as using animal eggs. In principle, where women are allowed to donate eggs for research, scientists and

Institutional Review Boards, which review the ethics of research proposals, should ensure that these women understand the procedures and risks involved before consenting to donate and that their interests and safety are adequately protected.

7. The views of researchers, professionals, religious bodies, interested organisations and the general public on these issues will help the BAC in the making of any recommendations.

DONATION OF HUMAN EGGS FOR RESEARCH

CONSULTATION PAPER

Introduction

1. The Bioethics Advisory Committee (BAC) in its 2002 report on human stem cell research, reproductive and therapeutic cloning (Stem Cell Report), noted that recent developments in stem cell research have raised hopes of discovering new cures for debilitating and fatal illnesses and of alleviating suffering.[1] It also recognised that important ethical concerns were entailed. Since the publication of the Stem Cell Report, legislative and regulatory frameworks have been established in Singapore to address some of these concerns. Singapore does not act alone in these endeavours, as many leading scientific nations have done likewise. However, several issues remain ethically challenging, and one that has drawn considerable attention in many countries relates to the donation of human eggs (or oocytes) for research, in particular embryonic stem cell research, which holds great promise of benefit for mankind.

2. Eggs are donated mostly for the treatment of infertility, although a number have been donated for research. Donating eggs for fertility treatment has been practiced for more than two decades and is now considered a well-established method for helping women who have problems conceiving. In contrast, the donation of eggs for research is more recent, and follows from advances especially in embryonic stem cell research. Such research is important in contributing to our understanding the nature and potential of stem cells, and this understanding is generally viewed as the key to unlocking the vast potential of stem cell therapy for serious and currently untreatable diseases, such as diabetes, Alzheimer's disease and Parkinson's disease.

3. Although there has been significant progress in stem cell science and technology since the publication of the Stem Cell Report, many more years of research are required before its therapeutic benefits may be realised. A more immediate obstacle to achieving these is the limited availability of human eggs, given the requirement of patients undergoing fertility treatment, the invasiveness of the medical procedures involved in obtaining the eggs, and broader concerns with protecting women from exploitation.

4. The process of obtaining eggs is not straightforward. It involves medical procedures and carries some risk to the donors. Thus safety and ethical concerns arise, the most important being the possibility that vulnerable women may be

1 Bioethics Advisory Committee. *Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning*. Singapore, 2002, page 1.

exploited, through various forms of inducement to provide eggs for research. At a practical level, the difficulty lies in determining whether any payment or compensation should be given to egg donors beyond the reimbursement of expenses actually incurred, and if so, the appropriate form or amount, and how to regulate it. It is also necessary to consider if researchers can be allowed to obtain eggs from women who are not undergoing fertility treatment. In any case, it is important to ensure that the safety and welfare of women are adequately safeguarded regardless of their status.

5. The main objective of this Consultation Paper is to consider the ethical, legal and social issues that relate to the donation of human eggs for research. The BAC seeks the views of researchers, professionals, religious bodies, interested organisations and the general public on:

(a) Whether healthy women not undergoing fertility treatment should be allowed to donate eggs for research, and if so under what conditions;

(b) Whether egg donors for research should be compensated for time, inconvenience and risk, and if so, what type of compensation or monetary amount would be acceptable, and not amount to an inducement;

(c) Whether there are circumstances in which the compensation for eggs could amount to a sale and if so whether such a sale should ever be contemplated;

(d) Any prohibitions, limits or regulatory mechanisms that should govern the supply and use of human eggs for research in Singapore; and

(e) Any other matters related to the donation of human eggs for research.

6. The feedback received will help the BAC review and build on the ethical and regulatory framework that has been established since the Stem Cell Report. As with our previous public consultations, recommendations will be made in a Report to the Steering Committee on Life Sciences.

Human Eggs in Research

7. Human eggs are required for embryonic stem cell research and research into assisted reproductive technologies. The eggs can be studied without being fertilised, for example, studies into methods of egg maturation and preservation, or they can be used to create embryos or other entities (such as parthenotes, described in paragraph 15 below), from which stem cells can be derived for research.

8. Stem cells are unspecialised (or undifferentiated) cells that are able to replicate themselves and become specialised (or differentiated) cells.[2] There are primarily two types of stem cells that scientists work with – adult stem cells and embryonic stem cells. Adult stem cells are present in a tissue or organ and are able to become (or differentiate into) specialised cell types of that tissue or organ, and some other cell types. Embryonic stem cells are unique cells, which can be derived from early embryos. They are able to continuously replicate themselves and are pluripotent i.e. they have the capacity to become or differentiate into all cell types. There is currently little evidence that adult stem cells are pluripotent.

9. Scientists are learning how to control and direct stem cell differentiation in ways that would lead to the production of specialised cells for the treatment of various diseases. Understanding the nature of embryonic stem cells is a critical step towards realising the potential of these cells in regenerative medicine, where new approaches to repairing and replacing injured and diseased tissues and organs are being explored.

10. An embryo can be created from an egg and a sperm using *in vitro* fertilisation (IVF) or through somatic cell nuclear transfer (SCNT), also sometimes referred to as research cloning or therapeutic cloning. SCNT involves the transfer of the nucleus of a somatic cell[3] into an egg cell, whose nucleus has been removed. This is then followed by stimulation of the cell to start dividing. After five to six days, stem cells can be extracted from the resulting embryo and used for research.

11. SCNT may be used to study nuclear reprogramming, which is a process whereby a somatic cell is converted into one that has the capacity of an unspecialised cell to develop into a living organism (totipotence) or differentiate into all types of cells (pluripotence). Understanding this process may lead to the possibility of achieving direct reprogramming, which does not involve the use of eggs or the need to create embryos.

12. When the nucleus of a somatic cell from a patient is used in SCNT, patient-specific stem cells may be derived from the resulting embryo. These cells have the advantage of not causing an immune reaction or tissue rejection, when used for treatment. Figure 1 shows how SCNT may potentially be used to produce patient-specific stem cells.

2 Specialised or differentiated cells are mature cells with specific functions, for example, skin cells and liver cells.

3 A somatic cell is any mature (or differentiated) cell in the body that is not an egg or a sperm.

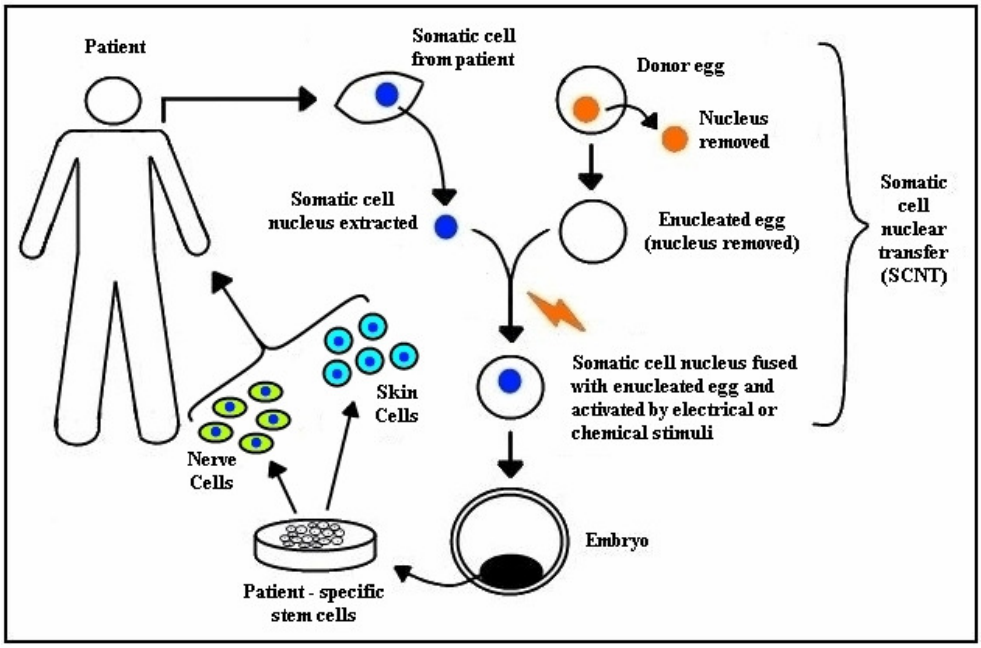


Figure 1. How SCNT may potentially be used to produce patient-specific stem cells

13. SCNT may also be used to study inherited diseases, when the somatic cells from patients with such conditions are used to generate disease-specific stem cells. These cells, which carry the genetic characteristics of the person suffering from the disease, could be used to study the development and progression of the disease in question. This may then lead to the discovery of better treatment or ways to reverse or prevent further progression of the condition.

14. Pluripotent stem cells can also be derived through parthenogenesis, which again requires eggs. Parthenogenesis, which means 'virgin birth' in Greek, occurs when the process of development of a new organism is initiated in an unfertilised egg.

15. Reproduction through parthenogenesis occurs naturally in certain insects and amphibians but not in mammals (including humans). However, the eggs of mammals can be stimulated by electrical or chemical stimuli to become embryo-like entities called 'parthenotes'. Mammalian parthenotes were thought to be unable to develop into offspring, but in 2004, a team of Japanese scientists reported the births of mice created via parthenogenesis.[4] In 2005, the Roslin Institute, which cloned Dolly the sheep, reported the creation of six human parthenotes with the intention of deriving stem cells for research.[5] These

4 Kono T et al. Birth of parthenogenetic mice that can develop to adulthood. *Nature*. 428 (2004): 860-864.

5 Amos J. 'Virgin conception' first for UK. BBC News, 9 September 2005. http://news.bbc.co.uk/2/hi/science/nature/4228992.stm (accessed 1 November 2007).

parthenotes were the first to be created in the UK. In June 2006, researchers at the University of Milan in Italy reported the creation of two stem cell lines from human parthenotes[6] and more recently a team of researchers claimed that they had succeeded in deriving pluripotent patient-specific stem cells from human parthenotes.[7] However much more research in this area is required before such cells can be used clinically.

Sources of Human Eggs for Research

16. While human eggs are very important for the advancement of embryonic stem cell research, they are not readily available. Currently, most eggs for research are obtained from women who have undergone fertility treatment. These could be surplus eggs which are not used for treatment, or they could be immature eggs that are either unsuitable for fertilisation or failed to fertilise following IVF. Other sources of eggs for research include cadavers, aborted foetuses and women undergoing medical procedures such as removal of ovaries. However, eggs from these latter sources may not be sufficiently effective for SCNT as they are usually immature, and access to these sources is nonetheless very limited for ethical and other reasons.

17. Theoretically, it might be possible to create eggs from human embryonic stem cells, and eggs created in this way could then be used in research. However, while it has been possible to create mouse eggs from mouse embryonic stem cells,[8] research on creating human eggs from human embryonic stem cells are in the preliminary stages. In 2005, researchers in the UK demonstrated that human embryonic stem cells displayed a capacity to generate immature gametes.[9]

18. In SCNT research, fresh eggs or surplus eggs from women undergoing fertility treatment are preferred to immature eggs or eggs that have failed to fertilise after IVF. Eggs that have failed to fertilise after IVF are less effective as they have been shown to have limited developmental potential.[10]

19. Moreover, surplus eggs from fertility treatment are often retained for use by the woman herself or donated to other couples undergoing fertility treatment. For this reason, insufficient eggs are available for research. Indeed, scientists have indicated that the scarcity of human eggs is a key limiting factor in stem cell

---

6 Merchant J. Human eggs supply 'ethical' stem cells. *Nature*. 441 (2006):103.

7 Revazova ES et al. Patient-specific stem cell lines derived from human parthenogenetic blastocysts. *Cloning and Stem Cells*. 9 (2007):432-449.

8 Hubner K et al. Derivation of oocytes from mouse embryonic stem cells. *Science*. 300 (2003):1251-1256.

9 Aflatoonian B and Moore H. Germ cells from mouse and human embryo embryonic stem cells. *Reproduction*. 132 (2006):669-707.

10 Lavoir et al. Poor development of human nuclear transfer embryos using failed fertilized oocytes. *Reproductive Biomedicine Online*. 11 (2005):740-744.

research. In many leading scientific nations, the possibility of obtaining eggs from women not undergoing any form of medical treatment (i.e. healthy women) is being considered. There are however significant ethical questions to be considered if this is done.

Procedures and Risks Involved in Egg Donation

20. The procedures which a woman has to undergo in order to obtain eggs for fertility treatment or for research are essentially the same. In both cases, it is important that she understands the procedures and risks involved.

21. Obtaining eggs is a time-consuming process, which has a certain degree of discomfort and possible health risks. A woman has to undergo stimulation of the ovaries through multiple hormone injections, followed by close monitoring of the development of her eggs in the ovaries through ultrasound scans and blood tests. Thereafter, the eggs are collected under mild anaesthesia via a special needle attached to an ultrasound vaginal probe. One can expect an average of between 20 to 40 injections under the usual regimes of ovarian stimulation.

22. The health risk entailed in egg donation is related to ovarian stimulation, where a condition called ovarian hyperstimulation syndrome (OHSS) may result. In addition, egg retrieval may cause excessive bleeding or infection. As the procedure of egg retrieval is done under mild anaesthesia, there are also risks associated with the type of anaesthesia administered. However, the risk in egg retrieval is relatively low. For example, in a review of 1000 cases of egg donors over a period of 13 years, it was found that there were two cases of severe adverse reactions to anaesthesia and two cases of bleeding. None of the patients who suffered these complications required hospitalisation and they recovered without any significant consequences.[11]

23. Mild OHSS is relatively common, usually occurring between five to nine days after egg retrieval and may affect up to 10% of women undergoing ovarian stimulation. The condition can be easily managed without hospitalisation and usually resolves spontaneously within several days. Severe OHSS is rare (occurring in less than 1% of egg donors)[12] and will require urgent medical attention. It is of late-onset (occurring between ten days to three weeks after egg retrieval) and often associated with pregnancy. Women undergoing ovarian stimulation specifically for the purpose of donating eggs for research are unlikely to develop severe OHSS as pregnancy is not expected to follow the retrieval of eggs.

---

11 Sauer MV. Defining the incidence of serious complications experienced by oocyte donors: A review of 1000 cases. *American Journal of Obstetrics & Gynecology*. 184 (2001):277-278.

12 *Ibid*.

24. Women who are less than 30 years of age, with a low body weight, irregular menstrual cycles or polycystic ovaries are at increased risk of developing OHSS. OHSS can be prevented by careful selection of egg donors, judicious use of the drugs given for ovarian stimulation and close monitoring of the individual's response to the drugs.

25. There is some documented evidence that ovarian stimulation may lead to an increased risk of future cancers of the breast, ovary and uterus, although the risk appears low, particularly for ovarian cancer.[13] While the possibility of long term effects still needs further study, and current findings are not uniform or conclusive, it is not possible to rule out such effects, especially as ovarian stimulation exposes women to increased concentrations of hormones and such increases have been linked with cancers of the breast and uterus.

Ethical Considerations and Regulatory Approaches to Egg Donation for Research

26. Legislative and regulatory policies on egg donation vary from country to country. In some countries, egg donation is prohibited or limited to particular purposes. In Japan and Norway[14] for instance, egg donation for reproductive purposes is prohibited. This would prevent a couple undergoing fertility treatment from seeking 'egg donors' with certain preferred characteristics (such as physical appearance or academic accomplishment). In Denmark,[15] egg donation for reproductive purposes is restricted to women receiving treatment themselves, so that while 'egg sharing' among these women is permissible, a woman is not allowed to undergo ovarian stimulation in order to donate eggs for the infertility treatment of another woman.

27. Two issues that are most relevant for the purposes of this Consultation Paper are:

(a) Whether women should be allowed to donate eggs for research; and

(b) Whether any payment may be made to, or received by, the egg donor.

28. Table 1 provides a summary of the laws and regulatory guidelines of various countries on egg donation, which may be used as a general reference for the discussion on these issues.

---

13 Brinton L. Long-term effects of ovulation-stimulating drugs on cancer risk. *Reproductive Biomedicine Online*. 15 (2007):38-44.

14 *Act on the Medical Use of Biotechnology*. Norway, 2003, section 2-18.

15 *Order No 728 of 17 September 1997 on Artificial Fertilization.* Denmark, chapter 1, paragraph 9.

Should women be allowed to donate eggs for research?

29. The permissibility of egg donation in a number of countries depends on the health status of a woman. Generally speaking, in countries where the practice of assisted reproductive technologies is allowed, women undergoing fertility treatment may donate eggs that are left over from their treatment for research. However, this may not be the case for healthy women who have to specially undergo ovarian stimulation to contribute eggs. The difference lies in the risks that these healthy women have to bear in order to donate their eggs.

Obtaining eggs from women undergoing fertility treatment

30. Before a woman undergoes ovarian stimulation for fertility treatment, she has to consider the possible options for the disposition of her excess eggs, should there be any. The options available are to store them for her own future use, to donate them to another couple, to make them available for quality assurance activities, to donate them for research, or to dispose of them. If she decides to donate her surplus eggs for the treatment of another woman's infertility, such a donation tends not to be ethically challenging since the donor is not subject to additional risk and her gift benefits the recipient directly.

31. However, if she is to be invited to consider donating her eggs for research, there are typically various safeguards to ensure her safety and that her contribution is informed and voluntary. For instance, a general requirement is that a woman should not be subjected to more risks than what her treatment requires and the number of eggs obtained should not be excessive. It follows that when a researcher is also the woman's attending physician, there may be an ethical expectation (as is generally the case in Singapore)[16] that requires her consent to be taken by an independent party wherever possible. This is because the prospective donor may feel under some obligation to the medical team which is providing the treatment.

Obtaining eggs from healthy women

32. When a research proposal seeks to involve healthy women as egg donors, the research tends to be subject to a higher level of ethical scrutiny. This follows from the general opinion that most women will not ordinarily subject themselves to unnecessary discomfort, possible health risks and inconvenience in order to provide eggs for research. With an increasing need of eggs for research as biomedical science progresses, there is a real concern that the giving of eggs by healthy women may be unethically induced (by monetary or other benefits).

16 Bioethics Advisory Committee. *Human Tissue Research*. Singapore, 2002, paragraph 8.8; Bioethics Advisory Committee. *Personal Information in Biomedical Research*. Singapore, 2007, paragraph 5.9.

33. However, it may be argued that a woman should in principle be free to decide whether or not to donate her eggs for research regardless of her health status, provided that ethical and legal requirements are met. Even though egg donation for research is of no benefit to a healthy donor, whose donation is primarily altruistic in character, it can be argued that it is up to an informed donor to decide whether the risk is acceptable, in the same way as occurs with other research participants in other areas of clinical research. For example, when clinical trials are conducted, there is an element of risk, especially when the trial represents the first time a new drug is tried out in a human being. Yet, the risk being explained, people can freely decide to enter the trial and so voluntarily agree to accept the risk. It can be argued that a similar principle of participant autonomy can be invoked in the case of healthy egg donors.[17]

34. The case for allowing healthy women to donate their eggs for research rests heavily on such a libertarian principle – that people should not be prevented from volunteering for valuable research at some personal risk – and on the interest of society to advance the common good. This argument notwithstanding, the safety of the research participant or egg donor is paramount and the researcher is under obligation to provide all necessary assistance should any harm or complications arise in the course of the research or as a result of the egg donation.

35. In Singapore, the use of human eggs, whether for research or for treatment is regulated by the Ministry of Health (MOH).[18] Treatment and procedures involving human eggs must be carried out by qualified personnel in assisted reproduction centres licensed by the MOH. Under the current regulatory framework, a healthy woman may donate eggs for research. Research on human eggs require the explicit consent of the donor, the prior written approval of the MOH and the approval of the relevant ethics committee or institutional review board (IRB).[19] A prospective egg donor must be interviewed by a designated panel (which will take into consideration the public interest and community values) to ensure that the donor is of sound mind, has a clear understanding of the nature and consequences of the donation and has freely given consent.[20]

36. Similarly, egg donation for research or for treatment is allowed in the UK. In February 2007, the Human Fertilisation and Embryology Authority (HFEA) decided to allow the altruistic giving of eggs for research, provided there are strong safeguards in place to ensure that the donors have been properly

---

17 Capps has reviewed the ethics of human egg donation for research, and his background paper *Oocyte Procurement for Research* (2007) is available at: www.bioethics-singapore.org.

18 Ministry of Health. *Directives for Private Healthcare Institutions Providing Assisted Reproduction Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations (Cap 248, Reg 1).* Singapore, 2006.

19 *Ibid*, paragraphs 8.1 and 8.5.

20 *Ibid*, paragraph 8.6.

informed of the risks and were not coerced.[21] It found that the medical risks for donating eggs for research are no higher than for fertility treatment and felt that a woman should be able to decide how she chooses to use her eggs, which includes donating them for research. Australia[22] and India[23] share this position in allowing healthy women to donate eggs for research.

Should there be any payment for donating eggs for research?

37. The recruitment of healthy women as egg donors and the amount of payment made to them are controversial as the procedures involved are risky and the payment may be seen to be an inducement or considered as commercialisation of human tissue, which is generally unacceptable. Consequently, there is at present no uniformity in the practices among countries on the amount of payment that a woman should receive for the donation of eggs, or indeed, if any compensation should be made at all.

38. Commercial trading in human eggs is explicitly prohibited by law in Singapore, and any contract or arrangement made in contravention of this will be void. However, any service (by receiving, storing, processing and subsequently implanting) undertaken for facilitating the donation and receipt of the egg is not regarded as commercial trading in human eggs.[24] Similar laws prohibiting the sale of human eggs have also been enacted in various countries including Australia, Canada and South Korea.

39. Commercial trading aside, there are three general approaches to financial compensation of women providing eggs for research:[25]

    (a) No compensation but only reimbursement of expenses incurred. This implements a philosophy of altruistic donation that is relatively free of any risk of inducement;

    (b) Reasonable compensation for time, risk and inconvenience, in addition to reimbursement of incurred expenses. This is not inconsistent with a philosophy of altruistic donation provided the quantum of

---

21 Human Fertility and Embryology Authority. HFEA statement on donating eggs for research. UK, 21 February 2007. http://www.hfea.gov.uk/en/1491.html (accessed 1 November 2007).

22 National Health and Medical Research Council. *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*. Australia, 2004, revised June 2007, paragraph 17.21.3.

23 Indian Council of Medical Research. *National Guidelines for Stem Cell Research and Therapy*. 2006, paragraph 11.4.

24 *Human Cloning and other Prohibited Practices Act* (Cap 131B of Singapore, 2005 Rev Ed), section 13.

25 Isasi and Knoppers have proposed a broadly similar analytical framework comprising three categories (expense reimbursement, financial compensation and financial incentives), with an analysis of the advantages and disadvantages of each category; Isasi RM and Knoppers BM. Monetary payments for the procurement of oocytes for stem cell research: In search of ethical and political consistency. *Stem Cell Research.* (2007):doi:10.1016/j.scr.2007.09.003.

reimbursement is not excessive and neither the quantity nor the quality of the donor's eggs affects the compensation; and

(c) Substantial compensation that amounts to outright payment of eggs as a commodity.

40. Only the first approach – reimbursement of expenses – is not affected by ethical concerns with inducement. Inducement to donate is generally regarded as unethical because it bears most strongly on the least economically empowered women, and thus is inequitable and could be socially divisive. As was earlier discussed, the concern with recruiting healthy women as egg donors is not the same as those raised by recruiting women who are undergoing fertility treatment, as there are no increased risks for the latter, who will be undergoing ovarian stimulation and retrieval of eggs anyway. It has also been noted earlier that the procedures for obtaining eggs are invasive with certain health risks entailed. These complicate the issue of compensation that may be provided in egg donation solely for research.

41. Some may consider that women who donate eggs for research should be compensated just as participants in some other research are compensated. However, it is difficult to determine a level of compensation that will not amount to undue influence or inducement as this would depend on a number of factors including the financial status of the woman concerned. This is made even more difficult as biomedical research assumes an increasingly global character. Owing to differences in payment or compensation schemes among countries, women from a country that does not allow compensation for the donation of eggs for research may be induced to make the donation in another country that allows a large payout to be made. Furthermore, there is concern that researchers from wealthy countries may attempt to obtain eggs from women in poor countries, where the compensation, if required would be financially less burdensome for these researchers in comparative terms. There is no simple response to this concern, but many countries are mindful that globalisation has a bearing on what might be considered as reasonable compensation for egg provision.

42. The European Parliament and the Council of the European Union indicated in a Directive the importance of ensuring that donations of tissues and cells (which include eggs) are voluntary and unpaid. However, donors are allowed "to receive compensation, which is strictly limited to making good the expenses and inconveniences related to the donation. In that case, Member States define the conditions under which compensation may be granted."[26] In a specific resolution on human egg cells, the European Parliament expressed its desire to "see egg cell donation, like organ donation generally, strictly regulated in order

26 *Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on Setting Standards of Quality and Safety for the Donation, Procurement, Testing, Processing, Preservation, Storage and Distribution of Human Tissues and Cells*, article 12.

to protect both donors and recipients and to avoid all forms of human exploitation".[27]

43. While payment beyond reimbursement of expenses incurred for the donation of eggs for research could be made in the US and the UK, there is a general recognition of the need to guard against such payment as inducement. For instance, both the International Society for Stem Cell Research (ISSCR)[28] and the California Institute for Regenerative Medicine (CIRM)[29] have issued a number of guidelines that include details on the informed consent process, information to be provided to prospective donors, monitoring of recruitment practices, rigorous review to ensure that reimbursements or financial considerations of any kind do not constitute undue inducement, and the requirement that egg procurement procedures be done by medically qualified and experienced physicians, using carefully controlled ovarian stimulation regimes to reduce the risk of OHSS. Should an egg donor require medical care as a result of providing eggs for research, there should be a provision to pay for the medical cost incurred. In addition, the ISSCR has recommended that "at no time should financial considerations of any kind be given for the number or quality of the eggs themselves that are to be provided for research."[30]

44. It may be considered that the compensation of time, risk and inconvenience is necessary in order to ensure that egg donors are not made worse off by their altruistic giving. A rationale for this has been provided by the European Society on Human Reproduction and Embryology (ESHRE) Task Force on Ethics and Law, which argued that the general principles of research ethics on the subject of compensation should apply to egg donation for research. Thus women who donate eggs for research should be treated similarly to research participants in clinical trials, so that they should receive reimbursement for all costs incurred, as well as compensation for time lost and inconvenience and discomfort suffered in the process.[31]

45. In the UK, the HFEA allows donors to be compensated for loss of earnings (but not for other costs or inconveniences) up to a daily maximum of £55.19 (about S$168) and an overall limit of £250 (about S$760) for each cycle of egg donation.[32] In addition, the HFEA states that there is no restriction on the value

---

27 *European Parliament Resolution on the Trade in Human Egg Cells,* 10 March 2005, resolution 9.

28 International Society for Stem Cell Research. *Guidelines for the Conduct of Human Embryonic Stem Cell Research*. Northbrook, Illinois, US, 2006.

29 California Institute for Regenerative Medicine. *The CIRM Medical and Ethical Standards Regulations*. California, US, 2007, chapter 2.

30 International Society for Stem Cell Research. *Guidelines for the Conduct of Human Embryonic Stem Cell Research*. Northbrook, Illinois, US, 2006, paragraph 11.5b (ii).

31 European Society for Human Reproduction & Embryology, Task Force on Ethics and Law. Oocyte donation for non-reproductive purpose. *Human Reproduction*. 22 (2007):1210–1213.

32 Human Fertility and Embryology Authority. *Directions given under the Human Fertilisation and Embryology Act 1990: Giving and Receiving Money or Other Benefits in Respect of Any Supply of Gametes or Embryos*. UK, 2006, paragraph 4.

of other benefits which may be given to a donor, but the only such benefits offered for this purpose may be treatment benefits provided in the course of the donation cycle unless medical considerations dictate otherwise.[33] This applies to donation for both clinical and research purposes.[34] Under the compensated 'egg sharing' arrangements with researchers by women undergoing fertility treatment, some cost of fertility treatment might be offset, as compensation, in return for the provision of eggs for research. The Medical Research Council has expressed support for this position by providing funds for subsidising the IVF treatment of women who choose to donate some of their eggs for a research project undertaken by the North East England Stem Cell Institute.[35] This scheme is the first of its kind in the world.[36]

46. The possibility of a compensated egg sharing scheme as an "ethically justifiable" way to obtain eggs for research has been earlier proposed in a paper by Heng, Tong and Stojkovic.[37] However, Isasi and Knoppers indicate that the presence of options of various schemes of monetary payment does not automatically rule out the possibility of exploitation, such as when participating in an egg-sharing programme with researchers is the only means to gain access to IVF treatment. Although there is no easy solution to this ethical dilemma, they emphasised the importance of making the ethical dimensions of the approach adopted (compensatory or otherwise) transparent.[38]

47. There is no uniform practice in the US. The Bedford Stem Cell Research Foundation in Massachusetts, founded in 2000 and the first in the world to recruit women specifically for stem cell research, reimburses egg donors for travel, time and child care expenses. The National Research Council and the Institute of Medicine of the National Academies recommend that women who undergo ovarian stimulation specifically for research "should be reimbursed only for direct expenses incurred as a result of the procedure, as determined by an Institutional Review Board. No cash or in kind payments should be

---

http://www.hfea.gov.uk/docs/D2006_1_Directions_on_giving_and_receiving_money.pdf (accessed 1 November 2007).

33 *Ibid*, paragraph 5.

34 Human Fertility and Embryology Authority. HFEA statement on donating eggs for research. UK, 21 February 2007. http://www.hfea.gov.uk/en/1491.html (accessed 1 November 2007).

35 Medical Research Council. Women undergoing IVF to donate eggs for stem cell research in return for reduced treatment costs. UK, 13 September 2007. http://www.mrc.ac.uk/consumption/groups/public/documents/content/mrc003971.pdf (accessed 1 November 2007).

36 North East England Stem Cell Research Institute, News. Egg sharing: Women to get help with IVF treatment costs for donating eggs to research. UK, 13 September 2007. http://www.nesci.ac.uk/news/item/egg-sharing-women-to-get-help-with-ivf-treatment-costs-for-donating-eggs-to-research (last accessed 1 November 2007).

37 Heng BC et al. The egg-sharing model for human therapeutic cloning research: Managing donor selection criteria, the proportion of shared oocytes allocated to research, and amount of financial subsidy given to the donor. *Medical Hypotheses*. 66 (2006):1022-1024.

38 Isasi RM and Knoppers BM. Monetary payments for the procurement of oocytes for stem cell research: In search of ethical and political consistency. *Stem Cell Research.* (2007):doi:10.1016/j.scr.2007.09.003, pages 3-4.

provided".[39] However, the Ethics Committee of the American Society for Reproductive Medicine is of the view that egg donors, whether for infertility treatment or for research should be compensated for their time, inconvenience and discomfort and decided that "at this time sums of $5,000 or more require justification and sums above $10,000 are not appropriate."[40]

48. In Singapore, the general ethical framework relating to the donation of tissue (which includes eggs) for research was established by the BAC in 2002. Such donation should be outright gifts and there should be no financial incentives, although reasonable reimbursement of expenses incurred should be allowed.[41] This ethical requirement in relation to the donation of gametes and embryos was taken up in legislation. Under Section 13 of the Human Cloning and Other Prohibited Practices Act (Cap 131B, 2005 Rev Ed), a person is prohibited from giving or receiving valuable consideration for the supply of human eggs, or to otherwise make an offer to that effect. Valuable consideration has been defined as including "any inducement, discount or priority in the provision of a service to the person, but does not include the payment of reasonable expenses incurred by the person in connection with the supply." Reasonable expenses include expenses relating to the collection, storage or transport of the eggs. However, the possibility of compensation for time, risk and inconvenience has not been addressed. Based on the general ethical principle of fairness, it appears that there could be circumstances where allowing reasonable compensation for time, risk and inconvenience is consistent with the existing ethical framework.

49. Some people might argue that compensation for participating in or contributing to research is justified when the research is done for profit by a commercial organisation, as when, for example, a pharmaceutical company compensates research participants in trials of a new drug. The rationale is that, because the venture is for profit, a participant should not be expected to donate time or take a risk altruistically, on a purely reimbursement basis. On this argument, eggs could be sold for private sector research. However, there is also an argument that it is unacceptable to create a situation where there are two standards operating, one for the private sector and one for the public sector, and it seems inconsistent to suggest that risks become ethically acceptable in contexts where commercial profit is a motive but not otherwise. There is, in general, a tradition of altruism in research participation, in much the same way as there is for organ donation, and in previous reports, the BAC has taken this tradition for granted in considering the ethics of research with human subjects and the idea that research should be considered a public good.

---

39 National Research Council and Institute of Medicine. *Guidelines for Human Embryonic Stem Cell Research*. Washington DC, The National Academies Press, 2007 rev, recommendation 16.

40 Ethics Committee of the American Society for Reproductive Medicine. Financial compensation of oocyte donors. *Fertility and Sterility*. 88 (2007):305-309.

41 Bioethics Advisory Committee. *Human Tissue Research*. Singapore, 2002, paragraphs 13.1.8 to 13.1.10.

Conclusion

50. Compensation for contributing eggs for research in an amount and manner that is fair and without inducement is likely to require the attention of ethicists, policy makers and regulators in the foreseeable future. As embryonic stem cell research gains a stronger foothold in Singapore, it is timely for this subject to be considered.

51. The availability of human eggs is a key limiting factor in embryonic stem cell research. Indeed, the number of eggs that is likely to be obtained from healthy donors will probably remain low. Scientists may have to continue with the current practice of using eggs contributed by women undergoing fertility treatment or look for alternative means to achieve their scientific goals, such as using animal eggs. In principle, where women are allowed to donate eggs for research, scientists and IRBs should ensure that these women understand the procedures and risks involved before consenting to donate and that their interests and safety are adequately protected.

Table 1

Regulatory Approaches of Selected Countries to Human Egg Donation[1]

Country[2]	Egg Donation for Assisted Reproduction (AR)	Payment[3] (Egg donation for AR)	Egg Donation for research[4]	Payment[3] (Egg donation for research)
Austria	✗	na	✗	na
Australia (Commonwealth)	✓	R	✓	R
Belgium	✓	C	✓	NI
Brazil	✓	NI	✓	R
Canada	✓	R	✓	R
China	✗	na	✓	G
Czech Republic	✓	R	✓	R
Denmark	✓	C	✓	NI
Estonia	✓	R	✓	R
Finland	✓	R	✓	R
France	✓	R	✓	R
Germany	✗	na	NI	NI
Greece	✓	✗	✓	✗
Hong Kong	✓	C	✓	C
Hungary	✓	C	✓	C
India	✓	C	✓	R
Israel	✓	NI	NI	NI
Italy	✗	na	NI	NI
Japan	✗	na	✓	R
Korea (South)	✓	G	✓	G
Netherlands	✓	R	✓	R
New Zealand	✓	R	✓	R
Norway	✗	na	✗	na
Singapore	✓	R	✓	R
Slovenia	✓	R	NI	NI
South Africa	✓	R	✓	R
Spain	✓	C	✓	C
Sweden	✓	NI	✓	NI
Switzerland	✗	na	NI	NI
Taiwan	✓	C	NI	NI
Turkey	✗	na	NI	NI
United Kingdom	✓	C	✓	C
USA (Federal)	✓	C	✓	C

Legend:

✕	Prohibited
✓	Allowed
C	Compensation allowed
R	Reimbursement of expenses allowed
G	General prohibition against purchase and/or sale of eggs
na	Not applicable
NI	No information that directly addressed the issue was found or the position on the issue was unclear

(1) The information set out in the table is indicative and need not necessarily be a complete representation of the regulatory approach of the specified country. In particular, the regulatory approach of the country presented has been interpreted in relation to that of Singapore and for the purposes of this Consultation Paper.

(2) Countries are selected based on several factors including availability of information (in the English language), availability of legislation and regulatory guidelines (both legally binding and non-binding) on the issues considered, and the extent that these issues have been deliberated on and debated in those countries.

(3) In this Consultation Paper, compensation is considered distinct from reimbursement. Reimbursement is defined as repayment for incurred expenses. In contrast, compensation is defined as recompense for presumptive loss of income and/or for risk and inconvenience. It is not intended to include any transaction for the purpose of monetary gain.

(4) Many countries have specific provisions for certain types of research involving eggs, such as the creation of an embryo, and therapeutic or research cloning. These specific types of research are not considered here. Rather, this column indicates whether eggs may be contributed for research in general. Countries with legislation or regulatory guidelines on egg donation for assisted reproduction may not have made similar (or explicit) provisions for egg donation for research. However, many of the countries that allow egg donation for assisted reproduction would generally allow a similar donation to research that is concerned with reproduction.

GLOSSARY

Adult stem cell – An unspecialised cell present in a tissue or organ, that is able to replicate itself and develop into specialised cell types of that tissue or organ, or some other cell types.

Alzheimer's disease – A common degenerative brain disorder, characterised by progressive deterioration of mental functions leading to impaired memory, thinking, judgment and ability to concentrate, emotional instability and increased reliance on others for daily activities.

Assisted reproductive technologies – The use of clinical and laboratory techniques to increase chances of conceiving a baby. An example is *in vitro* fertilization, or IVF.

Differentiation – The process whereby an unspecialised cell (eg stem cell) undergo changes to become a specialised cell.

Embryo – The earliest stage of development of an organism.

Embryonic stem cell – An unspecialised cell derived from an embryo, that is able to replicate itself and develop into various specialised cell types, for example, skin, nerve or heart cells.

Gamete – Sperm or egg cell.

Hormone – A chemical substance produced by an organ which can travel through the blood and exert functional effects on other organs.

Immune reaction – A response by the defence mechanism of the body that is able to recognise and attack foreign material (such as viruses or transplanted material) within the body.

Institutional review board (IRB) – A committee appointed by an institution to review the ethical standards of biomedical research proposals.

In vitro fertilisation (IVF) – A clinical and laboratory procedure whereby the eggs and sperm from a couple are extracted and fertilised outside their bodies. Such a procedure is a kind of assisted reproduction aimed at increasing the chances of a couple conceiving a baby.

Reprogramming – The process whereby a somatic cell (a specialised cell) is converted into one that has the capacity of an unspecialised cell to develop into a living embryo or into all types of cells or tissues in the body.

Nucleus – The part of a cell that carries most of the cell's genetic material.

Oocyte – An egg cell.

Ovarian stimulation – The administering of medication to stimulate egg development in the ovaries.

Ovarian hyperstimulation syndrome – A medical condition that may result from stimulation of the ovaries. Symptoms include nausea, vomiting, weight gain, pelvic pain, and difficulty breathing. In rare cases, the condition may be fatal.

Ovaries – The internal reproductive organs of a female that produce eggs.

Parkinson's disease – A disorder characterised by progressive degeneration of nerve cells in the brain, resulting in muscular tremors, rigid movement, stooped posture, and mask-like face.

Parthenogenesis – The process whereby the development of an organism starts in an egg that has not been fertilised. This is a form of non-sexual reproduction in some animals.

Patient-specific stem cells – Stem cells that are genetically matched to a specific patient and thus would not be rejected when transplanted into the patient's body.

Pluripotent – The capacity of unspecialised cells to develop into all types of specialised cells.

Polycystic ovaries – A hormonal disorder characterised by multiple cysts in the ovaries and irregular menstrual cycles. This is a common reason for infertility in women.

Reproductive cloning - The process of creating a genetically identical copy of a human being or animal.

Research cloning (also known as therapeutic cloning) – The use of cloning technology for research and therapeutic purposes that do not result in the creation of a complete animal or human being.

Somatic cell – Any mature (or differentiated) cell in the body that is not a sperm or an egg.

Somatic cell nuclear transfer – The process whereby the nucleus of a somatic cell is transferred into an egg cell, whose nucleus has been removed. This process may be used to create a cloned embryo so as to derive stem cells for research.

Stem cell – An unspecialised cell that is able to replicate itself and develop into specialised cell types (such as a skin, nerve, or heart cell).

Specialised (differentiated) cell – A mature cell with a specific function, for example, skin cells and liver cells.

Therapeutic Cloning – see Research Cloning

Tissue – An aggregation of similar cells that perform a particular function.

Totipotence – The capacity of an unspecialised cell to develop into any cell type, as well as developing into an organism.

Ultrasound scan – The use of high-frequency sound waves to create images of structures within the body.

Uterus – Also known as the womb, where a fertilised egg implants and a foetus develops.

List of Useful Documents

Balen A. *Ovarian Hyperstimulation Syndrome – A Short Report for the HFEA*. UK, February 2005.
http://www.hfea.gov.uk/docs/OHSS_Report_from_Adam_Balen_2005(1).pdf (accessed 1 November 2007).

Bioethics Advisory Committee. *Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning*. Singapore, 2002.
http://www.bioethics-singapore.org/uploadfile/60517 PMHSC Research.pdf (accessed 1 November 2007).

Bioethics Advisory Committee. *Human Tissue Research*. Singapore, 2002.
http://www.bioethics-singapore.org/uploadfile/60104 PMHT Research.pdf (accessed 1 November 2007).

Bioethics Advisory Committee. *Personal Information in Biomedical Research*. Singapore, 2007
http://www.bioethics-singapore.org/uploadfile/60247 PMPI in Research.pdf (accessed 1 November 2007).

Bioethics Advisory Committee. *Research Involving Human Subjects: Guidelines for IRBs*. Singapore, 2004.
http://www.bioethics-singapore.org/uploadfile/55527 PMHS Research.pdf (accessed 1 November 2007).

California Institute for Regenerative Medicine. *The CIRM Medical and Ethical Standards Regulations*. US, January 2007.
www.cirm.ca.gov/reg/pdf/Reg100010_CompRegs.pdf (accessed 1 November 2007).

Ethics Committee of the American Society for Reproductive Medicine. "Financial Compensation of Oocyte Donors." *Fertility and Sterility* 88 (2007): 305-309.
http://www.asrm.org/Media/Ethics/financial_incentives.pdf (accessed 1 November 2007).

European Society of Human Reproduction & Embryology, Task Force on Ethics and Law. "Oocyte donation for Non-Reproductive Purpose." *Human Reproduction* 22 (2007): 1210-1213.

Human Fertilisation and Embryology Authority. *Directions on Giving and receiving money or other benefits in respect of any supply of gametes or embryos.* UK, April 2006.
www.hfea.gov.uk/docs/D2006_1_Directions_on_giving_and_receiving_money.pdf (accessed 1 November 2007).

Human Fertilisation and Embryology Authority. *Statement on Donating Eggs for Research.* UK, February 2007.
www.hfea.gov.uk/en/1491.html (accessed 1 November 2007).

Human Fertilisation and Embryology Authority. *Donating eggs for research: safeguarding donors*. UK, September 2006.
http://www.hfea.gov.uk/docs/donating_eggs_for_research_safeguarding_donors_consultation_FINAL.pdf (accessed 1 November 2007).

Human Fertilisation and Embryology Authority. *Directions on Giving and Receiving Money or Other Benefits in Respect of any Supply of Gametes or Embryos*. UK, April 2006.
www.hfea.gov.uk/docs/D2006_1_Directions_on_giving_and_receiving_money.pdf (accessed 1 November 2007).

International Federation of Fertility Societies. "IFFS Surveillance 07". *Fertility and Sterility*. 87 Suppl 1 (2007): S1-67.
http://www.iffs-reproduction.org/documents/Surveillance_07.pdf (accessed 1 November 2007).

Indian Council of Medical Research. *National Guidelines for Stem Cell Research and Therapy*. 2006.
http://www.icmr.nic.in/stem_cell/stem_cell_guidelines.pdf (accessed 1 November 2007).

International Society for Stem Cell Research. *Guidelines for the Conduct of Human Embryonic Stem Cell Research*. December 2006.
www.isscr.org/guidelines/ISSCRhESCguidelines2006.pdf (accessed 1 November 2007).

Ministry of Health. *Directives for Private Healthcare Institutions providing Assisted Reproduction Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations (Cap 248, Reg1).* revised March 2006.
https://www.moh-ela.gov.sg/ela/docroot/html/assisted_reproduction_services_directives.pdf (accessed 1 November 2007).

National Health and Medical Research Council. *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*. Australia, 2004, revised 2007.
http://www.nhmrc.gov.au/publications/synopses/_files/e78.pdf (accessed 1 November 2007).

National Research Council and Institute of Medicine. *Guidelines for Human Embryonic Stem Cell Research*. US, 2005, revised 2007.
http://www.nap.edu/catalog.php?record_id=11278 (accessed 1 November 2007).

National Research Council and Institute of Medicine. *Assessing the Medical Risks of Human Oocyte Donation for Stem Cell Research: Workshop Report*. US, 2007. http://www.nap.edu/catalog.php?record_id=11832#toc (accessed 1 November 2007).

Ng SC. *Oocyte Donation – Clinical and Scientific Aspects*.
A background paper for the Bioethics Advisory Committee, Singapore. June 2007.
http://www.bioethics-singapore.org

Capps B. *Oocyte Procurement for Research*.
A background paper for the Bioethics Advisory Committee, Singapore, April 2007.
http://www.bioethics-singapore.org

Consultation Paper on "Donation of Human Eggs for Research"
7 November 2007

Distribution List

1. Academy of Medicine, Singapore
2. Alexandra Hospital
3. Association of Women for Action & Research
4. Bioinformatics Institute
5. Bioprocessing Technology Institute
6. Buddhist Fellowship
7. Catholic Medical Guild of Singapore
8. Centre for Research on Islamic and Malay Affairs, Association of Muslim Professionals
9. Changi General Hospital
10. College of Family Physicians Singapore
11. Duke-NUS Graduate Medical School
12. ES Cell International
13. Faculty of Arts and Social Science, National University of Singapore
14. Faculty of Dentistry, National University of Singapore
15. Faculty of Law, National University of Singapore
16. Faculty of Science, National University of Singapore
17. Genome Institute of Singapore
18. Graduates' Christian Fellowship
19. Hindu Advisory Board
20. Institute of Bioengineering and Nanotechnology
21. Institute of Medical Biology
22. Institute of Mental Health/Woodbridge Hospital
23. Institute of Molecular and Cell Biology
24. Jewish Welfare Board
25. Johns Hopkins Singapore International Medical Centre
26. KK Women's and Children's Hospital
27. Law Reform Committee, Singapore Academy of Law
28. Lee Kuan Yew School of Public Policy, National University of Singapore
29. The Law Society of Singapore
30. Majlis Ugama Islam Singapura (Islamic Religious Council of Singapore)
31. Mount Alvernia Hospital
32. National Cancer Centre
33. National Council of Churches of Singapore

34. National Dental Centre
35. National Heart Centre
36. National Medical Ethics Committee
37. National Neuroscience Institute
38. National Skin Centre
39. National University Hospital
40. NUH-NUS Tissue Repository
41. Obstetrical and Gynaecological Society of Singapore
42. Office of Life Sciences, National University of Singapore
43. Parkway Hospitals Singapore Pte Ltd
44. Raffles Hospital
45. School of Arts and Social Science, SIM University
46. School of Biological Sciences, Nanyang Technological University
47. School of Human Development and Social Science, SIM University
48. School of Humanities and Social Science, Nanyang Technological University
49. School of Law, Singapore Management University
50. School of Science and Technology, SIM University
51. School of Social Sciences, Singapore Management University
52. Sikh Advisory Board
53. Singapore Association of Social Workers
54. Singapore Association of Women Lawyers
55. Singapore Association of Women Doctors
56. Singapore Buddhist Federation
57. Singapore Council of Women's Organisations
58. Singapore Chinese Buddhist Association
59. Singapore General Hospital
60. Singapore Institute for Clinical Sciences
61. Singapore Medical Association
62. Singapore Medical Council
63. Singapore National Academy of Science
64. Singapore National Eye Centre
65. Singapore Nurses Association
66. Singapore Nursing Board
67. Singapore Psychological Society
68. Society of Bioscience & Technology
69. The Spiritual Assembly of the Bahá'is of Singapore
70. Tan Tock Seng Hospital

71. Taoist Mission (Singapore)
72. Thomson Medical Centre
73. Yong Loo Lin School of Medicine, National University of Singapore

IVF and Fertility Clinics

1. Centre For Assisted Reproduction Pte Ltd
2. Chan K H Clinic For Women
3. Charles M P Lim Clinic & Surgery For Women
4. Christopher Chen Centre For Reproductive Medicine
5. Dr L K Yap Clinic & Surgery For Women
6. Fong's Clinic For Women & Fertility
7. Gynecology Consultants Clinic & Surgery
8. MD Specialist Healthcare
9. Motoko Clinic For Women
10. Mount Elizabeth Fertility Centre
11. Noel Leong Fertility & IVF Clinic Pte Ltd
12. Pacific Specialist Practice
13. Rapha Specialist Clinic
14. S H Teoh Clinic & Surgery For Women
15. Teoh Clinic for Women
16. The Tow Yung Clinic
17. The Women's Specialist Centre
18. Thomson Fertility Centre
19. TLC Gynaecology Practice Clinic & Surgery
20. Women and Fetal Centre
21. Women's Health and Fertility Centre

.

Written Responses to the Consultation Paper on "Donation of Human Eggs for Research"

Organisations / Institutions / Fertility Clinics

1. The Catholic Medical Guild of Singapore
2. Christopher Chen Centre for Reproductive Medicine
3. Graduates' Christian Fellowship
4. Institute of Bioengineering and Nanotechnology
5. Institute of Mental Health
6. The Law Society of Singapore
7. Majlis Ugama Islam Singapura
8. National Council of Churches of Singapore
9. National Dental Centre Institutional Review Board
10. National Medical Ethics Committee, Ministry of Health
11. Noel Leong Fertility & IVF Clinic
12. Singapore Eye Research Institute Institutional Review Board
13. Singapore Nursing Board

Individuals

14. Mr Farhan Ali
15. Professor Chan Soh Ha
16. Dr Chuah Khoon Leong
17. Mr Patrick Goh
18. Dr Alexis Heng (2 sets of comments)
19. Dr Suresh Nair
20. Professor George Wei
21. Associate Professor Allen Yeoh
22. Member of the Public 1
23. Member of the Public 2

Bioethics Advisory Committee
11 Biopolis Way, #10-12 Helios
Singapore 138667

The Catholic Medical Guild of Singapore
2 Highland Road
#01-05 Catholic Archdiocesan Education Centre
Singapore 549102

Dear Sirs,

RE: Donation of Human Eggs for Research

We are grateful for this opportunity to provide feedback on the above issue.

Attached is the submission of The Catholic Medical Guild of Singapore.

Dr Gabriel Seow
Deputy Master
The Catholic Medical Guild of Singapore

DONATION OF HUMAN EGGS FOR RESEARCH

We are grateful for this opportunity to provide feedback on the above issue.

We agree with the BAC that the safety and welfare of donors are paramount, and that they should be "adequately safeguarded regardless of their status." We also agree with the BAC that another concern in this issue is the "possibility that vulnerable women may be exploited, through various forms of inducement to provide eggs for research."[1]

These are valid concerns, and we are glad that the BAC has brought them up in the course of discussion on the subject.

We base our discussion on certain universally accepted moral principles.

PRINCIPLES:

1. Every human being is to be respected for his own sake and cannot be reduced in worth to an instrument for the advantage of others.[2]

2. His rights as a person must be recognized and respected from the first moment of his existence. The first of these is the inviolable right to life. [3]

3. As we accord the human person immense dignity, the pursuit of science as a means to improve the human condition, to treat disease, and to save human life is laudable and to be encouraged. However, the primacy of human dignity must always be maintained.

4. Science, powerful instrument that it is, remains but a tool to be ethically used to serve man, and never the reverse. Not everything that is scientifically possible is for that reason morally permissible. Ethics committees exist because we recognize the fact that the pursuit of science without a right conscience can only lead to humanity's ruin.[4]

5. Informed consent is an important, but not the only, condition for an act to be considered ethically sound. Other considerations include that of ascertaining that the act, for which informed consent is given, is one that is good in itself.

---

1 BAC Consultation Paper on Donation of Human Eggs for Research, point 4.
2 Donum Vitae, I.5
3 Donum Vitae, I.1
4 Donum Vitae, I.2

SAFETY OF DONATION OF HUMAN EGGS

There is genuine concern about the possible harm that can befall women who donate their eggs, in particular the problem of Ovarian Hyperstimulation Syndrome (OHSS), which can range from mild to severe life threatening forms. In addition, we also note the BAC's concern that ovarian stimulation "may lead to an increased risk of future cancers of the breast, ovary and uterus."[5]

Even though it may be argued that the risk of such serious side effects may be small, the fact is that these risks are real. Furthermore, considering that many, many women are required to donate their eggs in order that enough eggs are produced for research purposes, the absolute numbers of women who suffer such serious side effects will increase accordingly.

PAYMENT FOR DONATION OF HUMAN EGGS

Financial compensation for egg donors is a means of encouraging women to donate their eggs in spite of the medical risks and inconvenience of doing so. Even though the commercialisation of human body parts is illegal, it is possible that the most likely contributors for the procedure of egg harvesting would be women in need of the accompanying financial gain, that is, women from lower socio-economic strata.

Furthermore, such practice will encourage us to see humans, in particular women, as mere commodities, where a price has been put on their bodies and their parts. In this way too, the perception that others can be instrumentalised for our benefit will take root, with long-term negative implications for society.

IMPACT ON THE MEDICAL COMMUNITY

"Do no harm" is the core ethical norm that is upheld by the medical profession. The goal of medicine has traditionally, and rightly, been to "cure sometimes, relieve often, and comfort always."

Once the sale of human eggs is legislated and doctors get involved as co-operators in this trade, this core ethical norm of the medical profession will be violated.

Doctors may be seen to be opportunistic professionals who are prepared to cause potentially significant harm to their patients (donors) for the sake of financial or scientific gain. The unique doctor-patient relationship, one that has been based on trust in the former's interest in the welfare of the latter, may likely be compromised.

---

[5] BAC Consultation Paper on Donation of Human Eggs for Research, point 25.

THE USE OF DONOR EGGS FOR CLONING/STEM CELL RESEARCH

While donated human eggs can be studied without being fertilized, we note that the main use of donor eggs has been in the area of cloning for stem cell research. This involves the creation of a new human being through the insertion of a nucleus from a somatic cell into an enucleated oocyte (somatic cell nuclear transfer or SCNT). It is followed by the destruction of this new human individual in the blastocyst stage, in order to obtain its stem cells for research. This is done in the hope that such work will yield treatment for diseases such as Parkinson's disease, Alzheimer's disease and diabetes.

We fully support the research and development of new treatment options for diseases in order to improve the human condition. We affirm that such research should only be conducted in a fully ethical manner, which does not compromise the dignity of any human being at any stage of his life. In particular, we find morally unacceptable the practice of creating new embryos through SCNT, parthenogenesis, variations of chimerisation or any other method and subsequently destroying them or manipulating them for research.

At this juncture, we also note the following problems with SCNT as it is practised:

1. The stem cells derived from this procedure share the same problem as other embryonic stem cells, namely that of tumour formation. This problem has been a bane to scientists involved in embryonic stem cell research, and despite the best efforts of scientists the world over, appears to be one that is extremely difficult, if not impossible, to surmount.
2. There are serious ethical concerns with SCNT, in particular the fact that human beings are cloned with the view to their being destroyed in order that their stem cells be utilized for research.

In fact, such concerns have been serious enough to prod many scientists to pursue other more scientifically viable, and in particular, more ethical, ways of obtaining stem cells for treatment.

Stem cells from adult sources (such as the bone marrow and umbilical cord) have seen many exciting new developments in research and therapy in recent times.

Dr Ian Wilmut, who led the team that created Dolly the cloned sheep, made a statement recently. For scientific reasons, he was abandoning human SCNT to pursue research in the area of “direct reprogramming” of adult human cells to generate stem cells known as induced pluripotent stem cells (iPSCs), a method pioneered by Dr Shinya Yamanaka of Kyoto University in Japan. While it is regrettable that embryonic stem cells were utilized in the process, the development of iPSCs points to the fact that adult cells can be used in many more ways than previously imagined. It adds to the view that therapy can indeed be developed while avoiding the ethical problem of destroying human embryos to obtain stem cells for research.

CONCLUSION

We thank the BAC for this opportunity to provide feedback on this important issue of financial compensation for egg donation. We strongly urge the BAC to look seriously into its implications on women's health, safety, and status. We, as doctors and scientists, are edified by research that is steered in a direction that respects the life of every human being in all states and stages.

CHRISTOPHER CHEN
CENTRE *for*
REPRODUCTIVE
MEDICINE
PTE LTD

ROC No: 199301062 H

5 January 2007

Professor Lee Eng Hin
Chairman
Human Embryo and Chimera Research Working Group
Bioethics Advisory Committee
11 Biopolis Way
#10-12 Helios
Singapore 138667

Dear Prof Lee

INVITATION TO COMMENT ON CONSULTATION PAPER

Thank you for your letter of 7 November 2007 inviting me to comment on the consultation paper entitled "Donation of Human Eggs for Research".

At the outset, BAC must be very clear and direct in its final recommendations to the SCLS as both the scientific investigators and the public require clear directives over the issue of donating human eggs for research. Whilst various countries around the world may have their own rules and regulations, we in Singapore must produce our own rules and regulations to suit our local conditions. To further emphasize the issue, we need to make up our minds and the BAC must ultimately give clear directions. There is no room for vacillation.

Singapore, undoubtedly, is trying to project itself as one of the world leaders in scientific research and progress, having invited top scientists to work here to supplement our local ones. It is therefore clear that Singapore must provide favourable conditions to realise its goal, and in the national interest. Biomedical research must therefore be given a helping hand.

It is very clear that human eggs are required for research, especially for embryonic stem cell research. The BAC must therefore keep this objective in mind, whilst at the same time not go overboard but keep within the confines of ethical, legal and social acceptability.

6A NAPIER ROAD #04-38 ANNEXE BLOCK GLENEAGLES HOSPITAL SINGAPORE 258500
TEL: (65) 6474 3900 FAX: (65) 6474 4011 ANSWERING SERVICE : 6333 5550
EMAIL: info@cccrm.com WEBSITE: www.cccrm.com

In order to obtain and increase donation of human eggs for research, it is of paramount importance that the right message be given to the public, promoting the public to donate eggs in the national interest, for research. We should avoid negative publicity.

For practical purposes, a realistic and major source of human eggs for donation will come largely from spare eggs during IVF treatments. Patients can be encouraged to donate their spare eggs; it is important that informed consent be obtained and that they be given full explanation as to what will happen to their donated eggs when used for medical research. Only after they have given their signed and informed consent should they be given monetary assistance to subsidise part of their expenses in their IVF treatment. This will overcome any criticism of obligation or inducement to donate their eggs.

The possibility of healthy females who wish to donate their eggs for medical research and who are not undergoing IVF treatment will be remote, if not exceptional. For those who are altruistic enough, they should be encouraged, and any potential obstacles removed.

An area that has not been given focus is the donation of **immature** eggs. IVF technology is continuing to advance, and one source of eggs for research which can be obtained, (perhaps in the not too distant future) can be further matured in the laboratory and then used for embryonic stem cell work. Women who require laparoscopy for investigation of infertility can donate some immature eggs during the procedure for medical research, which can also provide information to them about their egg quality. This information will be helpful in the further management of their infertility problem. I suggest the BAC pay some attention to this avenue of egg donation.

Thank you for your attention.

Yours sincerely

PROF CHRISTOPHER CHEN
Honorary Professor, School of Medicine, University of Queensland, Australia

Professor, Faculty of Health, School of Biomedical Sciences, University of Newcastle, Australia

Honorary Professor, Ricardo Palma University, Lima, Peru, South America

Honorary Professor, Sri Ramachandra Medical College & Research Institute, Sri Ramachandra University, India - A Harvard Medical International Associated Institution

World President Elect, International College of Surgeons, USA.

CEO & Medical Director, Senior Consultant Obstetrician & Gynaecologist and Infertility Specialist, of Christopher Chen Centre for Reproductive Medicine

Director of Gleneagles IVF Centre, Gleneagles Hospital

6A NAPIER ROAD #04-38 ANNEXE BLOCK GLENEAGLES HOSPITAL SINGAPORE 258500
TEL: (65) 6474 3900 FAX: (65) 6474 4011 ANSWERING SERVICE: 9802 5555
EMAIL: secretary@cccrm.com WEBSITE: www.cccrm.com

To: Bioethics Advisory Committee
11 Biopolis Way, #10-12 Helios
Singapore 138667
Attn: Prof Lee Eng Hin

RE: Response to the Consultation Paper fro Donation of Human Eggs for Research dtd 7th Nov 2007

The Graduates' Christian Fellowship (GCF) thank the Bioethics Advisory Committee (BAC) for your invitation to comment on the above mentioned paper. We applaud the continued efforts of BAC to ensure high ethical standards in a very delicate balance of pushing for cutting edge research for the possibility of saving and enhancing lives and protecting dignity of human lives.

It has been our position, as in the last submission, that GCF is not in favor of Embryonic Stem Cell Research (ESCR) because it involves the creation of a human life and subsequently the killing of it. It is also very sad that for an endeavor which for the time being (and after much financial and human resource) has not yielded any therapies that could be used for the cure of any existing disease. In the meantime, many lives had been sacrificed.

The key to this paper as we read it has one presenting issue and two main points; the lack of eggs to create embryos for ESCR and 1) should women be allowed to donate their eggs for research and 2) should there be payment for such donations?

Need for Human Eggs

We are certain that BAC has been keeping tabs with the most recent development in the Adult Stem Cell Research (ASCR) which was announced probably after the completion of the above mentioned consultation paper. These recent developments is critical in our response as we see the recent breakthrough by Prof James A. Thomson and his colleagues at the University of Wisconsin in Science and by Prof Shinya Yamanaka of Kyoto University and the Gladstone Institute of Cardiovascular Disease in San Francisco in Cell as the answer for the need for the presenting issue, the lack of human eggs.

We see that research institutes require the need for embryonic stem cells because of their pluripotent nature. It is stated in your paper that, 'There is currently little evidence that adult stem cells are pluripotent.' The above recent breakthroughs have found techniques which can manipulate adult stem cells so that they become pluripotent in nature. **There is therefore no real or critical need to harvest widely for human eggs from healthy women.**

This side steps most the ethical mine fields which currently plagues us in both the limitations to research and preserving the dignity of human lives. Though in its'

preliminary stages, we believe that this will be the new way forward to conduct future research which will be based on adult stem cells that are pluripotent in nature. Rather than putting much financial and human resources in the harvesting of human eggs and risking the lives of healthy women in the process, we implore the BAC to advice our government and biotechnology research institutes to develop and stabilize these new techniques and lead the way forward for biotechnological discoveries.

To quote Scottish stem cell pioneer Ian Wilmut (who led the team that in 1997 cloned Dolly the sheep) in his response reported in the Boston Globe regarding these new discoveries by Thomson and Yamanaka, announced that 'his University of Edinburgh laboratory will abandon embryonic cloning in favor of reprogramming. Wilmut, in remarks to journalists, said he is motivated not by ethical concerns, but by the conviction that Yamanaka's approach holds better chances for near-term scientific research and long-term medical therapies and cures. "The technique of changing cells directly from a patient into stem cells, without the step of making a clone, has better potential," he said. "Plus, it's socially more acceptable. This is the way science is going."[1]

Should women be allowed to donate eggs for research?

Deriving from our constant position that the beginning of a human live is at conception, and further from our view point in the above section, **GCF is not in favor to further harvest human eggs from healthy women.** We concede as a compromise that women who are currently undergoing IVF treatment can choose to 'sign over' surpluses for research with informed consent as is currently practiced. This compromise is with the view that these surpluses will otherwise be destroyed anyway.

We have found that there was no statement in the paper of any particular target number (women per year for example). It was only mentioned that 'the risk of egg retrieval is relatively low'. Some facts and figures would be very helpful for assessments of the risk and provides objectivity to the proposal. According to a report from the World Health Organization, 'The worldwide incidence of severe OHSS has been estimated at 0.2%–1% of all ART cycles *(206)* and the associated mortality at 1:45 000–1:50 000 per infertile women receiving gonadotrophins *(207)*.'[2] It was cited in an article by Dr. Pia De Solenni of the Family Research Council in Washington D.C that 'If we return to the lowest number of women required in order to use embryonic stem cell treatments for diabetes in the US, just one disease, 29 million women, that would translate into 580 deaths.'[3] It is therefore only reasonable for us to ask, how much risks are we talking about precisely. We need to make sure that we are not knowingly taking lives in order to 'potentially' save lives. It does not make logical sense. One death is one too many, especially when the person is a healthy individual.

---

[1] Colin Nickerson, Breakthrough on stem cells. Boston Globe, 21 November 2007

[2] Jean-Noel Hugues, http://www.who.int/reproductive-health/infertility/14.pdf

[3] Dr. Pia De Solenni, www.humanevent.com.

In view of the risks which the consultation paper have presented and the complexity of the procedure to stimulate eggs growth and donors subjection to multiple injections of Lupron™ (leuprolide acetate), we are of the view that 2 critical matters were not mentioned and could be enhanced.

1) There is insufficient clarity on the risks and side effects that are involving the use of leuprolide acetate as clearly spelled out in FDA web-site.[4] Such information will also help access the risks involved, particularly for those who intend to make such a donation.
2) There is also no mention of restrictions as to how many times a year can someone donate eggs.
3) The onus of responsibility for medical expenses and future healthcare has to be absorbed by the government agency in the event of a reaction or complication due to the extraction procedure for human eggs. We believe there is currently insufficient safeguards to protect the women who are targeted as donors. There has been cases were women were not given proper aftercare due to Ovarian Hyperstimulation Syndrome (OHSS).

Anyway, the primary use of Lupron is to reduce the amount of testosterone or estrogen in the body. It is used for conditions such as cancer of the prostate, endometriosis (growth of uterine lining outside of the womb), uterine fibroids, and early puberty (before 8 years of age in females and 9 years of age in males).[5] According to FDA approval, it was not specifically used for ovarian stimulation in the first place. Approval was given for

1) the management of endometriosis, including pain relief and reduction of endometriotic lesions; and

2) preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata (fibroids) when used concomitantly with iron therapy. [6]

There was no specific mention of ovarian stimulation for human eggs extractions.

Should Women receive any payment for egg donation?

GCF is of the view that women who come forward should be reimbursed but not compensated.

[4] http://www.fda.gov/medwatch/SAFETY/2004/oct_PI/Lupron_PI.pdf.
[5] http://www.drugs.com/lupron.html
[6] http://www.fda.gov/cder/foi/nda/97/20708_LUPRON%20DEPOT%203-MONTH,%2011.25MG_APPROV.PDF

We appreciate the BAC for making clear in section 39 of the 3 approaches and we affirm that there should be no substantial compensation (approach c.) that amounts to outright payments.

Our suggestion is to follow from current practices from Healthcare Services Authority (HSA) at the Center for Transfusion Medicine. Previously, blood donors were compensated with medical benefits at polyclinics. However, such practice was taken away due to abuses in the system. Currently, blood donation is mostly an altruistic act. Donors are not even reimbursed and have to pay their own way to the donation centers although schools give out CCA points and military provide days off or light duties at times.

Reimbursements such as transport and food would deem acceptable. Provisions for days off in collaborations with companies are also acceptable. However, it is impossible to gauge the 'proper' level of compensation for loss of earnings. For some, such 'compensation' amounts to 'significant salary', particularly a person from the low income group. Take for example the Ethics Committee of American Society for Reproductive Medicine guideline of USD 5000 is equivalent to 3 months pay for a single mom family, particularly if she is not able to find employment.[7]

On whether foreigners should be allowed to make egg donations, **GCF is of the view that only Singaporeans and Permanent Residents should be allowed to donate and not foreigners or work pass/permit holders.**

This stems from the wide socio-economical gap between Singaporeans / PRs and foreign workers in our midst. For example, domestic helpers (maids) receive only approximately S$250 to S$350 per month for their long hours of services. 'Compensation' for S$100 as an example, is therefore very significant, though for many Singaporeans and PR may seem like a 'fair' amount.

The long term healthcare of donors is also another factor which as a caring and gracious nation which we aspire to be, need to manage the complications and side-effects of the extraction procedure. This can only be taken care of for Singaporeans and Permanent Residents. We will not be able to provide such longer term healthcare for foreigners and foreign workers. The cost of such after care will also have significant impact on taxpayers depending on the target number of donors required.

We also need to be wary of accusation by foreign governments in falsely charging Singapore in exploiting their people, particularly for Singapore who intends to be one of the leading countries for ASEAN. The costs, economically, socially and politically is great in return for the benefits of ESCR which at this point has yielded little.

[7] The portion of Americans living in poverty declined to 12.6% in 2005…about 37 million people lived in poverty in 2005. Poverty was defined as annual income of $19,971 or less for a family of four. (USA Today, 29 Aug, 2006 by Dennis Cauchon)

GRADUATES' CHRISTIAN FELLOWSHIP

Conclusion

GCF strongly proposes the BAC to consider and advice government to take a fresh look into Adult Stem Cell Research as to Embryonic Stem Cell Research. Re-direct resources for ASCR and save significant time, money and literally pain (for going through the extraction procedure) of our people. This will not only side step many ethical issues but also put our research in pace with cutting edge research and methodologies. This approach to research using reprogrammed adult stem cell will also preserve the dignity of human lives rather than prancing on the edge of an ethical cliff from which our fall will mean loss of or significant scaring of lives.

Presented by

Timothy Liu
President for 2007-2008
On Behalf of the Graduates' Christian Fellowship.

Institute of
Bioengineering and
Nanotechnology

Institute of Bioengineering and Nanotechnology
31 Biopolis Way
The Nanos, #04-01
Singapore 138669
Tel : +65 6824 7000 Fax : +65 6478 9080
www.ibn.a-star.edu.sg

25 November, 2007

Professor Lee Eng Hin
Chairman
Human Embryo and Chimera Research Working Group
Bioethics Advisory Committee

Dear Professor Lee:

I am writing in response to your letter, dated on 7 November, 2007 to Professor Jackie Ying, Executive Director of Institute of Bioengineering and Nanotechnology (IBN), inviting to comment on the consultation paper entitled "Donation of Human Eggs for Research". I am a group leader in IBN working in the area of human embryonic stem (hES) cell bioengineering and glad to be given this opportunity to share with you our thoughts as follows.

Dedicated to improving the health and quality of life, Institute of Bioengineering and Nanotechnology (IBN) focuses its research activities on the following six areas:

- Pharmaceuticals Synthesis and Nanobiotechnology
- Delivery of Drugs, Proteins, and Genes
- Cell and Tissue Engineering
- Artificial Organs and Implants
- Biological and Medical Devices
- Bioimaging and Biosensing

Although we are not directly involved in generating hES cell lines, several aspects of our on-going studies in IBN involve the use of hES cells, mainly in the areas of cell and tissue engineering, and delivery of drugs, proteins and genes.

Almost all existing hES cell lines were isolated from human embryos generated from fertilized human eggs during *in vitro* fertilization (IVF). Alternatively, somatic cell nuclear transfer (SCNT) has been proposed to produce genetically personalized hES cell lines, in which the nucleus of an unfertilized egg is replaced with the nucleus from a somatic cell. The method holds great promise both for understanding human developmental biology and disease development/progression, and for regenerative medicine with organ and tissue replacement. However, the efficiency of deriving hES cell lines in this way is estimated to be extremely low, requiring about 100 human eggs to generate a customized hES cell line for a single individual. This is why human eggs become highly sought after, which further triggers the concern in compensating egg donors.

Fortunately, advances published in the journals *Science* and *Cell* last week in the area of stem cell research have totally changed the landscape. The new method creates pluripotent human stem cells by gene delivery of 4 functional genes to reprogram human somatic cells, eliminating the use of human eggs. The advance overcomes ethical, political and practical obstacles in the generation and use of hES cells. Facing this successful breakthrough, even the British creator of the cloned sheep Dolly, Dr. Ian Wilmut, has voiced to abandon SCNT technique for cloning human cells.

With this progress, I would suggest reconsidering the issue raised in the consultation paper of "Donation of Human Eggs for Research" and placing more emphasis on issues related to the new technology. For example, gene transfer into human somatic cells to produce human stem cells will become a hot topic in stem cell research. Somatic genetic modification is also viewed as gene therapy. The related issues were discussed before by the Bioethics Advisory Committee under Human Genetics. We probably need to revisit the issues by incorporating the considerations based on the recent progress in human stem cells. In terms of the use of human stem cells, these cells have been tested for transplantation into human bodies, with some of these stem cells being genetically modified before the transplantation. While the general issues have probably been covered in the sets of recommendations for Human Genetics, the genetic manipulation of stem cells might need to be discussed separately.

Sincerely yours,

WANG Shu, PhD
Group Leader
Institute of Bioengineering and Nanotechnology

cc: Prof Jackie Y. Ying, Executive Director
Noreena AbuBakar, Director, Administration

INSTITUTE of MENTAL HEALTH

Loving Hearts, Beautiful Minds

Buangkok Green Medical Park
10 Buangkok View
Singapore 539747
Tel: (65) 6389 2000 Fax: (65) 6385 1050
www.imh.com.sg

Business Registration No. 52930996C

13 Dec 2007

Professor Lee Eng Hin
Chairman
Human Embryo and Chimera Research Working Group
Bioethics Advisory Committee
11 Biopolis Way #10-12 Helios
Singapore 138667

Dear Professor Lee

INVITATION TO COMMENT ON CONSULTATION PAPER
IMH'S COMMENTS

Thank you for inviting IMH's comments.

Our views (which are the consensus of myself, the VCMBs, and the Clinical Chiefs), in respect of paragraph 5 of the Consultation Paper on "Donation of Human Eggs For Research" are:

(a) Healthy women not undergoing fertility treatment should be allowed to donate eggs for research so long as

- all steps are taken to protect their interests and safety,
- they are mentally fit to give consent,
- informed consent is properly taken by a third party who is not involved in the research

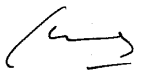
(b) Egg donors should be compensated for their time (including loss of earnings), inconvenience and risk. If individuals were sufficiently altruistic to volunteer as donors, it is fair to compensate them appropriately but not excessively so as to avoid any suggestion of inducement. Compensation should include the full costs of medical treatment incurred as a result of adverse events from the egg donation. Donors should be compensated on a standard basis that does not discriminate or favour particular groups of women. A team of appropriate professionals familiar with the research process should work out the exact formula for compensation.

(c) Sale of eggs should not be condoned while at the same time, compensation for voluntary donation should not be construed as a commercial transaction. Thus economically disadvantaged populations should not be specific targets of drives to encourage eggs donation. On the other hand, financially challenged volunteers should not be rejected on the basis of their financial status; eligible women should be afforded the opportunity to decide for themselves if they wished to donate. We acknowledge that the line between altruism and financial gain can be blurred in some situations but the onus is on the researchers not to specifically target the vulnerable population.

(d) Women without the mental capacity to make informed decisions should be excluded from voluntary donation. Consent for the donation may have to be taken by a medical practitioner in this respect. It is appropriate for the Ministry of Health to set up regulatory mechanisms with the relevant interested bodies to govern the supply and use of human eggs for research.

(e) The potential gains of such research are immense and will benefit millions of people worldwide. Mental capacity, informed consent, proper process of obtaining consent, and adequate (but not excessive) compensation are important to ensure the protection of the donors. Donations should be truly voluntary and entirely free of coercion or threat. An act of altruistic donation may help the donor fulfil a sense of humanity which is immeasurable but can improve self-esteem and actualisation.

Yours sincerely



CI A/P Wong Kim Eng
Chairman, Medical Board
Institute of Mental Health

THE LAW SOCIETY OF SINGAPORE

39 South Bridge Road
Singapore 058673
Tel: 6538 2500
Fax: 6533 5700
Email: lawsoc@lawsoc.org.sg
Website: www.lawsociety.org.sg

Pro Bono Services Office
1 Havelock Square
Level 5
Subordinate Courts Complex
Singapore 059724
Tel: 6536 0650
Fax: 6534 5237
Email: ProBonoServices@lawsoc.org.sg
Email: CLAS@lawsoc.org.sg

Our Ref: LS/87/2007 Your Ref:

7 January 2008

BY FAX AND POST
Fax No. 6478 9956
No. of Pages: 6
(including this page)

Professor Lee Eng Hin
Chairman
Human Embryo and Chimera Research Working Group
Bioethics Advisory Committee
11 Biopolis Way
#10-12 Helios
Singapore 138667

Dear Sir

INVITATION TO COMMENT ON CONSULTATION PAPER

We refer to your letter dated 7 November 2007 inviting the Law Society to provide its comments on the issues set out in the consultation paper entitled "Donation of Human Eggs for Research".

The Society appointed an ad hoc committee to review the consultation paper.

We are pleased to enclose our ad hoc committee's feedback on the matter for your consideration.

Thank you for giving the Society the opportunity to give our views on the matter.

Yours faithfully

Alvin Chen
Director
Representation and Law Reform

Enc.

4 JANUARY 2008

THE LAW SOCIETY OF SOCIETY

AD HOC COMMITTEE'S FEEDBACK ON THE BIOETHICS ADVISORY COMMITTEE'S CONSULTATION PAPER ON DONATION OF HUMAN EGGS FOR RESEARCH

THE LAW SOCIETY
OF SINGAPORE

LScommentsBAC(070108)Final

COMMENTS ON THE BIOETHICS ADVISORY COMMITTEE'S CONSULTATION PAPER ON DONATION OF HUMAN EGGS FOR RESEARCH

1. We have been appointed by the Law Society of Singapore to provide our comments on the Consultation Paper by the Bioethics Advisory Committee ("BAC") on Donation of Human Eggs for Research ("the Consultation Paper").

2. All members of this ad-hoc committee are involved in advising and representing individuals and organisations in the health care industry as part of their legal work.

3. We set out below our views on the issues raised at paragraph 5 of the Consultation Paper, in the order that they appear.

(1) Whether healthy women not undergoing fertility treatment should be allowed to donate eggs for research, and if so, under what conditions

4. It appears that the donation of eggs for research by women not undergoing fertility treatment is currently already permitted. In principle we have no objections to this being so, but are of the view that this should be subject to the following conditions:-

(1) detailed and informed consent to be obtained and documented. We would advocate that the consent be obtained by someone other than the healthy donor's doctor;

(2) there should not be any undue influence or incentives being paid to the donors;

(3) at the same time, we acknowledge that for healthy women who donate their eggs for research, in the event that they suffer injury or some harm as a result of their altruistic actions, they should have recourse to treatment without the burden of paying the medical expenses. We would propose a mandatory no fault based insurance coverage for donors which will provide for full payment of medical expenses in the event of an

immediate complication or risk materialising during the egg collection process as well as a compensation for the longer term risks that can be attributed to the egg donation. We recognise that with regards the risk of future cancer from ovarian simulation, this appears to be low (paragraph 25 of the Consultation Paper) and that there may be difficulties in establishing that the cancer(s) have been caused by egg donation related procedures. Nevertheless, we are of the view that in principle compensation for these risks should be addressed in line with the current practice for clinical trials.

(2) Whether egg donors for research should be compensated for time, inconvenience and risk, and if so, what type of compensation or monetary amount would be acceptable and not amount to an inducement

5. We recognise that in clinical trials, particularly those involving healthy subjects, subjects are sometimes paid for their time and expenses during the course of their participation in the trial. We are of the view that similarly, some compensation should be paid to healthy women who donate their eggs for research because of the time and expenses that these donors would have to expend. This may indirectly help to increase the number of eggs obtained for research but we do not feel that merely compensating these donors in a modest sum to cover their time and expenses would necessarily amount to an undue inducement to them to participate. What may be appropriate to consider is a reasonable lump sum compensation for the time and inconvenience involved in the process on a per cycle basis and this would also bring this in line with current practices for clinical trials involving healthy participants.

6. We suggest the amount paid to donors be regulated by guidelines which prescribe a limited range of payment.

7. Compensation for risks can take the form of mandatory insurance as discussed above.

(c) Whether there are circumstances in which the compensation for eggs could amount to a sale and if so whether such sale should ever be contemplated

8. Egg donation can be said to be analogous to organ donation. Just as the sale of organs is prohibited under current legislation, the sale of eggs for whatever purpose should also be prohibited.

9. If a donor obtains payment in excess of reasonable compensation for time spent and inconvenience, and stands to profit financially from the donation, the donation could foreseeably amount to a sale. This is to be guarded against.

10. It is also important for there to be no co-relation between the amount of compensation payable and the quantity or quality of eggs obtained.

(d) Any prohibitions, limits or regulatory mechanisms that should govern the supply and use of human eggs for research in Singapore

11. Limits on donor age and the number of times a donor may make a donation should be considered. This can help to ensure that the risks to donors are minimized.

12. The issue of mandatory counselling for the donor should also be considered as the donation involves both immediate side-effects and possible long term consequences which are important for the healthy donor to know and deliberate upon. Consent should not be taken by treating physicians but by independent third parties.

13. We also suggest a formal regulatory framework which applies to research institutions, researchers and private companies involved in the procurement of eggs for research, which should all be licensed under the existing legislation and guidelines which apply to centres engaged in in-vitro fertilisation for treatment. This is to prevent a situation where the ethical standards of conduct may vary depending on whether or not the institution is regulated under the Private Hospitals and Medical Clinics Act.

(e) Any other matters related to donation of human eggs for research

14. In considering mandatory insurance, the possibility of donors exploiting the scheme for the benefit of insurance coverage for cancer should be addressed.

Dated this 4th day of January 2008

مجلس اكام اسلام سيغاڤورا
Majlis Ugama Islam Singapura
(Islamic Religious Council of Singapore)

Islamic Religious Council of Singapore • 1 Lorong 6 Toa Payoh • Singapore 319376 • www.muis.gov.sg • Tel : 6359 1199 • Fax : 6253 7572

MUI OOM/31/2/12008

DID: 63591441
FAX: 62591735

11 January 2008

Professor Lee Eng Hin
Chairman
HECR Working Group
Bioethics Advisory Committee
11 Biopolis Way,
#10-12 Helios
Singapore 138667

Dear Prof Lee,

REQUEST FOR FEEDBACK ON CONSULTATION PAPER

We refer to your letter of 7 November 2007, to Haji Mohd Alami Musa, President of Muis.

2 As requested, please find the enclosed attachment for our comments on the consultation paper entitled "Donation of Human Eggs for Research".

3 We hope the comments are helpful in BAC's deliberations on the ethical aspects of the issue.

Thank you.

Yours sincerely,

Mohd Murat Mohd Aris
Director
Islamic Development
Majlis Ugama Islam Singapura

Feedback from Majlis Ugama Islam Singapura (MUIS)
BAC Consultation Paper
Donation of Human Eggs for Research

Introduction

The Majlis Ugama Islam Singapura (MUIS) has been invited to comment on the issues and recommendations contained within the Bioethics Advisory Committee's (BAC) consultation paper entitled "Donation of Human Eggs for Research". The comments are provided on the following points:

i. Donation of Eggs for Research by Healthy Women Not Undergoing Fertility Treatment

ii. Conditions and Safeguards for Donation of Eggs for Research

iii. Compensation for Donation of Eggs

I. Donation of eggs for research by healthy women not undergoing fertility treatment

2 Islam encourages research that advances the welfare of human beings and removes harm and difficulties. The Muslim legal philosopher Ibn Al-Qayyim, state that the *Syariah* (Islamic jurisprudence) is established to promote the well-being of mankind in this world and the hereafter. The enhancement of human life by way of scientific research that can lead to the prevention and treatment of diseases is also recognised as an objective of the *Syariah* and a public welfare (*maslahah*) that should be secured.

3 In the pursuit of public welfare, harm must be avoided at all costs. As such, where there is a certainty that a research will be harmful to those involved in it, such as in this case, if a woman who donates her oocyte is certain to be exposed to some form of harm, then she is not allowed to participate in it. This is in accordance with the Islamic legal maxim that states "Removal of harm takes precedence over pursuing welfare/interest (*maslahah*)". However, if both benefits and harm are probable and not certain, then the potential benefits must outweigh the potential harm, in order to warrant the pursuit of such research work.

4 In light of the vast potential in increasing scientific knowledge that can benefit mankind resulting from oocytes donation, as discussed in the Consultation Paper, and taking into account the Islamic principles above, we take the position that healthy women not undergoing fertility treatment should be allowed to donate eggs for research, under the conditions explained in the next section. It is also highly crucial that researchers involved in such research projects exercise a great deal of caution, care and rigour, in assessing whether someone is an appropriate donor, as well as to ensure that the research participants are clear about the risks involved in such donations.

II. Conditions and Safeguards for Donation of Eggs for Research

5 True informed consent and extensive counselling, with regards to the full details of the research in which donors are involved in, as well as the whole donation process, including its medical, physical and psychological aspects, should be revealed and discussed with potential donors thoroughly.

6 Research projects requiring donation and use of oocytes should be carefully and extensively evaluated by the relevant review boards and ethics committees before permission

to proceed is granted. This is to ensure, in part, that such projects do not replicate any past or existing research conducted elsewhere, nor cause any unnecessary requests for donation of oocytes, which may lead to their wastage.

7 The recruitment of nulliparous women or those who have not completed their families as oocyte donors may need careful and further consideration as there is a small risk that the medical procedures involved may cause unintended consequences or side effects, and lead to potential infertility. Thus, the potential donor needs to be fully aware of all possible consequences in the event that she decides to proceed with the donation.

8 The medical risks involved in donation of oocytes should be minimised as much as possible. These may include the following suggested steps:

a) Individualized medication regimens and close monitoring of research donors are absolutely necessary so as to reduce the probability of the occurrence of ovarian hyperstimulation syndrome (OHSS). Ovulation induction regimens should be adjusted according to a donor's response to previous ovarian stimulation cycles. If the potential donor has previously experienced OHSS, it is highly likely that she will react in the same way in subsequent stimulation cycles. Such potential donor should be rejected as donor, or can receive a safer level of stimulation.

b) Researchers must opt to exclude certain potential donors altogether if they present high-risk factors such as young age and presence of polycystic ovaries. After all, these donors receive no direct benefit following their donation and the eggs can be obtained from different donors without any major drawbacks.

c) There should be a general trend towards moderation in ovulation induction regimens to decrease the probability of the occurrence of OHSS. It is best to avoid regimens that lead to overstimulation so as to obtain as many eggs as possible. A well-informed research donor will definitely not want to put herself under the same health risks as an IVF patient since they do not benefit from a maximal number of retrieved eggs. If moderate regimens still lead to strong response in potential donors, the procedure should be abandoned immediately. Careful monitoring is therefore essential to ensure that the procedure is adjusted or cancelled whenever necessary.

d) Potential donors should also be informed of the risks associated with long term effects on the use of drugs relating to ovarian simulation and egg retrieval. Long term follow-up is necessary to assess any possible dangers. There is also the possibility of cancer development in research donors who reach the age at which hormonally related cancers are common. As data on more recent treatment methods become available for such hormonally related cancers, further research is certainly advised especially those studies focusing on fertile egg donors. This is because infertility may itself be a factor influencing cancer susceptibility that is difficult to correct in research that are based on IVF treatments. Data on adverse effects of the procedure is preferably collected and analyzed by independent physicians. It is also advisable to avoid repeated donations by the same woman as long term effects of drug usage in these procedures are unclear and it is better to err on the safe side.

e) Follow-up care is very important. Research donors should be entitled to free medical treatment for injuries resulting from research participation and

should be compensated for any resulting impairment, disability or handicap. This is an important issue because their personal health insurance may not want to cover medical expenses resulting from a procedure that was carried out without medical indications or necessity. Thus, research centers should guarantee free follow-up care for their research donors such as ensuring generous insurance coverage.

III. Compensation for Donation of Eggs

9 Islam does not allow for the commodification of the human body, or parts of it, as the Islamic theology teaches that the human body belongs to God. Oocytes fall under this category. However, Islam allows for the compensation of an individual for a work accomplished, or a contribution offered. Compensation or reimbursement for oocyte donation should be carried out to not only redress the burdens and inconveniences suffered by donors, but also to acknowledge their contributions. This is especially fair since the commercial potential of stem cell research is expected to be vast, but like all research subjects, oocyte donors have no ownership rights, nor are they considered stakeholders in any resulting technology and so will not share its financial or other benefits.

10 However, the shape of manner such compensation or reimbursement takes will need to be cautiously drawn so as not to represent unjustified financial inducement or undue psychological pressure. This will also help to prevent the exploitation of low-income women who may otherwise be inclined to become donors for monetary gains.

Co. Reg No. ROS 146/51/REL

National Council of Churches of Singapore
新加坡基督教會協會
சிங்கப்பூர் திருச்சபைகளின் தேசிய மன்றம்

3 January 2008

Professor Lee Eng Hin
Chairman
Human Embryo and Chimera Research Working Group
Bioethics Advisory Committee
11 Biopolis Way
#10-12 Helios
Singapore 138667

Dear Prof Lee

Donation of Human Eggs for Research

Thank you for seeking feedback from the National Council of Churches of Singapore on the above subject.

We enclose herewith our response to the Consultation Paper on "Donation of Human Eggs for Research."

We trust that this feedback will receive careful and serious consideration.

Thank you.

Yours sincerely

Bishop Dr Robert Solomon
President
National Council of Churches

B1-27 The Adelphi,
1 Coleman Street,
Singapore 179803
Tel: 6336 8177 Fax: 6336 8178
Email: admin@nccs.org.sg
Website: www.nccs.org.sg

"Many members... One Body... with Christ." 1 Cor 12:12

Response to the Bioethics Advisory Committee's Consultation Paper entitled, *Donation of Human Eggs for Research*

Presented by the National Council of Churches of Singapore

The National Council of Churches of Singapore (NCCS) is grateful to the Bioethics Advisory Committee (BAC) for the opportunity to respond to the consultation entitled, *Donation of Human Eggs For Research*. It is encouraged by and welcomes the BAC's attempt to promote public discussion and consultation on this important issue. In this response, the NCCS wishes to address the two fundamental issues presented by the paper, namely, (1) should women be allowed to donate their eggs for research? and (2) should there be payment for donating eggs for research?

DONATION OF HUMAN EGGS FOR RESEARCH

Although the focus of this consultation paper is egg donation and the welfare of donors and not the ethical implications of the research itself, the NCCS must reiterate its position on embryonic stem cell research (ESCR). This is because the view taken by the NCCS regarding such research has direct bearing on its position regarding egg donation.

The NCCS maintains that ESCR, which involves the destruction of human embryos, should be prohibited. This is because human life begins at conception, and the human embryo, regardless of its age, is worthy of the respect and dignity accorded to all human beings. The NCCS therefore rejects the distinction between embryo and pre-embryo as academic and arbitrary because it fails to take seriously the ontological status of the being in question. In similar vein, the NCCS rejects the distinction between therapeutic and reproductive cloning because the cloning process is the same in both 'types'. The only difference is the intended use of the manufactured embryo. For the same reasons, the NCCS maintains that the creation of human embryos through parthenogenesis should be prohibited. Although some ethicists have argued that this method of manufacturing embryos poses less ethical problems because the parthenote is not considered a human person, the NCCS finds this line of argument untenable.[1] The primary reason as to why procuring eggs from women for the manufacturing of embryos for research should be prohibited is that such research results in the destruction of human beings.

There are other reasons why women should not donate their eggs for research. The procedure that is currently employed to obtain eggs from donors involves considerable risks. Some of these risks are discussed on page 9 of the consultation paper. One of the main health risks associated with egg donation is that donors may develop a condition called ovarian hyper stimulation syndrome (OHSS). While according to the paper, 'the risk of egg retrieval is relatively low', it does continue to be a serious problem for specialists working in the field of infertility. As Annick Delvigne and Serge Rosenberg have pointed out, 'as this is an iatrogenic complication of a non-vital treatment with a potentially fatal outcome, the syndrome remains a serious problem for specialist dealing

[1] Presently the human parthenogenic embryo is unable to complete gestation unless it is combined with normal trophoblast cells, the outer ring of cells in an early embryo that ultimately form the placenta. But the gestational incompetence of the parthenote due to lack of the paternal 'imprinting' of genes should not lead us to conclude that it is therefore a 'lesser human' or 'not human at all'. The NCCS maintains that the parthenote who contains the full human DNA complement but is unable to complete gestation must be viewed as a human being, albeit one with serious genetic flaws. The NCCS opposes the parthenogenic creation of human embryos for the purpose of experimentation and research. It maintains that parthenogenic embryos already created must be given the same respect that is due to an incapacitated person or a person with serious genetic flaws.

with infertility'.[2] The former Chief Medical Officer at the Food and Drug Administration (FDA), Dr Suzanne Parisan, describes other risks associated with OHSS:

> OHSS carried an increased risk of clotting disorders, kidney damage, and ovarian twisting. Ovarian stimulation in general has been associated with serious life threatening pulmonary conditions in FDA trials including thromboembolic events, pulmonary embolism, pulmonary infarction, cerebral vascular accident (stroke) and arterial occlusion with loss of limb or death.[3]

The common drug used on egg donors is Lupron™ (leuprolide acetate). A range of side effects associated with this drug has been reported to the FDA.[4] This is not mentioned in the consultation paper, but such information is important for a closer assessment of the risks of egg donation. Such information is also vital for healthy women who are considering donating their eggs for research. The hormones used to stimulate ovaries to produce eggs such as gonadotropins, human chorionic gonadotropin therapy and gonadotrophin-releasing hormone (GnRH) agonists are known to produce adverse side effects ranging from headaches to organ damage.

Alongside these risks human embryonic stem cells have enjoyed little success in clinical trials. Even in animal models of disease they not only have a lacklustre success but have also in fact carried significant risks including immune rejection and tumour formation. Thus in its December 2006 response to the British Human Fertilisation and Embryology Authority's (HFEA) consultation paper on 'Donating Eggs for Research: Safeguarding Donors', the Scottish Council of Human Bioethics states that '[T]he potential value of research on embryo is over-stated. Although the reasons given to justify embryo research are usually that it will lead to cures of various serious disorders, any benefits are, at best, likely to be in the distant future and there are grave doubts that "cures" will ever be realised using these techniques'.[5]

Principle 16 of the Declaration of Helsinki states that 'Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others'. Although it is not always easy to compute the risk-benefit ratio, it may be argued that in this case the ratio is not favourable. The NCCS therefore maintains that a woman should not be subjected to such a risky procedure that has no benefit to her and very doubtful benefit to others.

Additionally and importantly, it must be pointed out that while the potential outcomes of research on human embryonic stem cells have been overstated, those of adult stem cells have been grossly understated. It is important to note that adult stem cells, which include stem cells taken from umbilical cords, have already been used successfully in human therapies for years, including the treatment of spinal cord injury, leukaemia, and Krabble's Leukodystrophy. To date, however, no therapies in humans using embryonic stem cells have been successfully carried out.

---

[2] 'Epidemiology and Prevention of Ovarian Hyperstimulation Syndrome (OHSS): A Review', *Humans Reproduction Update*, Volume 8, no. 6, 2002, pp. 559-577.

[3] www.ourbodiesourselves.org.

[4] They include rash, vasodilation(dilation of blood vessels causing a 'hot flash'), paresthesia (sensation of burning), tingling, pruritis, headache and migraine, dizziness, urticaria (hives), alopecia (hair loss), arthralgia (severe joint pain, not inflammatory in character), dyspnea (difficulty breathing), chest pain, nausea, depression, emotional instability, loss of libido (sex drive), amblyopia (dimness of vision), syncope (fainting), asthenia (weakness), asthenia fravis hypohyseogenea (severe weakness due to loss of pituitary function), amnesia (disturbance in memory), hypertension (high arterial blood pressure), tachycardia (rapid beating of the heart) muscular pain, bone pain, nausea / vomiting. Asthma, abdominal pain, insomnia, swelling of hands, general edema, chronic enlargement of the thyroid, liver function abnormality, vision abnormality, anxiety, myasthenia (muscle weakness), and vertigo. See http://www.fda.gov/medwatch/SAFETY/2004/oct_PI/Lupron_PI.pdf.

[5] http://www.schb.org.uk/

PAYMENT FOR HUMAN EGG DONATION

The position of the NCCS regarding egg donation for research has, in a sense, made the question concerning payment for egg donation less relevant. However, because the question of financial incentives for donors is not only restricted to women who donate their eggs, the NCCS would like to state that it categorically opposes any inducement of or payment to tissue and organ donors. The NCCS therefore fully agrees with the statement of the 1998 HFEA consultation on the *Implementation of Withdrawal of Payments to Donors* which maintains: 'In order to ensure beyond doubt that donors were not motivated by financial gain, it would be necessary to abolish all payments and benefits (other than necessary expenses)'.[6]

At the outset it must be pointed out that the term 'commercial egg donation' is an oxymoron. As Thomas Murray has argued, 'Despite the repeated reference to "donors" of both ovum and sperm, paying individuals for their biological products makes them vendors, not donors'.[7] While critics may be right to point out that gametes are not strictly speaking the 'product' of donors and receiving payment for them therefore do not make them vendors, there can be no side-stepping the issue that such a practice would result in the commodification and commercialisation of tissues and body parts. The buying and selling of human tissues would lead to the increased objectification of the human body, where the concept of the 'body-as-self' is replaced with the 'body-as-property'. This shift in perspective, which Murray tries to point out with his metaphor of the vendor, will no doubt encourage people to view individual humans as saleable commodities and this would surely compromise and degrade human dignity.

How we perceive the body is profoundly important because it will influence the policies that we put in place in securing important and valued body tissues. In recent history, the human body is not simply a subject of observation and study, but an object of manipulation. Biomedical science and technology has in the past quarter century found many revolutionary lifesaving potentials of the body in medicine as new life is created through reproductive technologies, and lives are sustained through organ and tissue transplant. In addition, biomedical science also seeks to preserve life through research on tissues and cells. The image of the body as property has become more prominent now more than ever before. But there is a need to ask whether it is appropriate to see the human body through the conceptual lens of 'property', and examine what radical changes are introduced to our sense of self-identity when this paradigm is embraced uncritically.

Yet, there is widespread if often inarticulate unease in society about the very idea of offering parts of the human body for sale at the right price. The sense of repugnance, which is firmly rooted in our collective psyche and moral sensibility, must not be taken lightly. This is because it reveals a resistance to the view that the human body is just a natural object that can be used at our disposal. We realise the need to increase the supply of organs for life-saving transplantations, and we know that doing so exacts a cost. By insisting that organs must be given freely and must not be bought and sold we are finding a way to live with this cost. We know that by allowing organs to be bought and sold we could possibly increase their supply and save many more lives. But we have resisted this approach because we know that by doing this we would make the body or parts of the body simply natural objects, at our disposal if the price is right. There is, of course, nothing degrading about buying and selling, and there is a sense in which commerce can enhance human life. But life itself must never be viewed as a commodity. Our sense of repugnance is therefore rooted in the belief that some things are simply not for sale. In our society, we recognise that public offices and criminal justice may never be bought or sold. To this list we must include the human body.

---

[6] *The Regulation of Donor-Assisted Conception*. HFEA, 2003, paragraph 8.
[7] Thomas Murray, 'New Reproductive Technologies and the Family', *New Ways of Making Babies: The Case of Egg Donation*, C.B. Cohen (ed.) (Bloomington and Indianapolis: Indiana University Press, 1996), 51-69.

The NCCS therefore supports the position expressed in para 48 of the consultation paper that the donation of tissues 'should be outright gifts and there should be no financial incentives, although reasonable reimbursement of expenses incurred should be allowed'. The NCCS is therefore in broad agreement with the principles delineated in para 48 of the consultation paper (and other documents such as *Human Tissue Research* and Section 13 of the Human Cloning and Other Prohibition Practises Act [Cap 131B, 2005 Rev Ed]). The NCCS therefore recommends that this policy be retained because it is founded on sound ethical principles. These principles are articulated in other major guidelines, particularly those issued by the European Union and the Council of Europe, for example the *Additional Protocol to the European Convention on Human Rights and Biomedicine Concerning Transplantation or Organs and Tissues of Human Origin* (ETS No. 186), [8] alluded to in the consultation paper.

Terms like 'compensation' and 'payment' commonly used in such documents are often ambiguous and fluid and must be therefore carefully defined. The compensations or payments that a donor might receive must be such that they can never be perceived as financial incentives to donate. These payments must only serve to compensate for loss of earnings or other justifiable expenses so that the donor will not suffer from any financial disadvantage due to the donation. Any form of payment that exceeds reasonable compensation must be deemed unethical. In similar vein, any benefits in kind such as reduction of fertility treatment costs for donors would be unethical. The NCCS therefore does not support 'egg sharing' in which a woman undergoing fertility treatment is induced either by reduced fees or a shorter waiting time to donate her excess eggs for research. Such a practice would tantamount to the commercialisation of human bodily parts by obtaining financial gains or comparable advantages.

[8] Para 1 of Article 21:

> The human body and its parts shall not, as such, give rise to financial gain or comparable advantage.
>
> The aforementioned provision shall not prevent payments which do not constitute a financial gain or a comparable advantage, in particular:
>
> - Compensation of living donors for loss of earnings and any other justifiable expenses caused by the removal or by the related medical examinations;
> - Payment of a justifiable fee for legitimate medical or related technical services rendered in connection with transplantation;
> - Compensation in case of undue damage resulting from the removal of organs or tissues from living persons.

National
Dental Centre
SingHealth

Tel: (65) 6324 8910
Fax: (65) 6324 8810
National Dental Centre
5 Second Hospital Avenue
Singapore 168938
www.ndc.com.sg

Reg No 199505641 M

4 January 2008

Professor Lee Eng Hin
Chairman, HECR Working Group
Bioethics Advisory Committee
11 Biopolis Way
#10-12 Helios
Singapore 138667

Dear Professor Lee

FEEDBACK ON CONSULTATION PAPER "DONATION OF HUMAN EGGS FOR RESEARCH"

I refer to your letter to Dr Yuen Kwong Wing, Clinical Advisor, National Dental Centre, requesting for feedback on the above consultation paper. I have been tasked to provide my comments.

Guidelines on donation of human eggs for research are timely and will be much appreciated by all involved in such research. National Dental Centre acknowledges the great effort put forth by the Bioethics Advisory Committee in consolidating the paper.

My comments in relation to the questions raised on Pg. 5 of the paper are as follows:

a) **Whether healthy women not undergoing fertility treatment should be allowed to donate eggs for research, and if so under what conditions.**

Healthy women not undergoing fertility treatment should be allowed to donate eggs for research if the process is voluntary, the subject understands clearly there are some risks involved in the procurement of the eggs and that she will derive zero benefit from the exercise. The selection of potential egg donors should be stringent, and subjects at greater risks for Ovarian Hyperstimulation Syndrome (OHSS), etc should be excluded. To avoid the possibility of foreigners from less privileged financial circumstances from being induced to participate in the donation of eggs for research, foreigners should be disallowed to make egg donations in Singapore. Permanent residents may be excluded from this caveat. Frequent monitor by an appointed panel should be carried out on the consent taking for the eggs donation.

b) **Whether egg donors for research should be compensated for time, inconvenience and risk, and if so, what type of compensation or monetary amount would be acceptable, and not amount to an inducement.**

I am not adverse to compensated "egg sharing" provided that the cost of undergoing fertility treatment by these donors may be offset partially but not excessively in return for the donated eggs for research.

Egg donors for research should be reimbursed for all expenses incurred in the procurement of the eggs. They could be reasonably compensated for their time, discomfort and inconvenience out of goodwill. Compensation should not be given for associated risk involved in the process. This is because the potential donor has been fully made aware of these risks. Nor should compensation be given for loss of earnings. Compensation given for "involved risks" or "loss of earnings", even if capped, will raise some concern of element of commercialism. But should the egg donor require medical care as a result of complication of the egg procurement process, there should be a provision to pay for the medical costs incurred.

c) **Whether there are circumstances in which the compensation for eggs could amount to a sale and if so whether such a sale should ever be contemplated.**

Any compensation given to egg donors should not be excessive which may then amount to an inducement. An Ethics Committee or an IRB that reviews the study can keep the amount of compensation in check. Sale of eggs should be strictly prohibited, and laws/regulations governing this should be highly deterrent.

d) **Any prohibitions, limits or regulatory mechanisms that should govern the supply and use of human eggs for research in Singapore.**

There are usually check processes eg. by IRB, MOH, in the procurement of donated eggs for research. For laboratory research involving eggs that had been collected and banked, is the use of these eggs subject to the scrutiny of a committee/panel (equivalent to that of the SingHealth Tissue Repository Committee) that oversees the release of banked eggs to investigators upon application? If not currently in place, this should be looked into and guidelines be set up.

The use of human eggs to clone humans should not be allowed and to avoid this, any laboratory process that can potentially create an embryo capable of developing into a human baby should be disallowed. While it may be argued that the research will stop at derivation of stem cells from created embryos, the temptation to go further to create human clones will always be present.

The above are my personal views. I have further included the comments of my IRB members. They are as follows:

View 1

I agree with the comments put forth by Dr Teh. Apart from Singaporeans and permanent residents, foreigners should not be allowed to donate. As mentioned, there's possibility of foreigners who would donate for the sake of rewards. The acts of altruism are good but

realistically how many participants of research studies do it for altruistic purposes? Monetary compensation should commensurate with the level of risks involved and be regulated by the IRB.

View 2

All women should be allowed to exercise their option to donate their eggs if they choose to even if they are not on fertility programme. This choice should be applied to everyone - citizens, permanent residents and foreigners who wish to donate their eggs in Singapore. They have to be adults of sound mind and know of all possible risks and harm to themselves before they make the decision.

Donations are gifts made through acts of altruism. Altruism is rendering help with no thoughts of reward, capitalistic returns or compensations, so it is unwise to pay donors for transport, loss in earnings and the like - this way, there are no risks or perceptions of inducements or barter.

Costs of egg-harvesting and medical treatment to manage complications are necessary project-running expenditure and should be borne by research sponsors or funding agencies.

There should be oversight and regulation of such research so that there will be no misuse of human embryos, cloning or reproduction of a genetically modified child.

View 3

I have carefully considered this issue and spoken to other lawyers in my team on this issue. I agree with the position as expressed in View 2, but wish to emphasize that this whole exercise must be very strictly regulated and supervised to prevent the creation of abominable life forms e.g. crossing humans with animals comes to mind.

View 4

Foreigners should be allowed to donate their eggs. But if the race / nationality needs to be revealed, then confidentiality issues may arise.

Due to the difficulty to clearly demarcate compensation from inducement, I support the position in View 2- that no compensation is allowed. However, all the medical costs arising from complications involved in the procurement of eggs should be borne by the research institution / sponsor.

View 5

All women (after being informed of the possible risks) should be allowed to donate their eggs for research purposes. They should be reimbursed for their transport expense, compensated for their time, inconveniences and discomfort.

Donation of eggs for research is for the advancement of science, therefore foreigners can also donate their eggs in Singapore. But there is a high possibility of foreigners being induced to participate. Hence, there should be some restrictions on their participation e.g. they can donate once only.

View 6

a) Healthy individuals should be allowed to donate. Selection of donors should be stringent.
b) I agree to the views of Dr Teh with regard to compensation for donor subjects.
c) No to sale of eggs and human cloning experimentation.
d) Checks should be done in accordance to regulatory mechanisms by Ministry of Health and IRB.

View 7

Foreigners should be allowed to donate their eggs in Singapore, as long as they are residents.

Compensation should be looked at and not totally cut out. Donor subjects should be treated like subjects in other drug trials or product trials where they do receive some form of compensation or free treatment. In those trials - they are not considered inducements.

I hope the above feedback is useful to you.

Yours Sincerely

Dr Teh Luan Yook
Chairman, Institutional Review Board,
National Dental Centre

Cc. Dr Yuen Kwong Wing, Clinical Advisor, National Dental Centre
Dr Kwa Chong Teck, Executive Director, National Dental Centre

MINISTRY OF HEALTH
SINGAPORE

MH 24:63/1-26

20 Feb 2008

Professor Lee Eng Hin
Chairman
Human Embryo and Chimera Research Working Group
Bioethics Advisory Committee
11 Biopolis Way #10-12 Helios
Singapore 138667

Dear Prof Lee

INVITATION TO COMMENT ON CONSULTATION PAPER

Thank you for your letter, dated 7 Nov 07, inviting the National Medical Ethics Committee (NMEC) to comment on the issues set out in the Bioethics Advisory Committee (BAC) consultation paper entitled "Donation of Human Eggs for Research".

2 In an earlier reply, dated 31 Dec 07, the NMEC expressed its regrets for not having been able to provide its comments on the consultation paper by 7 Jan 08 as requested. Thank you for your kind understanding.

3 The NMEC has since discussed the consultation paper. The NMEC's comments are at Annex A.

4 The NMEC is grateful for the opportunity to provide its comments on the consultation paper.

Thank you.

Yours sincerely,

DR LEE SUAN YEW
CHAIRMAN
NATIONAL MEDICAL ETHICS COMMITTEE

Ministry of Health, Singapore
College of Medicine Building
16 College Road
Singapore 169854
TEL (65) 6325 9220
FAX (65) 6224 1677
WEB www.moh.gov.sg

Annex A

NMEC'S COMMENTS ON BAC'S CONSULTATION PAPER: DONATION OF HUMAN EGGS FOR RESEARCH

(a) Whether healthy women not undergoing fertility treatment should be allowed to donate eggs for research, and if so under what conditions.

The NMEC has no objections to allowing healthy women not undergoing fertility treatment to donate eggs for research, on the proviso that certain conditions are fulfilled.

Women undergoing assisted reproductive technologies should not be egg donors as such individuals may feel unduly obliged to comply with the requests from attending medical and scientific personnel who might face competing interests in obtaining best quality eggs.

2 There should be a minimum donor age to protect younger women who may not fully appreciate the long-term sequelae of the procedure at the point of donation, which may include unknown irreversible effects on reproductive capacity. There should be an upper limit on donor age, and the number of times a donor may undergo egg donation, established on the basis of medical risks of the procedure to the donor.

3 The actual and potential risks of the procedure, including any correlation with increasing donor age, should be adequately addressed in the informed consent process.

(b) Whether egg donors for research should be compensated for time, inconvenience and risk, and if so, what type of compensation or monetary amount would be acceptable, and not amount to an inducement.

4 The NMEC notes the BAC's earlier recommendation in its Report on Human Tissue Research that "donors should not be paid any financial incentives for the donation, although they may be given reasonable reimbursement of any expenses incurred in the donation for the sample".

5 The NMEC acknowledges that some may argue that reasonable compensation for egg donors for time and risks could be acceptable, as it has been offered for subjects of clinical trials. However, the NMEC also notes that, if any compensation for time, inconvenience and risk, were to be allowed, it would be difficult to determine the amount of compensation that would be reasonable and which would not amount to an inducement, as benchmarks vary with the perspective taken. Some members feel that compensation should not be provided at all, as this could be the start of a slippery slope for the commercialization of eggs.

6 If compensation were to be allowed at all, a predetermined fixed fee should be paid to all donors. The less preferred alternative would be to fix a limit to the maximum amount allowed for compensation to avoid exploitation of the poor. Any compensation could also be paid to the donor's Medisave, or prevailing health

insurance policy. Neither donor nor the professionals involved in the harvesting of the donor oocytes should gain, or be seen to gain financially from the procedure.

7 Any system of payment should be made transparent, uniform and limited. Guidance could be taken from international stands on acceptable payment practices.

(c) Whether there are circumstances in which the compensation for eggs could amount to a sale and if so whether such a sale should ever be contemplated.

8 Compensation could amount to a sale if compensated procurement of eggs were conducted by private companies set up for the sole purpose of collecting eggs for research, whether within or outside regulated fertility treatment centres.

9 Such a sale of eggs should not be allowed under any circumstances.

(d) Any prohibitions, limits or regulatory mechanisms that should govern the supply and use of human eggs for research in Singapore.

10 The NMEC takes the stand that any procurement of eggs should be restricted to regulated fertility centres or other healthcare establishments with access to tertiary care facilities, and performed by the appropriate registered specialist.

11 All procurement of eggs for research should also be undertaken as part of a research protocol, subject to ethics review and approval by an institutional review board. No blanket approval should be given for the procurement of eggs for "research purposes" not directly linked to a specific research protocol. The procurer should be part of the research team, so that responsibilities may be imposed on both the procurer and the researchers.

12 There should be guidelines on the storage of eggs. In addition, there should not be any importation or exportation of eggs.

(e) ***Any other matters related to the donation of human eggs for research.***

Insurance coverage for complications

13 The NMEC opines that adequate medical insurance cover should be bought on behalf of donors, to provide adequate compensation for short-term and long-term medical complications. As the main beneficiaries of the egg donation, the research team should be responsible for providing the insurance.

Advertising for eggs

14 Advertising for egg donors should be regulated. IRBs could determine the acceptability of advertising as a means of recruitment, as part of the ethics review of the research protocol.

Definition of "egg"

15 As the term "egg" could refer to various stages of maturation of the gamete, there could be a clarification as to which stage of the egg was referred to for the donation.

Risk for ovarian hyperstimulation syndrome

16 It could be more accurate to state, in paragraph 24 of the consultation paper, that ovarian hyperstimulation syndrome (OHSS) could be "avoided", rather than "prevented", by careful selection of donors. Women could also donate eggs without undergoing ovarian stimulation, in which case, the risk for ovarian hyperstimulation would be markedly reduced.

NOEL LEONG FERTILITY & IVF
Healthcare from the Heart

Dr Noel K Y Leong
MBBS, M.MED (O&G), FRCOG, FAMS
Reproductive Endocrinology & Infertility
Obstetrics & Gynaecology
Advisor & Senior Consultant
Thomson Fertility Centre

10 January 2008

Professor Lee Eng Hin
Chairman
Human Embryo and Chimera Research Working Group
Bioethics Advisory Committee
11 Biopolis Way
#10-12 Helios
Singapore 138667

Dear Professor Lee

DONATION OF HUMAN EGGS FOR RESEARCH

I apologise for my delayed response and comments. I have missed out the deadline but I hope it is not too late. My comments are :

(1) The consent forms should state clearly that the eggs are to be used for research purposes only and will not be used for reproduction and fertility treatment for other women.

(2) The risk of severe ovarian hyperstimulation syndrome (OHSS) and the potential development of ascites, hydrothorax, renal failure, deep vein thrombosis with slight risk of pulmonary embolism should be included in the consent form.

(3) As egg donation is an invasive procedure requiring a few weeks of treatment, I am in favour of monetary compensation (subject to a maximum amount), for time, risks, inconvenience and loss of income.

Thank you for inviting me to comment on the consultation paper.

Dr Noel Leong

Noel Leong Fertility & IVF Clinic Pte Ltd
#06-05 Thomson Medical Centre 339 Thomson Road Singapore 307677
Tel : (65) 6255 6883 Fax: (65) 6255 6889 Email: noel@noelleong.com
Website: www.noelleong.com / www.ivf.com.sg
Company Reg. No.: 200103493R

Comments from Singapore Eye Research Institute IRB

6 March 2008

1) It is important that the Religious Bodies be consulted on this matter. We assume that BAC will have a dialogue with the various religious leaders.

2) BAC's present position is stated in the "BAC Report on Human Tissue Research":"Donation of Tissues (which includes eggs) should be outright gifts and there should be no financial incentives, although reasonable reimbursement of expenses incurred should be allowed".

   Is BAC thinking of changing this?

3) Is donation of an egg so different from donation of an organ, say a kidney? Both procedures are just as perilous, and the donor may die. Therefore no inducement (other than reimbursement of expenses) should be given.

4) You may argue that donation of a kidney is to save a life, but donation of an egg is for research work. So the donor of an egg will need more motivation to donate. But is donation of an egg for research work so different from volunteering for a Phase I (1st in man) study? In both cases the volunteers are healthy subjects and exposing themselves to serious risks. As in phase 1 studies, there should be no inducements (other than reimbursement of expenses), because of the risks involved.

   (In a Phase 1 study in UK recently (the TGN 1412 Trial); all six healthy volunteers became critically ill. One of the criticisms of the study was that the volunteers were unduly encouraged to participate as they were paid £3,000 each.)

5) There should be no soliciting for donors through advertising in the mass media. If advertising is done, there should be no mention of money. The problems with advertisements are:
   i) Risks of the procedures are downplayed.
   ii) The sale of tissues / body parts will be encouraged.
   iii) Undue encouragement to participate.

6) As the donation of eggs is for research, the process should be reviewed by a Research Ethics Committee (IRB / DSRB), which will ensure that there is informed consent and compensation.

Dr Khoo Chong Yew
Chairman
Singapore Eye Research Institute IRB

SINGAPORE NURSING BOARD

3 January 2008

Professor Lee Eng Hin
Chairman
Human Embryo
& Chimera Research Working Group
Bioethics Advisory Committee
11 Biopolis Way
#10-12 Helios
Singapore 138667

Dear Prof Lee

INVITATION TO COMMENT ON CONSULTATION PAPER

Thank you for inviting the Singapore Nursing Board to comment on the consultation paper on Donation of Human Eggs for Research.

The following are our comments on the two most relevant purposes.

(a) We are of the view that obtaining human eggs for research should be confined to women who are undergoing fertility treatment. The procedure is invasive and poses possible risks and adverse effects on the health and safety of healthy women.

(b) Women who donate eggs should be given monetary compensation for the time and expenses incurred provided that control measures are in place. The compensation amount or type should be periodically monitored and reviewed by an independent panel.

We would like to commend the Human Embryo and Chimera Research Working Group for a thorough and comprehensive coverage of the underlying issues.

Yours sincerely

MRS NELLIE TANG
CHAIRMAN
SINGAPORE NURSING BOARD

16, College Road, #01-01 College of Medicine Building, Singapore 169854 Tel: 6372 3082/3 Fax: 6221 1160
Website: http://www.snb.gov.sg

Comments from Mr Fahan Ali

Farhan Ali [farnali@yahoo.com.sg]

15 January 2008

Consultation Paper on Donation of Human Eggs for Research – An Individual Feedback

I refer to the above.

I am providing feedback as a private individual interested in the ethics of biomedical research. I divide my feedback below into three areas: the general ethics and impact of human egg donation, issues concerning donation of excess eggs, and issues concerning donation by healthy women. In addition to general ethical concerns, I also bring up issues that BAC may want to consider, while the rest of the points invite clarification from BAC in future reports. I hope my feedback would be useful for BAC in drafting the guidelines to govern the donation of human eggs for research.

The general ethics and impact of human egg donation

The consultation paper cites ESHRE's stance that "the general principles of research ethics on the subject of compensation should apply to egg donation for research (para 44). An argument can be made that egg donation, especially by healthy women, is a case qualitatively different from normal clinical trials. First, healthy women who donate eggs are at double-risk; not only are their general somatic health at risk as is the case in typical clinical trials, but their reproductive systems are being unnaturally disturbed, bringing in further future risks dealing with reproduction and germlines (e.g., risk of uterine and ovarian cancer). Second, egg donation can only be done by women, who are "minorities" and are less powerful in many contexts (e.g., economically less well-off, under influence of more powerful agents like husbands, etc). This situation may present special problems dealing with issues of lack of informed consent. Third, unlike some clinical trials, egg donation involves contributing cells capable of germline reproduction that may carry risks of subsequent illegal use. Although other cells donated (e.g, blood) may also suffer from such risks, illegal use of germline cells may pose even more serious future implications (e.g., illegal reproductive use). Given the above concerns, I hope BAC can apply judiciously the principle of fair compensation to balance such risks that go beyond those of normal clinical trials.

Also, are the ethical concerns and the health risks worthwhile given that the BAC itself admits that donations by healthy women are unlikely to be substantial enough to help alleviate the lack of eggs for research (para 51)? Moreover, as it is now, Singaporeans are quite reluctant in donating tissues, participating in clinical trials, and giving away

information[1]. Lack of egg donation may be reflective of a more general trend of reluctance in Singapore society that needs to be addressed beyond the current consultation process. However, in keeping with the current issue, BAC can perhaps clarify the impact of the 2002 "Human Tissue Research" guidelines on donations, specifically highlighting how many cases of healthy volunteers donating eggs exist heretofore in Singapore and if new guidelines providing a wider definition of payment can increase participation.

Donation of excess eggs

I would like to expand further the issue of consent sought by an independent person of women undergoing fertility treatment to donate excess eggs. The current practice is for someone other than the medical doctor tasked with the clinical care of the woman in a fertility clinic to ask for consent to harvest excess eggs for research. However, the medical sector in Singapore is changing rapidly with lines between clinical care and research being blurred[2]. Hospitals are increasingly becoming the place for basic research with medical doctors being scientific researchers too. In cases such as these, although the person asking for consent (e.g, another doctor in the hospital) may be considered independent enough, the institution where the fertility clinic resides may have a vested interest in seeking a consent (e.g, more eggs in the hospital for medical research in the hospital). It is recognised that a typical IRB would already consists of a layman not related to the institution or the healthcare group altogether. But it is still imperative that in donation of excess eggs, this importance of independence is properly enforced not just internally in the IRB but also in the eyes of the women concerned. Otherwise, these women may feel pressured to agree to donate excess eggs and place themselves under more risk.

Donation of eggs by healthy women

I would like to draw the BAC's attention to three issues surrounding donation of eggs by healthy women. First, there is the issue of egg donation by healthy women who are affiliated with the research institution. This issue is particularly important given recent reports of female staff in the laboratory of Dr Hwang, the disgraced South Korean stem cell researcher, donating eggs for their own research, possibly under pressure from the senior doctors as precondition for promotion. Can such women be allowed to donate? One could argue that it is hard to believe that the donation would be altruistic since they have a stake in the research or that they might have been under pressure to donate. Yet, it is still possible that these women donate out of a genuine sense of belief in the importance of research for humankind, a cornerstone of volunteering for clinical trials. Does BAC have special provisions for cases like these?

---

1 See recent reports in the Straits Times in the past few years on the lack of twin volunteers coming forward as well as the Shorvon controversy which was caused by a principal investigator too eager to conduct the research when there were not enough patient volunteers. The recent BAC guidelines "The Use of Personal Information in Biomedical Research" were aimed at addressing this problem of access to patient data and in making the case for the importance of use of personal information for medical advances.

2 For example, very recently, the National University of Singapore Medical School and National University Hospital were merged under one management, to allow greater synergies between clinical care and research, but also complicating further issues of care vs. research.

There is the second issue of medical subsidies being extended to healthy women donors. Some guidelines in other countries extend medical subsidies for fertility procedures to those women who donate excess eggs in the course of their fertility treatments. Can such arrangements be extended to healthy women donors? On the one hand, it seems like a fair arrangement for healthy women to receive subsidies perhaps for closely-related medical procedures (e.g, gynaecological examinations) in the same way that women undergoing fertility treatments enjoy some subsidies for fertility procedures if they donate excess eggs. Such arrangements are also routinely done for clinical trials (e.g, participants given free medical examination). However, there are related considerations of whether extending the same privilege to healthy women is ethical; whether healthy women may end up donating just to access otherwise inaccessible medical procedures; and whether there can be a fair way of deciding what treatments qualify for the subsidies and what do not.

The final issue pertains to when payment is given. In standard participation in experiments and trials, volunteers are given payments sometimes before they undergo the procedure. Can this be applied to egg donation? Can a woman also withdraw at any time without worry that her participation would not be compensated for? I am of the opinion that healthy women donors should be compensated immediately upon signing up and that any subsequent withdrawals be completely the prerogative of the women. There is, however, potential for abuse (e.g., women singing up just to get money but not committed to the treatment). But such considerations are relatively minor compared to the ethical minefield associated with women donors feeling compelled in continuing the egg donation treatment for fear of not being compensated for all her efforts thus far. On the flipside, such an arrangement of paying upfront may be a form of pressure to continue with the treatment despite discomfort and risks. This, however, can be limited by carefully explaining to the woman donor that she is under no obligation to continue if she wishes not to. Also, payment before embarking on the treatment is only possible under a compensation scheme and not under a reimbursement scheme where payment to donors is only given after all costs incurred are tabulated. I hope BAC can carefully weigh these considerations.

Conclusion

In general, I support the timely effort to reexamine the issue of egg donation in light of the progress of stem cell research in Singapore. However, I believe there is a need to consider human egg donation and its risks in greater detail as well as to address issues associated with it as outlined above.

Comments from Professor Chan Soh Ha

Yong Loo Lin School of Medicine
National University of Singapore

9 January 2008

---

a) Research on stem cells should if possible make use of the already existing stem cell lines that have been available for some time.

b) If experiments strictly require fresh eggs, the first choice is left over fertilized eggs, from successful in vitro fertilizations that are no longer required and written informed consent for this purpose has been made. No compensations are required.

c) Healthy females not undergoing fertilization treatment may be allowed to voluntarily donate eggs. Informed consent and counseling for possible dangers and risks should be done by an independent body. There must be no coercion or inducement. Reasonable compensation for time, inconvenience or lost earnings should be allowed.

Comments from Dr Chuah Khoon Leong

3 January 2008

Dear Sir/Madam

I am writing in response to the Bioethics Advisory Committee request for feedback from Fellows of the Academy of Medicine who are in the Chapter of Pathologists.

While scientific pursuit in the area of medical treatment is commendable and to be encouraged, this pursuit should be morally acceptable. Therefore in the area of human egg donation, there is great concern whether the safety and welfare of women are adequately protected regardless of their social status. Furthermore, the possibility of exploitation remains.

One cannot deny that there are risks involved in the procurement of human eggs. Firstly, there is the problem of ovarian hyperstimulation syndrome which may be life threatening and also the increased risk of subsequent breast cancers, ovary and uterus. Is there a need to subject healthy women to such risks even though these risks are supposedly small? For the woman bearing the effects of these risks, it will be looked upon as 100% tragedy for her. In addition, the woman will be subjected to anaesthesia which again is another procedure that carries a certain percentage of risks.

Among the suggestions made is the possibility of payment for women who donate eggs for research. I do see the potential of commodification of women and their body parts if this is to be pursued, leading to a loss of respect of women as human beings. In addition, medical professionals may look at this as a source of potential for personal gain regardless of the fact that there is a potential risk of harming the patient. This may have a long-term negative impact on the medical profession since as doctors; we must safeguard the patient's medical interests above our own interests.

Cloning is the main reason for the procurement of human eggs. The number of eggs required in the formation of a single successful human clone is not known and research with monkeys indicated 304 eggs were used for the creation of 2 embryonic stem cell lines using the somatic cell nuclear transfer technique (Reference: David Cyranoski. Cloned monkey stem cells produced. Nature News. 14 November 2007). One wonders how many women are needed to ensure an adequate supply of eggs for the production of a successful cell line and how many women will therefore be subjected to unnecessary risks. Besides, this method involves the destruction of human individual in order to obtain embryonic stem cells and I do find this unacceptable from an ethical perspective for human life begins at the moment of conception and as such, to be respected. Moreover, stem cells derived from such method are prone to the formation of neoplasms which limits the usefulness of such therapeutic cloning.

Given the above scientific and moral issues, alternate ethically sound methods of obtaining stem cells should be looked into. After all, the creator of the cloned sheep Dolly, Professor Ian Wilmut, had abandoned the so called somatic cell nuclear transfer technique and is now concentrating on direct reprogramming of adult human cells in the production of induced pluripotent state cells, a method devised by Dr Shinya Yamanaka of Kyoto University, Japan.

With the availability of non-controversial methods, is there a need to subject women to unnecessary risks?

Thank you.

Sincerely
Dr Chuah Khoon Leong, FRCPA, FAMS (Pathology)
Senior Consultant Histopathologist

Comments from Mr Patrick Goh

3 January 2008

I understand that those who donate are well informed so that the decision is theirs.

My questions:

1) What concrete proofs are there that this donation helps the betterment of science given that cloning of Dolly the sheep had taken turn for the worst?
2) Is there any emotional or psychological trauma that the donator goes through?
3) Also, even when the donator goes under anesthesia, I understand that the process can be exhaustive and the donator has to go through vigorous checks, procedure, etc, which may be detrimental to her health towards the later part of life? Therefore, is compensation meant to cover her throughout her life existence?

Perhaps, one should consider more on the emotional and psychological compensation as these are the hidden concerns of which many individual do not reveal and not so easily detected? Even, with this said I do not agree at all for any reason whatsoever, in human egg donations. It leads to the manipulation of life at it's minutest (littlest) form and since the researches are allowed to do so, any other individual person (human being) can be manipulated for one's selfish reasons and glory.

The case in Irvine California, USA where the couple was not told that their spare egg were sold to other couple, speaks volumes on the ethical issues and dilemmas we will face. We do not know or even understand that there are boundaries when we undertake what is meant to be of Nature. There are other methods that have proven more positive such as using of umbilical cords, skins, etc.

The IVF does not have high success rate and the cost is exorbitant which goes to prove that it is not feasible as well as we are wasting precious resources (time and money) in this area when other avenues (methods) should be looked into instead. An area is that there is to be an acceptance if one unfortunately is unable to conceive and there are orphans to adopt. There are also other proven natural ways of conceiving and it is a shared responsibility between the spouses. Other areas that couples could conceive is creating an awareness and better education that contraception can affect future births.

These are my consideration.

Comments from Dr Alexis Heng

13 November 2007

Feedback on egg donor compensation

I generally agree with the principle that donors should receive additional compensation for their time, effort and inconvenience in egg donation, over and above reimbursement for direct expenses [1-8]. Nevertheless, I would like to make the following proposals in response to various potential pitfalls and ethical challenges in egg donor compensation. The views and opinions expressed here are entirely my own, and do not reflect the stance of any institution or organization that I am affiliated with.

1) There should be a cap on the maximum amount of money that can be reimbursed for direct expenses

In some countries such as Hong Kong [8] and Canada [9], the reimbursement and compensation of egg donors is strictly limited to direct expenses incurred by the donor herself. This is easy to justify on moral and ethical grounds, based on the premise that if a healthy and fertile woman is genuinely altruistically-motivated to help a childless couple start a family, there should be no reason why she should suffer any financial loss from acting as an egg donor i.e. travel and accommodation costs. Nevertheless, it may also be prudent to put a cap on the total amount of direct expenses that can be reimbursed to the egg donor, as in the case of the Human Reproductive Technology Ordinance of Hong Kong [8]. As discussed previously, it is possible that the provision of travel opportunity and accommodation abroad [10] may in fact serve as undue inducement to foreign egg donors i.e. an 'all expenses-paid free holiday' for economically disadvantaged women. Hence, a clear line has to be drawn on the appropriate levels of travel and accommodation provided to egg donors that should ideally be comfortable, but not border on the lavish and luxurious [11]. It is imperative to ensure that free accommodation provided to the donor should not exceed the time-frame required for participation in the egg donation program. Of course, the pertinent question that arises is why should we pay for the highly expensive air-travel and hotel bills of foreign egg donors? Should not local women be recruited for egg donation instead? As highlighted by Schneider [12], it is unethical to export one country's infertility problem to another country. Egg donation is associated with significant health risks to the donor [13, 14], and it would be absolutely immoral to expose foreign women from poorer countries to such health risks, in order to solve the infertility problems of richer developed countries [12]. Instead, each country should ideally develop self-sufficiency in egg-donation, through the recruitment of local women as donors [12]. Perhaps a cap on the maximum amount of money that can be reimbursed for direct expenses may be utilized to discourage air-travel and hotel accommodation of foreign egg donors.

2) Reimbursement claims for loss of earnings and childcare expenses should be accompanied with documented proof.

Superficially, reimbursement of egg donors for loss of earnings and childcare expenses would appear rather easy to justify on moral and ethical grounds. Nevertheless in most countries, it is almost universally required by law for employers to give their workers a fixed number of days of paid holiday leave annually. Hence, the pertinent question that arises is what happens if a woman makes use of her paid holiday leave to participate in an egg donation program? She would not face any true loss of income, which would make her claim to any loss of earnings rather dubious. This does not imply that the donor should not be compensated for her time and inconvenience in donating her eggs during her holiday leave (which will be discussed later). Instead, the key issue of contention here is honesty and veracity in her claim for loss of earnings. In the case of prospective egg donors without regular full-time employment (i.e. housewives and university students), they should at least provide evidence that they are con-currently holding a part-time or holiday job, before making any reimbursement claims for potential loss of earnings. Another pertinent issue is childcare expenses faced by women in taking time-off to participate in egg donation. It is often the case that women with young children would rely on their network of female relatives (i.e. mothers, sisters and aunts) and friends for help in child-minding, whenever they need to take time-off for other commitments. Hence, there is a possibility of abuse in the form of dubious claims for childcare expenses, when in reality free child-minding is being provided for by the donor's own relatives and friends. It is therefore proposed that any claims for loss of earnings and childcare expenses should be accompanied with documented proof and evaluated on a case-by-case basis to prevent falsification and abuse. In particular, egg donors on paid holiday leave should be denied any form of reimbursement for loss of earnings. They can of course still be compensated for their time, inconvenience and effort in egg donation (which will be discussed in the next section). The underlying principle here is that reimbursement claims for loss of earnings must truthfully reflect genuine loss of earnings by the donor, so as to maintain accounting integrity and ensure transparency. For childcare expenses, reimbursement claims should be accompanied by bills and receipts from registered government-approved childcare centers.

3) Additional compensation based on minimum wages or fixed sum payment given to clinical trial volunteers is ethically justifiable, due to the inconvenience, discomfort, pain, loss of time and medical risks faced by the egg donor. However, payment should be pro-rated to the donor's actual wages, so as to avoid undue inducement to poorer women.

Besides reimbursement for direct expenses, potential loss of earnings and childcare expenses, it is often argued that egg donors should also be given additional compensation for the inconvenience, discomfort, pain, loss of time and medical risks faced in egg donation [15, 16]. A typical egg donation cycle takes up several hours of a donor's time [15, 16], in addition to the hassle of commuting to and from her home,

workplace and fertility clinic. It has been proposed that egg donors should be compensated for at least the statutory minimum wages per hour set by law for this period of time spent on egg donation [15, 16]. Additionally, it has also been suggested that extra financial compensation should be given for discomfort, pain and medical risks faced by the egg donor, similar to the fixed sum payment given to clinical trial volunteers. These proposals for additional financial compensation above that given for direct expenses, potential loss of earnings and childcare expenses may have some grounds for ethical and moral justification. Nevertheless, it is imperative that the amount of payment should not be too great so as to entice women to donate their eggs solely for the sake of money; without regard to their own health and safety (i.e. undue inducement). Special caution should be exercised in the case of poorer foreign women from developing countries. It is a well-known fact that differences in living standards, currency exchange rates and purchasing power parity, can easily magnify a petty sum of money in developed countries to an inordinately large amount in poorer countries. For example, the recommended £250 (≈ US$400) compensation for egg donors (SEED report, 2005 [17]) proposed by the Human Fertilization and Embryology Authority (HFEA) in the UK would appear to be a paltry sum by UK standards. However, to young working women in some Eastern European countries and the former Soviet Union, this could very well represent a couple of weeks' wages [11]. Hence, it is suggested that payment of egg donors should be pro-rated according to their actual wages, as attested by bank statements and income tax slips provided by donors themselves. This will avoid undue inducement to poorer women. For this purpose, the concept of purchasing power parity [18] in international currency exchange rates would prove particularly useful. The Big Mac Index [19] readily demonstrates this point by showing that the price of the same MacDonald hamburger varies considerably in different countries, based on local currency exchange rates with the American dollar.

4) Financial compensation should be given for time spent in the egg donation program, even if the donor opts out half-way

Based on the premise that egg donors should rightfully be compensated for their time, inconvenience and discomfort, in addition to being reimbursed for direct expenses and loss of earnings; the pertinent question that arises is whether compensation and reimbursement should also be given to women who opt out of the egg donation program half-way, if they are feeling genuinely unwell? It is often argued that payment to egg donors does not constitute direct purchase of her donated eggs per se, but instead serve as due compensation for her time, inconvenience and effort. To maintain ethical and legal consistency on this line of argument, prospective donors who opt out half-way from an egg donation program should also receive payment for the time that they had spent in the program. It is well-known that superovulation regimens involving administration of purified recombinant gonadotrophins (i.e. follicular stimulating hormone) to the egg donor, often result in the development of mild to moderate symptoms of ovarian hyperstimulation syndrome (OHSS) [13, 14, 20, 21], most commonly characterized by feelings of nausea and 'bloatedness'. Hence if the donor is feeling genuinely unwell and wishes to withdraw her participation in the egg donation

program, there should be no undue inducement or coercive pressure for her to continue, as this might lead to serious medical complications later. It is often the case that fertility clinics and doctors will give either the bulk or full sum of financial compensation to the egg donor upon her completion of the entire program. This is ethically and morally contentious, because there is now undue inducement and even some degree of coercive pressure on the egg donor to complete the entire program at the risk of her own health, if she is feeling genuinely unwell. Hence, it is proposed that some financial compensation should be given for time spent in the egg donation program, even if the donor opts out half-way. Preferably, the donor should receive payment on a daily basis. This would reduce coercive pressure and undue inducement for the egg donor to continue her participation at the risk of her own health.

5) Medical professionals and scientists directly involved in fertility treatment or research should be excluded from the recruitment, counseling and compensation of egg donors

Medical professionals and scientists directly involved in fertility treatment or research face conflicting interests in the recruitment, counseling and compensation of egg donors. At the crux of conflicting interests is the issue of informed consent, as highlighted by Spar [22], and the ESHRE task force on Ethics and Law [23]. There are both short and long-term health risks posed to women by egg donation [13, 14, 20, 21]; and the ability of medical professionals and biomedical scientists to provide sound advice and informative counseling on this particular issue to egg donors may be severely compromised by their 'commitment' to the fee-paying recipient patient or to their own research. In many countries with lax regulations on donor counseling and informed consent, it is often the case that prospective egg donors would only be told what brokers, fertility clinics and research laboratories choose to tell them [22]. Additionally, if medical professionals and biomedical scientists are directly involved in reimbursement/compensation of direct expenses, loss of earnings and childcare expenses, there is a risk of 'creative-accounting' being utilized to increase the sum of money given to egg donors, which might serve as undue inducement. Because the cost of donor compensation is likely to be paid-up by the recipient patient, the fertility clinic and medical doctor does not suffer any financial loss; but in fact can attract more egg donors by increasing the reimbursement/compensation pay-out from recipient patients. Hence, it is proposed that the Ministry of Health in Singapore should set up a specialized department or agency for the ethical recruitment, counseling and compensation of egg donors, which would function independently of medical professionals providing fertility treatment and biomedical scientists conducting research. Perhaps, the National Gamete Donation Trust (NGDT) in the United Kingdom could provide such a good example of an independent-functioning agency [24]. Moreover, it must be remembered that in many countries, transplant surgeons are not allowed to procure and allocate donated organs for their own patients, due to obvious and undeniable conflict of interests [25, 26]. There is usually a centralized registry and waiting list of patients requiring organ transplantation, and priority is given based on medical conditions and needs. If transplant surgeons were given a free rein to

decide which patients should receive priority for organ transplantation, there is a high probability that they would favor their own patients, who would eventually pay them medical fees. Likewise, a similar principle should be followed for the procurement and allocation of donated eggs for infertility patients, based on a centralized registry and waiting list maintained by the Ministry of Health in Singapore. A government monopsony on donor eggs would prevent profiteering by medical professionals; as well as maintain a reasonable donor compensation rate, so as to avoid undue inducement to vulnerable women.

6) The import of donor eggs should be prohibited, to ensure legal and ethical consistency in donor compensation and informed consent policy

In recent years, there have been increasing transactions of donor eggs across international borders [27, 28]. As discussed previously [27], there are varying policies on egg donor compensation and informed consent in different countries. Hence, the Ministry of Health in Singapore faces a legal dilemma and ethical conundrum, if they permit the import of donor eggs from foreign countries with significantly different legislation and policies on egg donor compensation and informed consent. For example, the Ministry of Health in Singapore has established rather stringent and rigorous procedures for egg donor counseling and informed consent. It is stated in section 8.6 of the Directives for Private Healthcare Institutions Providing Assisted Reproduction Services [2] that: "All prospective oocyte donors (i.e. patients who come primarily to donate their oocyte for research and not as part of fertility treatment) must be reviewed by a panel (may come from the hospital's ethics committee) consisting of a lay person and 2 medical practitioners, one of whom is an authorized Assisted Reproduction practitioner. The panel must interview the prospective donor before commencement of the ovarian stimulation and be satisfied that the prospective donor (a) is of sound mind (b) has clear understandings of nature and consequences of the donation and (c) has given explicit consent for donation (freely without coercion or inducements) before allowing procedures leading to the donation to proceed. In addition, the panel should take into consideration the public interest and community values when assessing an application for donation of oocyte for research." The pertinent question that arises is whether it is possible to maintain such rigorous and high standards of donor counseling and informed consent, if donor eggs are imported from abroad? There is clearly a risk that donor eggs imported from a foreign country may be procured from ill-informed women, with little awareness of both the short- and long-term health risks of egg donation [13, 14, 20, 21]. Also, even if the amount of financial compensation given to egg donors in Singapore is tightly-regulated to avoid undue inducement, there is no guarantee that such a lofty principle would be followed in a foreign country. As mentioned earlier, differences in living standards, currency exchange rates and purchasing power parity, can easily magnify a petty sum of money in developed countries to an inordinately large amount in poorer countries [11]. It would therefore be fallacious to claim that there is no undue inducement, if the amount of donor compensation abroad is the same as that in Singapore, after currency conversion. Hence, the import of donor eggs into Singapore should be prohibited, to ensure legal

and ethical consistency in donor compensation and informed consent policy. Additionally, it must be noted that imported donor eggs are usually frozen or cryopreserved to facilitate transportation, and there are significant health risks associated with the process of freezing and cryopreserving unfertilized Human eggs. The Practice committee of the American Society for Reproductive Medicine [29] states that: "The metaphase-II oocyte is extremely fragile due to its large size, water content, and chromosomal arrangement. In the mature oocyte, the metaphase chromosomes are lined up by the meiotic spindle along the equatorial plate. It has been well documented that the spindle apparatus is easily damaged by intracellular ice formation during the freezing or thawing process [30, 31]. In addition, hardening of the zona pellucida can adversely affect the normal fertilization process [32]." Subsequently, the committee recommended caution with regards to the use of frozen human eggs in assisted reproduction [29], by stating that: "Due to the known effects of cryopreservation on the meiotic spindle of the oocyte, there remain concerns regarding the potential for chromosomal aneuploidy or other karyotypic abnormalities in the offspring. Concerns similarly remain regarding the potential for organ malformations or other developmental problems. Despite the few promising studies on vitrification, even less is known about the potentially detrimental effects of vitrification when compared with conventional cryopreservation techniques."

7) Ovarian stimulation of foreign egg donors should not take place abroad.

In the case whereby foreign egg donors are recruited from abroad, it would be particularly convenient to start her ovarian stimulation regimen (i.e. 2 to 3 weeks of gonadotrophin administration) abroad through a foreign collaborating fertility clinic [28]. This would limit her duration of stay upon arrival in Singapore, which in turn could save on accommodation costs. Nevertheless, this is ethically and morally contentious for two major reasons. Firstly, there is a question of abdication of responsibility on the part of Singapore-based fertility doctors for the donor's welfare. If the donor develops life-threatening or debilitating ovarian hyperstimulation syndrome [20, 21] prior to arrival in Singapore, only the foreign collaborating fertility doctor administering the ovarian stimulation regimen would be held accountable, whilst his or her foreign partner in Singapore would remain unscathed. Ideally, both doctors should be held equally responsible for the welfare of the egg donor, as well as the recipient patient. Moreover, to ensure continuity in medical care, there should preferably be only one doctor taking charge of the egg donor superovulation regimen. Secondly, there is an issue of lower prescription price of fertility drugs being used to superovulate the foreign egg donor. In many economically less-developed countries, the prescription price of the same brand and dosage of various pharmaceuticals is often cheaper [33-35], commensurate with the lower income and higher purchasing power parity of the local currency. Additionally, cheaper generic fertility drugs that violate international patent laws may also be available. In many developing countries, there is often scant regard for international patent laws and intellectual property protection with regard to pharmaceutical drugs [36, 37], probably because of political pressure from the local populace who desire cheaper medications. Because Singapore is signatory to the World

Trade Organization (WTO) agreement on intellectual property and patent protection; it would be ironic if superovulation of egg donors from poorer countries were induced using cheaper generic fertility drugs and the donor eggs thus obtained are utilized in Singapore by local patients or researchers. It must be remembered that in clinical assisted reproduction, the prescription cost of fertility hormones used in superovulation makes up a substantial proportion of the medical fees. Cost savings from lower prescription prices would probably not be passed down to the recipient patient in Singapore, but could instead be exploited to boost the already substantial profit margin of medical doctors and fertility clinics. To prevent such abuses, it is thus recommended that ovarian stimulation of foreign egg donors should not take place abroad.

8) Egg donors should preferably be restricted to Singapore citizens and permanent residents.

It is recommended that egg donors be restricted to Singapore citizens and permanent residents for three major reasons. Firstly, if foreign donors were to develop life-threatening or debilitating medical complications upon returning to their home country, it may be difficult to carry out legal redress against Singapore-based fertility doctors, as well as claim health insurance; since it is mandated by law that all patients undergoing fertility treatment in Singapore must have insurance cover [2]. Secondly, there is no medical follow-up and aftercare of egg donors by Singapore-based fertility doctors, which could be tantamount to shirking professional responsibility. Thirdly, medical records of Singaporean citizens and permanent residents are readily accessible, for checking the personal medical history of prospective egg donors, as well their familial record of hereditary diseases. By contrast, it is much more difficult to check on the past medical records of foreign egg donors coming from abroad, which may even be written-up in a foreign language.

References

[1] Human Cloning and Other Prohibited Practices Bill, July, 2004. Accessible at the following website address: http://www.parliament.gov.sg/Publications/0400034.pdf (Date accessed: 1 August 2007).

[2] DIRECTIVES FOR PRIVATE HEALTHCARE INSTITUTIONS PROVIDING ASSISTED REPRODUCTION SERVICES : REGULATION 4 OF THE PRIVATE HOSPITALS AND MEDICAL CLINICS REGULATIONS (CAP 248, REG 1), March 2006. Accessible at the following website address: https://www.moh-ela.gov.sg/ela/docroot/html/assisted_reproduction_services_directives.pdf (Date accessed: 1 August 2007).

[3] Robertson JA. Compensation and egg donation for research. Fertil Steril. 2006 Dec;86(6):1573-5.

[4] Heng BC. Alternative solutions to the current situation of oocyte donation in Singapore. Reprod Biomed Online. 2006 Mar;12(3):286-91.

[5] Heng BC, Zhang X. Perspectives on compensated egg-sharing in the People's Republic of China. Reprod Biomed Online. 2007 May;14(5):664-5.

[6] Heng BC. International egg-sharing to provide donor oocytes for clinical assisted reproduction and derivation of nuclear transfer stem cells. Reprod Biomed Online. 2005 Dec;11(6):676-8.

[7] Blyth E. Subsidized IVF: the development of 'egg sharing' in the United Kingdom. Hum Reprod. 2002 Dec;17(12):3254-9.

[8] Code of Practice on Reproductive Technology & Embryo Research, December 2002. Health, Welfare and Food Bureau, The Government of the Hong Kong Special Administrative Region. Accessible at the following website address: http://www.hwfb.gov.hk/download/press_and_publications/otherinfo/021230_h/e_cop_full.pdf (Accessed: 1 August 2007).

[9] Rasmussen C. Canada's Assisted Human Reproductive Act: is it scientific censorship, or a reasoned approach to the regulation of rapidly emerging reproductive technologies? Sask Law Rev. 2004;67(1):97-135.

[10] Heng BC. Ethical issues in paying for long-distance travel and accommodation expenses of oocyte donors. Reprod Biomed Online. 2005 Nov;11(5):552-3.

[11] Heng BC. Regulatory safeguards needed for the travelling foreign egg donor. Hum Reprod. 2007 Aug;22(8):2350-2.

[12] Schneider I. Oocyte donation for reproduction and research cloning--the perils of commodification and the need for European and international regulation. Law Hum Genome Rev. 2006 Jul-Dec;(25):205-41.

[13] Norsigian J. Egg donation dangers: additional demand for eggs leads to additional risks. Genewatch. 2005 Sep-Oct;18(5):6-8, 16.

[14] Ahuja KK, Simons EG, Edwards RG. Money, morals and medical risks: conflicting notions underlying the recruitment of egg donors. Hum Reprod. 1999 Feb;14(2):279-84.

[15] Steinbock B. Payment for egg donation and surrogacy. Mt Sinai J Med. 2004 Sep;71(4):255-65.

[16] International Stem Cell Forum Ethics Working Party, Knoppers BM, Revel M, Richardson G, Kure J, Lotjonen S, Isasi R, Mauron A, Wahlstrom J, Rager B, Peng PL.

Oocyte donation for stem cell research. Science. 2007 Apr 20;316(5823):368-70; author reply 368-70.

[17] Sperm, Egg and Embryo Donation (SEED). SEED Report: A Report on the Human Fertilisation & Embryology Authority's Review of Sperm, Egg and Embryo Donation in the United Kingdom. London: Human Fertilisation & Embryology Authority. Available at:https://centres.hfea.gov.uk/AboutHFEA/HFEAPolicy/SEEDGuidanceandDirections/SEEDReport05.pdf [Accessed: 1 August 2007].

[18] Dornbusch R. Exchange Rates and Prices. American Economic Review, March 1987, 77(1), pp. 93-106.

[19] The Big Mac Index. The Economist Magazine. Accessible at the following website: http://www.economist.com/markets/indicators/displaystory.cfm?story_id=8649005 [Accessed: 1 August 2007].

[20] Budev MM, Arroliga AC, Falcone T. Ovarian hyperstimulation syndrome. Crit Care Med. 2005 Oct;33(10 Suppl):S301-6.

[21] Pearson H. Health effects of egg donation may take decades to emerge. Nature. 2006 Aug 10;442(7103):607-8.

[22] Spar D. The egg trade--making sense of the market for human oocytes. N Engl J Med. 2007 Mar 29;356(13):1289-91.

[23] ESHRE Task Force on Ethics and Law III. Gamete and embryo donation. Hum Reprod 2002;17:1407–1408.

[24] The National Gamete Donation Trust Website, 2006. Accessible at the following website address: http://www.ngdt.co.uk/ (Date accessed: 1 August 2007).

[25] Dimond B. Law concerning organ transplants and dead donors in the UK. Br J Nurs. 2005 Jan 13-26;14(1):47-8.

[26] Samuels A. Human Tissue Act 2004: the removal and retention of human organs and tissue. Med Leg J. 2004;72(Pt 4):148-50.

[27] Heng BC. Legal and ethical issues in the international transaction of donor sperm and eggs. J Assist Reprod Genet. 2007 Apr;24(4):107-9.

[28] Heng BC. The advent of international 'mail-order' egg donation. BJOG. 2006 Nov;113(11):1225-7.

[29] The Practice Committee of the American Society for Reproductive Medicine; Practice Committee of the Society for Assisted Reproductive Technology. Ovarian tissue and oocyte cryopreservation. Fertil Steril. 2006 Nov;86 Suppl 5:S142-7.

[30] Shaw JM, Oranratnachai A, Trounson AO. Fundamental cryobiology of mammalian oocytes and ovarian tissue. Theriogenology 2000;53: 59–72.

[31] Baka SG, Toth TL, Veeck LL, Jones HW Jr, Muasher SJ, Lanzendorf SE. Evaluation of the spindle apparatus of in-vitro matured human oocytes following cryopreservation. Hum Reprod 1995;10:1816 –20.

[33] Matson PL, Graefling J, Junk SM, Yovich JL, Edirisinghe WR. Cryopreservation of oocytes and embryos: use of a mouse model to investigate effects upon zona hardness and formulate treatment strategies in an in-vitro fertilization programme. Hum Reprod 1997;12:1550 –3.

[33] Ridley DB. Price differentiation and transparency in the global pharmaceutical marketplace. Pharmacoeconomics 2005;23:651–8.

[34] Danzon PM, Towse A. Differential pricing for pharmaceuticals: reconciling access, R&D and patents. Int J Health Care Finance Econ. 2003;3:183–205.

[35] Frank RG. Prescription drug prices: why do some pay more than others do? Health Aff (Millwood) 2001;20:115–28.

[36] Glass G. Pharmaceutical patent challenges: time for reassessment? Nat Rev Drug Discov 2004;3(12):1057 – 62.

[37] Attaran A. How do patents and economic policies affect access to essential medicines in developing countries? Health Aff (Millwood) 2004;23(3):155 –6.

Comments from Dr Alexis Heng

22 November 2007

Feedback on donation of surplus eggs by IVF patients for discount in medical fees - egg sharing

I would like to give an additional feedback on the donation of surplus eggs by IVF patients for a discount in medical fees – more commonly known as "egg sharing".

Egg sharing in return for subsidized fertility treatment has often been proposed as a more ethically acceptable means of procuring donor oocytes, as compared to the direct payment of egg donors (Ahuja et al., 1996; 2001). In recent years, the concept of egg sharing has caught on in popularity; and among the various countries that have permitted egg sharing in clinical assisted reproduction includes the United Kingdom (Blyth et al., 2004), Belgium (Pennings and Devroey, 2006) and the People's Republic of China (Heng and Zhang, 2007). Nevertheless, there are some pertinent ethical challenges that have largely been overlooked.

First and foremost is the issue of appropriate dosages of gonadotrophins (Follicular Stimulating Hormone) being prescribed for the ovarian stimulation of prospective egg-sharing patients. To maximize the number of oocytes retrieved, it is often the case that prospective egg sharing patients would be restricted to younger women with indications for either male-factor sub-fertility or mild female-factor sub-fertility (i.e. fallopian tube occlusion). Poor prognosis older patients with 'tricky' medical indications, such as polycystic ovarian disease and endometriosis are likely to be excluded. Hence, the pertinent question that arises is whether it is medically necessary to subject good prognosis younger patients to high dosages of gonadotrophins, just for the sake of maximizing the yield of retrievable oocytes for egg sharing? Should not natural cycle or minimal ovarian stimulation protocols be more appropriate for such patients (Edwards, 2007; Nargund et al., 2007; Heng, 2007)? Indeed, there is much evidence to show that the use of natural cycle or minimal ovarian stimulation protocols for good prognosis younger patients results in a more physiological endocrine profile (Ubaldi et al., 2007), which in turn leads to improved quality of retrieved oocytes (Fauser et al., 1999), as well as better endometrial receptivity and luteal support for subsequent embryo implantation (Devroey et al., 2004; Lindhard et al., 2006).

Moreover, it must be remembered that high dosages of gonadotrophins are associated with increased risk of debilitating and potentially life-threatening ovarian hyperstimulation syndrome to the patient (Budev et al., 2005), in addition to other not so well characterized long-term health risks such as future reduction in fertility and increased propensity to develop gynecological cancers (Pearson, 2006). This in turn touches on the core guiding principle of medical deontology, by which all treatment administered to the patient must be in the best interest of his/her welfare. A paradoxical

situation can thus develop as follows: "To maximize the yield of retrievable oocytes for egg sharing, high dosages of gonadotrophins are being administered to the patient. However, high dosages of gonadotrophins contribute to a significant portion of expensive medical fees in the first place (Gleicher et al., 2003; Ubaldi et al., 2007). Because poorer patients are unable to cope with high medical fees in fertility treatment, they participate in egg sharing to obtain a discount. Nevertheless, a discount in medical fees may not be needed, if poorer patients with good prognosis had instead opted for natural cycle or minimal ovarian stimulation protocols, in which nil or low dosages of gonadotrophins are administered."

Secondly, another pertinent ethical issue is the appropriate levels of discount in medical fees that should be given to the prospective egg-sharing patient. Currently, there is a dire lack of guidelines and regulations in this area, and different fertility clinics display considerable variation in the level of discount of medical fees given to egg-sharing patients, even in the same country. For example, in the People's Republic of China, the discount can range from as low as 50%, to as high as 100% of total medical fees billed to prospective egg sharing patients (personal communication with Dr. Zhang Xiao of Peking University Medical School). Hence, the pertinent question that arises in this case is which particular component of the medical fees should be eligible for discount? The first thing that comes to mind is the prescription price of gonadotrophins and other drugs (i.e. GnRH antagonist or agonist) utilized for ovarian stimulation of the egg-sharing patient. Besides this, medical fees for the surgical retrieval of oocytes from the egg-sharing patient can also be eligible for discount. Nevertheless, it would be morally and ethically dubious to given a 100% discount for these two components of the medical fees billed to the egg-sharing patient, since she should in principle bear some of the costs of her own treatment to avoid undue inducement. Instead, it is recommended that the level of discount in medical fees be pro-rated according to the exact proportion of retrieved oocytes being shared with the recipient. For example if ten oocytes are retrieved, and three of these are being shared with the recipient, then the percentage of discount given to the egg sharer should be 30%, to be paid-up by the recipient patient. Other components of the medical fees such as for consultation, IVF/ICSI procedures and embryo cryopreservation should ideally be borne separately by the egg-sharing and recipient patient, so as to ensure transparency and avoid undue inducement in the procurement of shared donor oocytes.

Thirdly, there must be rigorous auditing to ensure that the amount of financial subsidy given to the egg sharing patient is exactly equal to the surplus medical fees billed to the recipient patient. There is a possibility that medical professionals and fertility clinics might charge the recipient patient much more than the actual financial subsidy given to the egg sharing patient, thereby making a profit in the process. This is ethically and morally dubious; because the money earned in this case is not directly related to medical services rendered to the patient, but is instead attributed to the brokerage and transaction of donated human material.

Lastly, the abolishment of donor anonymity in many countries (De Jonge and Barratt, 2006) has potentially more ramifications for prospective egg sharing patients, as compared to non-patient donors. This is because egg sharing patients are themselves trying to conceive, and it would be a daunting prospect for them to be confronted by their own biological offsprings several years later, if they fail at clinical assisted reproduction themselves. In such an eventuality, they would likely feel being 'shortchanged' or 'cheated' by egg sharing in return for subsidized fertility treatment.

Although egg sharing is a novel concept that has proven to be of much benefit to patients undergoing clinical assisted reproduction, it is imperative that some thought should go into the ethical challenges outlined above; so as to prevent abuse by medical professionals and protect the welfare of the patient.

References

Ahuja KK, Simons EG, Fiamanya W, Dalton M, Armar NA, Kirkpatrick P, Sharp S, Arian-Schad M, Seaton A, Watters WJ. Egg-sharing in assisted conception: ethical and practical considerations. Hum Reprod. 1996 May;11(5):1126-31

Ahuja KK, Simons EG, Rimington MR, Nair S, Gill A, Evbuomwan I, Bowen-Simpkins P. One hundred and three concurrent IVF successes for donors and recipients who shared eggs: ethical and practical benefits of egg sharing to society. Reprod Biomed Online. 2000;1(3):101-5.

Blyth E, Crawshaw M, Daniels K. Policy formation in gamete donation and egg sharing in the UK--a critical appraisal. Soc Sci Med. 2004 Dec;59(12):2617-26.

Budev MM, Arroliga AC, Falcone T. Ovarian hyperstimulation syndrome. Crit Care Med. 2005 Oct;33(10 Suppl):S301-6.

De Jonge C, Barratt CL. Gamete donation: a question of anonymity. Fertil Steril. 2006 Feb;85(2):500-1.

Devroey P, Bourgain C, Macklon NS et al. 2004 Reproductive biology and IVF: ovarian stimulation and endometrial receptivity. Trends in Endocrinology and Metabolism 15, 84–90.

Edwards RG. IVF, IVM, natural cycle IVF, minimal stimulation IVF - time for a rethink.
Reprod Biomed Online. 2007 Jul;15(1):106-19.

Fauser BC, Devroey P, Yen SS et al. 1999 Minimal ovarian stimulation for IVF: appraisal of potential benefits and drawbacks. Human Reproduction 14, 2681–2686.

Gleicher N, Vietzke M, Vidali A. Bye-bye urinary gonadotrophins? Recombinant FSH: a real progress in ovulation induction and IVF? Hum Reprod. 2003 Mar;18(3):476-82.

Heng BC. Reluctance of medical professionals in adopting natural-cycle and minimal ovarian stimulation protocols in human clinical assisted reproduction. Reprod Biomed Online. 2007 Jul;15(1):9-11.

Heng BC, Zhang X. Perspectives on compensated egg-sharing in the People's Republic of China. Reprod Biomed Online. 2007 May;14(5):664-5

Lindhard A, Ravn V, Bentin-Ley U et al. 2006 Ultrasound characteristics and histological dating of the endometrium in a natural cycle in infertile women compared with fertile controls. Fertility and Sterility 86, 1344–1355.

Pearson H. Health effects of egg donation may take decades to emerge. Nature. 2006 Aug 10;442(7103):607-8.

Pennings G, Devroey P. Subsidized in-vitro fertilization treatment and the effect on the number of egg sharers. Reprod Biomed Online. 2006 Jul;13(1):8-10.

Ubaldi F, Rienzi L, Baroni E, Ferrero S, Iacobelli M, Minasi MG, Sapienza F, Romano S, Colasante A, Litwicka K, Greco E. Hopes and facts about mild ovarian stimulation. Reprod Biomed Online. 2007 Jun;14(6):675-81.

Comments from Dr Suresh Nair

7 January 2008

Prof Lee Eng Hin
Bioethics Advisory Committee
11 Biopolis Way #10-12 Helios
Singapore 138667

Dear Prof Lee

Thank you for asking me to comment on the "Bioethics Advisory Committee" consultation paper on "Donation of Human Eggs for Research". I have read the document and researched the topic and these are my comments.

First and foremost, I agree and fully support research involving human oocytes donated for non-reproductive purposes. However, as regards involving women already undergoing IVF fertility treatments themselves, I feel we should exercise extreme caution and not unnecessarily burden these women who are already under great duress from these treatments. As regards the issue of their benefiting from monetary compensation in the way of reduced and more affordable treatment – that is an issue that should be decoupled from oocyte donation for research. We should address the affordability of IVF in Singapore by reviewing the cost of drugs, services and the trend towards single embryo transfer and hence more subtle stimulation protocols using lesser quantums of stimulation drugs and hence decreasing the overall cost of IVF.

The reasoning behind keeping the IVF population as a secondary source of oocytes if at all for research is that this would absolve institutions providing IVF treatments and also involved in oocyte research or providing oocytes for research of concerns that the patient's ovaries may be stimulated more than is required for her reproductive needs leading to a greater propensity for ovarian hyperstimulation syndrome (OHSS). This issue persists even if two mutually independent institutions were involved in the stimulation/ART treatment and the other collecting surplus or immature eggs.

It could be argued that women undergoing IVF are a cohort who are well-informed and hence prepared for the risks that ovarian hyperstimulation that can result in OHSS. Further, they need to undergo these treatments that have the clear benefit of providing them children of their own. Critics might say that this will absolutely circumvent the dangers of ovarian hyperstimulation and the invasive oocyte recovery process requiring anesthesia and its attendant risks upon an otherwise healthy population not at all requiring to go through this potentially "dangerous" procedure.

To counter this argument, which I feel might not be adequately consolidated in the paper; the following points can be emphasized.

- That the risk of ovarian stimulation is low and through the conduct of stimulation by MOH accredited practitioners and ART centres who are already closely monitored by the regulatory authorities, and because of the good track record of ART in Singapore, the process of ovarian stimulation and OHSS risk upon oocyte donors would be very small.
- In addition, for oocyte donors, stimulation protocols that are gentler / milder can reduce the risk of OHSS far below the 1% quoted for ART cycles.

The suggestion that using only surplus or immature eggs of ART women for research would negate the need for healthy donors is also not feasible as the quantum of oocytes is extremely small and the ART patient may still not escape the fear, albeit inadvertent, of being lower in the priority ladder should they be not sufficiently prolific egg producers to be a "good" research oocyte source.

We must therefore endeavor to make the involvement of healthy individuals as oocyte donors as palatable a concept and eventually a reality for public and professional acceptance.

Firstly, all research involving oocytes must be centrally governed and scrutinize through the BAC. In this regard, all institutions involved in oocyte stem cell research must have their research protocols and the recruitment practices examined by the relevant authorities with independent unrelated counselling centres / counselors to ensure that potential donors are under no pressure / duress to submit themselves for the research and also be provided with informed consent in a language they fully understand. The requirement of a basic educational level e.g. secondary schooling, to be eligible as an oocyte donor and that there is freedom for the individual to "bail out" at any time during the stimulation process must be clearly spelt out and reinforced. Indeed, the segment of the paper that addresses informed consent should be further expanded such that a well-defined stringent step by step procedural pathway must be developed such that omission of one stage / step disallows the donor from progressing towards eventual recruitment into the study. The rigor with which this recruitment phase is spelt out will clearly appease those who are concerned about potential donors being mislead and unwittingly chanelled into the programme. This is to hopefully prevent another "Shorovsky debacle".

In addition, it must be more vehemently emphasized that any organization / university / research group intending to do research on human oocytes in Singapore will be held to the very stringent requirements that already exist and, in addition, that the regulatory authorities would ensure that there is not a repetition of established research completed elsewhere but can include the studies meant to analyze the peculiarity, if any, in the genetic / physiological characteristics of oocyte / stem cell properties in the Eastern / Asian population in comparison to research done in Europe / USA. That no effort would be spared to see if the research cannot be conducted using non-human oocytes and that protocols that are wasteful of human oocytes and not efficiently utilizing oocytes for research would be disapproved must be reiterated and reinforced.

Should there be an age limit?

Clearly there should be an age limit to define the suitable donor. The lower age limit based on well accepted social norms of the definition of adulthood where it presumed that the individual has reached a sufficient degree of maturity and independent thinking both in the legal and societal context is 21 years of age.

As along as there is no demonstrable / detectable disease that can potentially jeopardize the health of an older individual, older women should also be allowed to donate oocytes for study so that research into ovarian and oocyte senescence can be conducted as well.

Oocyte from other sources – should be allowed but preference from healthy donors

As regards oocytes from other sources such as the fetuses from pregnancy termination (which is legal in Singapore) is a good source but there should be no connection between the decision to terminate the pregnancy and the potential for oocyte donation. Other sources are mid-trimester or later trimester pregnancy losses e.g. anencephalic babies, cadaveric (both young and old) are also valuable sources of oocytes that can help in elucidating problems in the different age groups through tactful in-vitro maturation. However, this point can be omitted or deferred for the time being as they present a very small albeit important resource of oocytes and might bring about other complex social and religious issues.

The issue of payments

Oocyte donors must clearly not only be reimbursed but definitely compensated for making this ultimate sacrifice of going through a not painless regimen of treatment and an invasive procedure to retrieve eggs.

In Singapore, the regulatory bodies can work out what is a reasonable compensation (taken into consideration current costs of living which must be updated regularly) in regards time away from work not only during the process but if the individual is not well enough to go back to work. I feel that we should not just compensate but provide such women with more tangible support be it in cash or kind.

My argument in support of this is that provided the sum of money is a widely accepted fixed quantum and is not ludicrously high in which the incentive of huge riches would blind women into adopting high-risk behavior, I think our society is mature and sensible enough to accept the concept / idea of payment to oocyte donors for making this major sacrifice for the betterment of all, particularly when the public is educated and made to realize the somewhat arduous process toward oocyte donation.

In order to counter the knee-jerk reaction of critics and those who fear that this would lead to a huge number of under-privileged women into the "business" of egg donation, having stringent regulatory agencies applying checks through independent localities with officers and independent reviewers unrelated to the research organization / IVF centres to monitor and marshal the practices is the sensible and prudent way to safeguard these women from allegations of abuse or exploitation. This is not to suggest a policing / watch-dog function but more to monitor the public's response and if it is too exuberant a response to the "oocyte donation for research" programme then we have to rethink the remuneration scheme. This is very unlikely as it takes a lot of convincing in order for a woman to want to put herself through the process of oocyte donation before she agrees to it.

The issue of compensation should not be considered inappropriate in "oocyte donation for research" because the context within which it is conducted is similar to the realm of research involving participants recruited into a drug trials when the risks to health can be different and higher because the therapeutic element is likely to be recent and not well-established like the protocols of ovarian stimulation which has a long history of use with an established safety record.

Safety of treatment protocols – recent developments increasing the safety profile and convenience

The process of ovarian stimulation and collecting eggs is now a finely tuned low risk procedure. Currently very efficient drugs and regimens using highly purified recombinant drugs delivered by easy to use pens and fewer and shorter duration of injections i.e. using antagonists, and minimizing OHSS using agonist to trigger oocyte maturation are all very significant steps in making ovarian stimulation safe. This should be highlighted to assure those not knowledgeable about ART practices to understand that it is a fairly low risk and user-friendly process. The long term implications as regards breast ad ovarian cancer is thus far not unfavourable.

Non-monetary support and benefits

In order to improve the risk-benefit equation, potential donors can be provided with comprehensive health screening as it is necessary in any case to determine that they are healthy enough to be suitable donors free from disease, including genetic disorder that might interfere with the research.

Of course critics can argue that health screening of low risk healthy individuals have always had a low yield in detection of problems / diseases and that this is not as useful a benefit. Nevertheless, it provides the donor with useful information such as after the viral screen, to see if she needs important vaccinations so that if she decides to have her own pregnancy she would be protected e.g. hepatitis, rubella, chicken pox, etc.

In more recent times, HPV vaccination to prevent HPV infection in addition to Pap smear is also valuable to young women in prevention of cervical cancer – this hopefully might appease the public and critics who might view oocyte donation with disdain.

Yet another component of protection and benefit for the oocyte donors which is often a very key emotive issue that bogs down efforts at recruiting oocyte / embryo donors is that of the impact these treatment regimens have on the donor's fertility potential.

There is sufficient data to show that women continue to lose oocytes at a phenomenal rate of 1000 oocytes per cycle. This ovarian and oocyte senescence occurs in everyone, some deplete earlier because of a diminished primordial follicle pool to maternal illness / environmental effects during the intrauterine period or adulthood. This human phenomenon goes unabated irregardless of what we might do to maintain and promote our health. That being the case, oocyte donors must be assured that the act and process of egg donation does not accelerate the depletion of one's ovaries of eggs. These eggs if not utilized are destined to be lost and become atretic in any case.

Donors must be made aware of their rights to protect their own reproduction potential. Oocyte freezing particularly vitrification has come of age such that good revival and retrieval rates are now achievable coming close to the thaw survival rates of embryos. The Ministry of Health had recently sent out a notification to all IVF centres that the Ministry supports oocyte freezing for women undergoing cancer treatment.

Hence, another non-monetary benefit to oocyte donors is the opportunity to freeze and bank some of her own oocytes for her later reproductive use or if stem cell research produces useful

therapeutic benefit, that she, the donor, has access through her banked eggs to such treatments in the future. This is a strong counter argument to the criticism of the risk albeit small, of the impact if any, that the process of ovarian stimulation and / or oocyte retrieval might have on the donor's fertility reserves or potential. This I feel is an important enough point that should be stated and reiterated because from our experience with oocyte donors for infertile couples, it has been shown, time and time again to be a contentious issue.

New problems may arise as to how long the establishment involved in oocyte donated research should "bank" the oocytes of the donor. As the cost of oocyte banking is still inexpensive and the number of donors not likely to run into large numbers, I feel this component of the cost of cryopreservation should be incorporated into the funding for the research.

This is an important issue that I feel should be mentioned in our paper and in the research protocols as this would strengthen the ethical standing of the study that could help to not only to bring the study closer to regulatory approval but also successful award of funding as the welfare of the oocyte donor is clearly taken care of.

In the reckoning of the quantum of funding the research investigators can incorporate the cost of oocyte cryopreservation as a "compensation" for potential donors.

Extrapolating from this idea, the BAC and our government should steer legislation towards ensuring that all research projects involving oocytes donated by women undergoing invasive procedures have an insurance arrangement, best made, mandatory, to cover the donor against untoward complications because insurance companies usually do not cover any fertility treatments let alone donor oocyte research programme associated problems – this literally leaves the donor vulnerable and totally unprotected from untoward mishaps during the process of occyte donation.

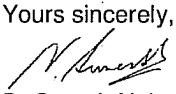
This is not a new or unusual concept as drug companies do take out insurances to safeguard against liabilities and costs of unexpected outcomes that might result in unexpected complications and hospitalizations during drug trials.

Will all these moneys set aside for "complimentary" oocyte banking or protective insurance coverage stifle oocyte research? I think not. On the contrary, placing high regard to human life and the sacrifice of the donors and placing the focus in protecting the individual's rights first and foremost will only pave the way to more successful research endeavors whose study subjects feel valued, know that they will be taken care of and therefore become committed to putting forth their best effort to the project.

This, it is hoped, will quell the nay-sayers and the critics who might "sing the same song" of exploitation and / or abuse of women for research that they mistakenly believe has not been adequately explored using alternative sources of oocytes.

I hope these comments will help the BAC to complete this already comprehensive guidelines. Please feel free to email me at or call me on my mobile at any time should any clarification be required.

Yours sincerely,



Dr Suresh Nair
MBBS, MMED, FRCOG, FAMS

Comments from Professor George Wei
School of Law
Singapore Management University
January 2008

Consultation Paper on Donation of Eggs for Research

Introduction

The Singapore Bioethics Advisory Committee (BAC) published a consultation paper on 7 November 2007 entitled "Donation of Eggs for Research". The comments set out below are in response to that paper. The comments of the author do not necessarily reflect the view of the Singapore Management University.[1]

The paper identifies 5 main areas for which comments are sought. These are:

- Whether healthy women not undergoing fertility treatment should be allowed to donate eggs for research and if so under what conditions;
- Whether egg donors for research should be compensated for time inconvenience and risk and if so, what type of compensation or monetary amount would be acceptable, and not amount to an inducement;
- Whether there are circumstances in which compensation for eggs could amount to a sale and if so whether such a sale should ever be contemplated;
- Any prohibitions, limits or regulatory mechanisms that should govern the supply and use of human eggs for research in Singapore; and
- Any other matters related to the donation of human eggs for research.

Given the significance of stem cell research (embryonic or otherwise) the broad open ended nature of the inquiry is unsurprising. However, for convenience, and as suggested by the BAC[2] the two key issues (for the paper) are (i) whether women should be allowed to donate eggs for research and, if so, (ii) whether any payment may be made to, or received by, the egg donor.

Before setting out some comments on these two key issues, a brief summary of the previous work of the BAC is set out to provide the context in which the present issues are to be discussed. This will be followed by a summary of the author's understanding of current regulatory framework. The Comments follow thereafter.

---

1 The Comments are not intended at date of writing for publication. The author is responsible for all errors and omissions.

2 BAC Paper at p.10.

Previous Work of BAC

The BAC was formed in early 2001 and is charged with the task of examining the legal, ethical and social issues arising out of human biological research and to suggest recommendations to the Government.[3] Since its inception the BAC has produced a number of consultation papers and published reports on various aspects of life sciences. Some of these have resulted in legislative responses by the Government. The papers and reports include:

- Report on Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning (June 2002);
- Report on Human Tissue Research (November 2002);
- Report on Research Involving Human Subjects: Guidelines for Institutional Review Boards (2004);
- Report on Genetic Testing and Genetic Research (2005); and
- Report on Personal Information in Biomedical Research (2007).

The first report (June 2002) made a number of important recommendations touching on the need for an independent regulatory body to supervise and control biomedical research, the banning of reproductive cloning of human beings whilst allowing medical research on embryonic stem cells (less than 14 days old). The main recommendations were subsequently implemented by the Human Cloning and Other Prohibited Practices Act (Cap 131B Rev Ed 2004) which sets out prohibitions against human cloning and related practices.

The second report (November 2002) concerned human tissue research and set out 4 main recommendations. The first concerns the adoption of ethical principles: that the health and welfare of the donor is the paramount consideration in taking any tissue; that no tissue should be taken without full, free and informed consent of the donor, that the human body and its remains should be treated with respect, that gifts of tissues should be accepted only on the basis that the donor renounces property rights or claims in the tissues, that all research involving human tissues be approved by research ethics committees or institutional review boards and that all researchers involved in human tissue banking be under a duty of confidentiality so as to respect the privacy of donors. The second recommendation was that research tissue banking only be conducted by or through approved institutions. The third recommendation was that there should be statutory regulation and supervision of research tissue banking and that a statutory body be set up for this purpose. The fourth recommendation was for a continuing professional and public dialogue on the principles to govern research tissue banking. Initially, it appeared that there might well be new legislation on these matters as the Regulation of Biomedical Research Bill was presented for discussion in 2003. The Bill was not, however, passed by Parliament.

[3] This is partly based on a Chapter on Biotechnology and the Law, prepared by the author and to be published shortly in Singapore Business Law by Thomson Learning (now Cengage Publishing).

The third report (2004) concerned research involving human subjects and guidelines for institutional review boards (IRBs and referred to in the second report). This Report resulted in a long list of recommendations. In brief some of the more important points are as follows. First, that all human biomedical research be reviewed and approved by properly constituted IRBs and these should be accredited by the Ministry of Health. Second, that IRBs be accountable to their appointing institutions and to be responsible for (amongst other things) conducting ethics reviews of proposed human biomedical research programmes. Third, that researchers must comply with all conditions laid down by IRBs that approved the project and (amongst other things) inform and discuss with research subject's attending physicians if the research interferes with the subject's medical management. Fourth, institutions should have the overall responsibility of ensuring the proper conduct of human biomedical research carried out by employees on their premises.

The fourth report (2005) concerned genetic testing and genetic research. The Report sets out a list of 22 recommendations. Key recommendations include: that genetic testing should be voluntary and subject to informed consent and that non-consensual or deceitful taking of human tissues should be prohibited. Further, germ-line genetic modification should not be allowed (at this time) and pre-natal genetic diagnosis should be limited to serious medical disorders and should not be used for selection of desired traits, gender or non-medical reasons. It was also recommended that laboratories carrying out clinical genetic tests are to be accredited by a relevant authority and that predictive genetic tests should not be offered direct to the public.

Since the fourth report, the BAC issued a consultation paper (2006) on the use of personal information in biomedical research. This consultation paper set out a number of complex recommendations for public feedback and discussion. In brief, these concerned the need to establish a legal framework for the use of personal information in biomedical research. The suggested framework touches on the need for specific consent when the research involves identifiable personal information or tissue samples and the use of general consent for subsequent research when this involves de-identified or remnant tissue. The consultation paper also suggested that the legal authorities clarify the legal basis for disclosure of medical information by health care institutions and physicians and to establish mechanisms enabling health care institutions and physicians to increase accessibility of personal information that significantly advance public welfare whilst safeguarding privacy concerns. The general tenor of the consultation paper was to advocate the anonymisation (de-identification) of the personal information as far as and as soon as possible so as to protect individual rights of privacy. The consultation paper also recommended that the Government consider a moratorium on the use of predictive genetic information for insurance purposes and that an authority should be set up to consider the long term implications of accessibility to predictive genetic test results by employers and the insurance industry.

After deliberation, the BAC produced a fifth report entitled Personal Information in Biomedical Research (May 2007). This embodied 11 recommendations touching on the legal protection of personal information, privacy and confidentiality, consent and

proportionality, consent and reciprocity, vulnerable persons, withdrawal of consent and access to predictive genetic information by employers and insurers.

It will be appreciated that the issues raised by the present Consultation Paper on egg donations overlap with some of the points discussed in earlier BAC Reports. Of especial significance is the 2002 Report on Human Stem Cell Research.

Current Regulatory Framework for Egg Donations

Human Organ Transplant Act (HOTA)

Prohibitive Provisions

This law, first enacted in 1987 deals with human organ transplantation as well as "trading in organs and blood." Of particular note is section 14(1) which provides that a contract (for valuable consideration) for the sale or supply of any organ or blood from any person is void. Section 14(2) sets out a parallel criminal provision punishable by fine ($10,000 maximum) and/or imprisonment (12 months maximum).

Do these provisions apply to egg donations? Organ for the purpose of section 14 is defined as "any organ of the human body".[4] Clearly, sale of ovaries will be caught by the bars in section 14. But, what of eggs that have been extracted in the manner outlined in the Consultation Paper? At first sight, it seems unlikely that a human egg will be regarded as an "organ" under the present HOTA provisions. Dictionary definitions suggest that organ refers in this context to any part of the human body adapted for a particular function. Thus, insulin is a product of the pancreas (the organ).

Ambiguity, however, arises in the guise of section 14(4). This allows the Minister to exempt specified classes of product derived from any organ or blood that has been subjected to "processing" or "treatment". Two points arise. First, given the technical interventions required to induce ovulation etc, can it be suggested that ova obtained in the manner described by the BAC amounts to "processing" or "treatment"? Whilst I have not looked for any relevant Parliamentary discussions in Hansard, as a matter of principle, it seems probable that treatment has indeed taken place, albeit, treatment of the ovaries *in vivo*. The induced ova are very much a product of technical human intervention (hormone injection etc) and the fact that natural biological processes are also involved should not mean that "treatment" has not occurred.

If the harvested ova can properly be regarded as a product derived from treatment of the ovary, the question arises as to whether section 14 applies. The point being that there would have been no need for section 14(4) if organ and blood was not intended to apply to derived products. At present, the Minister has used his power under section

[4] Compare the more limited definition of organ for other statutory provisions such as right to remove organs after death. For the latter, organ is defined as the kidney, liver, heart and cornea. See s.2 HOTA.

14(4) to exempt human blood products and plasma fractions, human hormones, vaccines and toxoids and diagnostic agents derived from human blood.[5] No mention here of ova or indeed stem cells derived from embryos developed out the ova. If "organ" in HOTA was intended to include parts of organs as well as derived products, then as a matter of policy, it is understandable that down stream products requiring human intervention and ingenuity should be capable of being exempted under Ministerial discretion. Otherwise, the reach of section 14 will be very broad and carry prohibitive implications for all sorts of useful products derived from human organs and blood.

It is also noted that section 14(5) sets out provisions catching sale or supply of derived products (other than exempted products). The contract is again void and the vendor/supplier subject to criminal sanctions.

So, if HOTA does extend its prohibitive provisions to derived ova (as distinct from ovaries), the question that arises is whether the Minister should exercise his powers of exemption. If section 14 does indeed apply to sale of induced ova (and query derived stem cells), clarification/amendment may be needed in the light of the conclusions reached by the BAC. Indeed, even if the decision is to leave the matter alone, for the time being, it may be good counsel to seek legislative clarification of the scope of the prohibitive provisions of section 14 and whether it is generally intended to apply to (any) products derived from (any) human organ or blood.

Re-imbursement of expenses

Whilst section 14(1) and (2) generally catches the sale of human organs and blood for valuable consideration, section 14(3) HOTA does permit:

(a) Reimbursement of expenses necessarily incurred by a person[6] in relation to the removal of any organ or blood in accordance with the provisions of any other written law; and
(b) Any scheme introduced/ approved by the Government granting medical benefits or privileges to any organ or blood donor (or their families or nominees).

Depending on the position reached by the BAC, this provision may also need clarification. Assuming, for example, that the view is to only allow reimbursement of expenses arising from the ova donation process, does section 14(3)(a) apply? Do induced ova fall within "removal of organ…"? What is the "other written law" that will activate this provision? In the present context this will most likely refer to the provisions in the Human Cloning and Other Prohibited Practices Act.

[5] Human Organ Transplant (Specified Products) Notification.
[6] This may cover costs of the procedure as well as costs necessarily incurred by the donor.

Human Cloning and Other Prohibited Practices Act (HCPP)

Relevance to the technology: somatic cell nuclear transfer etc.

It is understood that the ova (once induced and removed) can be used for a wide variety of research purposes. These will not necessarily involve the creation of a human embryo. In some cases, however, it seems that the creation of an embryo by somatic cell nuclear transfer (SCNT) etc is necessary as a prelude to the obtaining of stem cells. Section 7 of HCPP prohibits the development of any human embryo other than one created by fertilization of a human egg by human sperm for a period of more than 14 days. Human embryo is defined as any live embryo that has a human genome or an altered genome and that has been developing for less than 8 weeks since the appearance of 2 pro-nuclei or the initiation of its development by other means.

The implications for embryonic stem cell research are clear. My understanding is that SCNT results in the creation of a human embryo: one that possesses a human genome that is a clone of the donor of the somatic cell. If that is so, section 7 prohibits the development of such an embryo for a period of more than 14 days. My understanding is that this is not a problem (in this context) as embryonic stem cells are usually harvested within 5 to 6 days.

Prohibition against importing/exporting prohibited embryos

Section 11 prohibits import/export of prohibited embryos. The latter includes any human embryo developing outside of the body of a woman for more than 14 days. Whilst this is an important provision, it does not apply to derived stem cells and in any case is only relevant to 14 day plus human embryos. It is assumed that this provision will not have any immediate impact on the research into embryonic stem cells.

Prohibition against commercial trading in human eggs, embryos etc.

Section 13 prohibits commercial trading of human eggs, human sperm and human embryos. Any contract is void and the offender subject to criminal sanctions (fine not exceeding $100,000 and/or imprisonment for a maximum of 10 years).

Points worth stressing are (i) the prohibition specifically applies to human eggs (compare HOTA), (ii) commercial trading by way of sale to foreign research bodies will also be caught, (iii) the provisions catch both seller and the buyer and (iv) the criminal sanctions are somewhat more severe than those applying under HOTA.

Thus, whatever view is taken on the scope of HOTA (above) there is no doubt that the commercial supply of human eggs is caught by section 13 of HCPP. A female donor who enters into any such contract/arrangement will be caught by the provisions as they currently stand.

HCPP does not, however, currently prohibit the supply of human eggs *gratis* or otherwise than for valuable consideration. Reimbursement of "reasonable expenses" is allowed including expenses arising from the collection, storage or transport of the egg.[7] Whilst there may be some ambiguity in assessing what amounts to reasonable expenses, it is clear that Parliament intends a conservative approach whereby profit is to be excluded. Altruism (subject to reasonable expenses) is the cornerstone of the provision. In particular, it is to be stressed that HCPP does not permit any inducement, discount or priority in the provision of a service to the person supplying the egg. There is no discretion, for example, vested in the Minister to provide for better access to health care for donors[8].

Clearly, section 13 of HCPP will need careful consideration if the BAC forms the view that egg donors should be allowed to receive a benefit over and above reimbursement of reasonable expenses. Even if a view is formed that the status quo should be maintained, there may be need for a system whereby the Ministry can issue guidance regulations as to what amounts to reasonable expenses.

Private Hospitals and Medical Clinics Act and Related Material

This legislation deals with the control, licensing and inspection of private hospitals, medical clinics, clinical laboratories and healthcare establishments. Section 22 authorizes the Minister to issue regulations on the same.

Private Hospitals and Medical Clinics Regulations

Regulation 4 requires all licensees to comply with directives and guidelines issued by the Director of Medical Services. Failure to comply is currently punishable with a maximum fine of $2,000 and/or maximum imprisonment of 12 months.

Directive for Private Healthcare Institutions Providing Assisted Reproduction Services

Under the Directive dated 31st March 2006, paragraph 8 deals with research on oocytes and or human embryos. The details of paragraph 8 unsurprisingly mirror the provisions in HCPP. It is noted that this Directive is primarily concerned with assisted reproduction services (AR). It is understood that AR procedures may result in an excess supply of eggs and that in this regard, requests for permission to undertake research can arise.

It does not appear that the Directive is primarily concerned with oocytes obtained specifically for research purposes although clearly, similar issues can be expected to arise. Hence it is noted that there are in fact also provisions on donors who are not

---

7 Collection will presumably include expenses necessarily incurred by the donor in participating in the procedure. Perhaps this should be clarified.

8 Compare HOTA. Also note that section 13(4) HCPP makes clear that supply of human egg etc does not include supply for purpose of subsequently implanting the donated human egg etc in the body of another human whether or not for consideration.

involved in fertility treatment. I believe that it will be helpful to clarify the scope of the Directive in relation to excess eggs and AR treatment and non-therapeutic (non-AR) egg donations.

Key provisions in Paragraph 8 worth highlighting include:

- The principal physician and embryologist in charge of the patient's AR treatment must not be the same as the principal investigator of the research team.

- Human ova fertilized with human sperm not to be cultured *in vitro* for more than 14 days.

- No research is permitted on human embryos after 14 days from creation. (This presumably will also apply to embryos created by SCNT).

- No research or experiments on human gametes/embryos without explicit consent of donor. Information to be provided must be comprehensive and there must be no inducements, coercion or undue influence. (This really concerns three issues: sufficiency of information; consent and absence of inducement. A donor may have been given all information and still be induced by some proffered benefit or affected by undue influence etc.)

- In the case of prospective oocyte donors (patients who come primarily to donate oocyte for research and not as part of fertility treatment), there must be a review by a panel comprising a lay person and 2 medical practitioners one of whom is an authorized AR practitioner. The panel must be satisfied that the donor is of sound mind, has clear understanding of nature and consequences of the donation and has given explicit consent free of coercion or inducement before allowing the donation to proceed. In addition, the panel must take account of the public interest and community values when assessing the application. It appears (subject to clarification) that this covers human egg donation for non-therapeutic research purposes. (One might query why there is no reference here to undue influence although it may be said that this is subsumed within the requirement of consent).

Under the existing regulatory framework outlined above, donation of human eggs for research is permissible.

There are two main scenarios whereby eggs can be obtained. The first is where the donor is also an AR patient. Here, my understanding is that the research will involve "excess" eggs not needed for the AR treatment. The research program must be approved by the institutional review board/ethics committees and also by the Ministry of Health. Whilst it appears that some overlap in manpower may arise (between the AR teams and research teams) a clear distinction is drawn between the principal physician,

embryologist and the principal investigator. Explicit consent must be obtained and inducements, coercion and undue influence avoided.

The second are donors who are not seeking AR treatment and whose eggs are sought primarily or solely for research. Again, the research programme must be approved and the donor must give explicit consent, absence of inducement etc. I do not know how many egg donors fall into this category in Singapore. Even if there are very few, it seems that the Directive already contemplates non-therapeutic egg donations.[9]

Permission must also be obtained from the Ministry before any eggs are released to other research centres (presumably whether inside or outside Singapore).

In short, Singapore currently allows voluntary human egg donation subject to explicit consent, absence of inducement and coercion. Payment in cash or in kind so as to provide an inducement is not permitted by the Directive. The supporting legislative framework allows payment of reasonable expenses: but not an inducement.

The line between reasonable expenses and inducement is a real but fine line that may be hard to apply in practice. On one view, even payment of costs incurred by the donor might in one sense be regarded as an inducement of sorts. However, if that interpretation is taken, then the provision allowing for reasonable expenses will be rendered illusory! It is suggested that the better interpretation is that expenses look towards the donor's direct costs and that reimbursement of these should not be regarded as inducement. Some cost elements may be easy to quantify such as cost of transport to the hospital or costs of medication post procedure. Others may be much more difficult. Suppose the donor has taken 5 days leave for the medical procedures: will payment based on what she would or could have earned be allowed? What if she was given paid leave by her employer? Should be expenses be limited to direct out of pocket costs or extend to lost opportunities? Would compensation for time spent/lost amount to an inducement? What if the donor is unemployed: what will be the allowable reasonable compensation for the time spent given that there is no real expense as such? Is compensation driven by reasonable objective expenses incurred or can it also include judgmental components such as time spent and risks taken? Rather than leave this to the discretion of the hospital/research clinic, will it be better for the Ministry to issue guidelines so as to reduce the uncertainty?

[9] For convenience, this Comment uses the terms "therapeutic" and "non-therapeutic" research. The former refers to procedures involving both therapy for the donor/patient as well as medical research. The latter is concerned with "pure" research and with no immediate benefit for the donor. The author accepts that there will be cases where the line between the two types of research are less than distinct. See generally, G. Dworkin, Law and Medical Experimentation: Of Embryos, Children and Others with Limited Legal Capacity, MULR, Vol 13 1987 189 at 191. See also Michael Jones, Medical Negligence at p.570.

Comments

Singapore's drive to take a pole position in the life science industry is well known. The core of the industry is biotechnology: a marriage between the science of genetics and the life science industry including of course information technology.

Much of the raw material for modern biotechnology is genetic in origin. Human genetic resources is one thing that Singapore is not short of; although her limited indigenous bio-diversity will mean that she may need to gain access to biodiversity of other countries in certain areas of biotechnology such as plant and seed variety based research. It is thus not surprising that Singapore appears to have focused her biotechnology push on the life sciences and human genetic (medical and therapeutic) research. However, whilst there may be no intrinsic shortage of human genetic material, society will likely demand and expect restraints in the manner in which that material is obtained (and used) as a result of ethical and related concerns.

Modern biotechnology is big business that relies heavily on scientific discoveries and innovative applications. Modern biotechnology is knowledge intensive and capital intensive. The development of new successful commercial products may be months or years or decades away. But when they come: the social, economic and commercial impact is likely to be considerable. On the other-hand, failures and false leads are also likely to be common-place. Can the product or application in mind (example gene therapy based on cloning of human stem cells) be achieved and if so will the technology be socially/ethically acceptable: not just in Singapore, but in the international community as a whole where the innovation may be exploited? Some genetically engineered products that do appear to work (such as genetically enhanced soya beans) may not be socially acceptable because of perceived health risks or other ethical concerns. Modern biotechnology is not just knowledge and capital intensive: it is also risk intensive.

All knowledge intensive industries require protection of the economic or commercial fruits of intellectual effort, labour and the investment of capital against unauthorised use. It is here that the intellectual property right system comes to the fore. But, biotechnology, law and society, is not just about protecting business and commercial interests. It is also about the need for public regulation and control: the need for ethical standards for research and development of new practical applications, the need for ethical patenting and acquisition of intellectual property rights and also ethical use and exploitation of the products of biotechnology as in the case of claims of a bio-diverse rich country for equitable benefit sharing where inventions are made based on bio-diversity that their indigenous communities have conserved and made available for research. Good business practice is not been just about securing the commercial interests of the enterprise. A balance has to be achieved between commercial interests, the interests of consumers and the public at large. In the increasingly globalised world and open markets, the balance is becoming ever more complex: good corporate

governance and ethical standards for business operations are likely to become even more important than they already are.[10]

One of the most exciting areas of biotechnology concerns stem cell research. The medical and therapeutic applications are eagerly awaited. Even President George W. Bush is not against stem cell research (for medical and therapeutic applications). His problem is with the source of the material on which that research is heavily dependant: human eggs and embryonic stem cells. Hence the current US Government position to limit Federal Funding to stem cell lines derived from embryos whose "life/death" decision had already been taken before 9.00 pm EDT August 9 2001. In addition the stem cells must have been derived from an embryo that was created for reproductive purposes and which was no longer needed. Informed consent must also have been obtained for the donation of the embryo and that donation must not have involved financial inducements.[11]

How long the wait for success will be in areas such as Alzheimer's disease, Parkinson's disease, diabetes, spinal cord injury, macular degeneration etc is uncertain: what is clear is that thus far the promise and hope has been much more than the reality. Risks there are. Aside from financial risks (for the industry), there are the obvious risks to health, the environment and biodiversity as well as ethical risks aplenty for society as a whole. Singapore has recognised the significance of the ethical risks from an early point: hence the setting up of the Bioethics Advisory Committee in 2001.

The ethical question that has arisen for this Consultation Paper concerns not stem cell technology *per se* but the source and means by which a sufficient supply of stem cells can be acquired and maintained. Two issues in particular come to the fore. To begin, there are the pro-life arguments and the status (and argued sanctity) of a human embryo. Second there are the issues concerned with consent: information and inducement. A "conservative" resolution of these issues, lie at the heart of the current US Federal Funding Policy on Stem Cells. Singapore and many other countries have taken a different view especially in respects of the first issue. The status of a human embryo and the circumstances in which a human embryo can be "artificially" created and/or terminated for use in research are clearly extremely important and deserving of full consideration. The issue transcends biotechnology and embryonic stem cell research into other equally controversial and important areas including of course abortion. Hence the earlier work of the BAC especially on stem cell research was timely and necessary. The current position in Singapore has been summarised earlier and the debate over stem cells and use of human embryos will not be re-canvassed here. Stripped of the details, Singapore, along with many countries, permits the use of embryonic stem cells provided the 14 day rule is strictly followed. So it is the question of the supply of human eggs or oocytes that is now in issue.

---

[10] This section is partly based on a Chapter on Biotechnology and the Law, prepared by the author and to be published shortly in Singapore Business Law by Thomson Learning (now Cengage Publishing).

[11] http://stemcells.nih.gov/policy/

Whilst it is my understanding that stem cell research is not necessarily dependent on use of embryonic stem cells (stem cells with varying degrees of pluripotency being available from a number of other sources such as cord blood) obtained from human embryos, up to very recently, this was the "preferred" route. By "preferred" I refer to scientific and industrial research preferences.[12] My understanding is that early stage embryonic stem cells possess the highest pluripotency or ability to develop into specialised cells and indeed organs and tissues. Use of cloned embryonic stem cells also have the advantage of overcoming immune defence reactions and opens the door to patient specific (but presumably very costly) treatment programs. This is the context in which the present Consultation Paper raises the two questions: (i) whether women should be allowed to donate eggs for research and, if so, (ii) whether any payment may be made to, or received by, the egg donor.

But, before addressing these important questions it may be necessary to revisit the threshold scientific question as to whether embryonic stem cells are in fact the preferred or best or better basis on which stem cell research is to be conducted. Of especial importance are the exciting developments announced in November 2007 concerning induction of pluripotent stem cells from a variety of human somatic cells. As I understand it, two different teams (in US and Japan) have pioneered a method of re-programming specialized adult cells so that these return to their original undifferentiated or unspecialized state. These adult cells were taken from a number of non-ethically controversial and widely available sources such as skin cells, connective tissue and cells from the foreskin of a newborn.[13] According to the published reports and a variety of "news sources", the technology involves insertion of 4 transcription factors (genes) into the cell nucleus.[14] These factors effectively re program the cell back to its undifferentiated state: becoming an induced pluripotent cell. Shorn of the details, it is understood that a retrovirus is used as the carrier for inserting the factors into the cell nucleus. It is also understood that questions remain as to the risk of damage (to the genome) arising from the insertion, the use of onco-genes (such as C-MYC as one of the transcription factors) in the procedure and the danger of cancer and risks associated with use of viral vectors. Beyond this, it is assumed that there may still be questions as

---

12 It must also be recognized that a substantial body of researchers and scientists support the pro-life view that stem cell research should not focus on embryonic stem cells.

13 The Japanese team used adult skin cells and connective tissue. The US based team used foetal skin cells and cells from the foreskin of a newborn. See Takahashi et al., Induction of Pluripotent Stem Cells from Adult Fibroblasts by Defined Factors, Cell (2007) doi: 10.1016/j, cell.2007, 1.019. See also Junying Yu et al., Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells. Sciencexpress/ www.sciencexpress.org/20 November 2007/ Page1/10.1126/science.1151526. Use of foetal skin cells can of course give rise to concerns of source. The other sources do not appear to raise any ethical dilemma other than very broad questions as to whether science should tinker with nature. That is not an issue that is considered in these comments or indeed the Consultation Paper.

14 See for example: Ian Sample, Guardian Unlimited at http://www.guardian.co.uk/science/2007/nov/21/stemcells. Seattle Times at http://seattletimes.nwsource.com/cgi-bin/PrintStory.pl?document_id=2004031975&zsection_id=2003912685&slug=stemed26&date=20071126.

to whether IPS cells are as effective as embryonic stem cells obtained in the "traditional way".[15]

If we assume for the sake of argument that IPS cells do indeed possess all the characteristics of ES stem cells including those produced by cloning, the ethical issues surrounding the use of human eggs and human embryos for stem cell research can be neatly sidestepped.[16] But this appears to be a pretty substantial assumption that will require further research. The safety issues referred to above will also need to be dealt with although it is my understanding that some of these (such as use of oncogenes and retroviruses) may not be too difficult to overcome.[17]

Should Singapore switch tact and proceed down the line of IPS research? This is an issue for the scientific experts advising the BAC and Ministerial Life Sciences Committee. I don't know whether Singapore has any research teams using or hoping to use the newly published technique. Doubtless, the Japanese and U.S. research teams and their industrial backers/supporters will have filed for patents. If patents are granted any Singapore researcher will of course have to obtain the necessary licences from the patent holders. Whilst there will be an economic cost in complying with any new patents I understand that the position is no different with ES stem cell procedures since the University of Wisconsin is reported to hold key patents on ES technology in any case.

If we assume that the economic costs of complying with intellectual property rights over the two methods (ES and IPS) are comparable and if it accepted by the scientific community that IPS cells are "as good" as ES cells: then it seems that Singapore should

---

15 See BAC Consultation Paper at p.5-8. See also Chapter 2 of BAC Report on Ethical, Legal and Social issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning, 2002.

16 But query whether this will really be so? Assuming that the technique really does return the adult skin cell into a completely undifferentiated state: does this mean that the transformed cell is just like an embryo and which now has the capacity to develop into a viable newborn? See Gina Kolata, The New York Times, November 21 2007 where it is reported that the Japanese team had previously been able to add 4 genes to mouse cells and to turn these into mouse embryonic stem cells which then developed into mice! Apparently some 20% of the resulting mice developed cancer. Leaving aside cancer risks from using onco genes as transcription factors etc. how does society view the re-programmed somatic cell? Is it just a transformed skin cell or has it effectively become an embryo! If the latter, will this attract the same ethical debate as surrounds human embryos obtained/made in the "normal" way bearing in mind that SCNT cloning technology also requires technical intervention by a human. See http://www.nytimes.com/2007/11/21/science/21stem.html?em&ex=1196312400&en=bac7288684b3db31&ei=5087%0A.

17 In December 2007 it was reported that researchers were able to produce mouse IPS cells for treatment of mouse sickle cell anemia. See, Sickle-cell Mice Cured with Their Own Cells. New Scientist, Dec.6 2007 at http://www.newscientist.com/channel/life/genetics/dn13007-sicklecell-mice-cured-with-their-own-cells.html. See also Heidi Ledford, Stem cells treat Anaemia in Mice, Naturenews 6 December 2007 at: http://www.nature.com/news/2007/071206/full/news.2007.347.html. It has also been reported that Japanese scientists have found a way of producing IPS cells without use of onco genes. See Maker, Adult Cells Reprogrammed to Pluripotency without Tumours, Naturenews, Dec 6 2007 at: http://www.nature.com/stemcells/2007/0712/071206/full/stemcells.2007.124.html.

reconsider the use of human embryos for this area of life science research.[18] Indeed I note that the BAC in its 2002 report on stem cell research, whilst supporting ES research, recommended that:

> "The creation of human embryos specifically for research can only be justified where (1) there is strong scientific merit in and potential medical benefit from, such research; (2) no acceptable alternative exists, and (3) on a highly selective, case by case basis, with specific approval from the proposed statutory body".

It is also important to stress that the BAC had earlier recommended that emphasis should be placed on cell lines already in existence and surplus human embryos created for fertility treatment less than 14 days old. Writing in 2002, the BAC view was that as for source of ES cells "there should be a sufficient supply from ES cell lines (the established lines) followed by surplus embryos" and "that it is unlikely that it would be necessary to create new embryos by IVF for human stem cell research."[19]

Has the position, with the benefit of experience, changed since 2002? Are existing ES stem cell lines together with surplus AR embryos sufficient to meet the needs of research teams in Singapore for ES stem cells? If yes and the shortage of ES stem cells is in other countries which have very strict restrictions on use of embryonic tissues etc: caution will be a very wise counsel before expanding Singapore supply to meet research needs overseas.

The current Consultation Paper (2007) certainly takes the position that surplus eggs from fertility treatment are often retained for use in connection with fertility treatment and that insufficient human eggs are available for research (presumably whether for ES research or other research on human eggs apart from stem cell generation). The present BAC and the current Consultation Paper appear to accept that the scarcity of human eggs is a key limiting factor in stem cell research.[20] If this is indeed the position, then given the (apparent) general acceptance of the utility and desirability of stem cell research in connection with medical treatment of diseases and injuries, the question arises as to what steps can be taken, within ethical limits, to increase the supply of human eggs.

---

[18] See Economist. Report on Stem Cell Research, Nov. 22 2007 reporting that Dr Ian Wilmut (Dolly the Sheep) is so impressed by the new data on IPS that he intends to focus his efforts on "this alternative approach." See http://www.economist.com.

[19] BAC Report, Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning, 2002 at p.28.

[20] See Consultation Paper at p.8. Note however that Dr Benjamin Capps in his helpful background paper entitled "Oocyte Procurement for Research", April 2007 puts the matter more neutrally: "the issue has again come to the fore because of claims that there may not be enough human oocytes to facilitate the advance of embryonic stem cell research. See http://www.bioethics-singapore.org/.

Has the recent announcement over IPS stem cell technology avoided the issue?[21] Whilst this must depend on the views of the scientists and researchers, it is probable that it will be quite some time before the full impact of the "breakthrough" is known and a consensus reached. A quick glance at news sources on the Internet reveal a polarization of views. Some hail the development as a major breakthrough that will obviate the need for any further liberalization of the law on embryonic stem cells. Others beg to differ arguing that a twin track approach will be needed for some time yet: that IPS technology currently supplements but does not replace ES techniques.[22]
For the purposes of this comment, I will assume that exciting though the IPS technology doubtless is that there is still a clear and present need for an adequate supply of human eggs for ES stem cell research. I am also prepared to accept, but on a necessarily tentative basis, that supply of ES stem cells from existing cell lines and surplus AR embryos is inadequate to meet current research needs *in Singapore*.

I turn then to the two issues at the heart of the current Consultation Paper. First, there is the question whether women should be allowed to donate eggs specifically for research purposes. As indicated already, my understanding is that under the HCPP and the Private Hospitals and Clinics Act (together with the Directive), donation of human eggs for research is already permitted subject to compliance with the established procedures. If that is so, there seems to be no sufficient reason to change that position: at least not until the impact and implications of IPS technology becomes much clearer.

Consent and the Law

Leaving aside specific statutory requirements, consent is driven by the common law torts of battery and negligence. Battery in this context is primarily concerned with individual autonomy whilst negligence is mainly concerned with ensuring that medical/research conduct does not fall below standards of reasonable medical practice. Adequate consent is essential to avoid liability under either tort. That much is clear. The question of what constitutes a valid consent is less certain: different common law

---

[21] The BAC Consultation Paper at page 6 recognises that IPS may reduce need to rely on human embryos. There it is stated that "SCNT may be used to study nuclear reprogramming which is a process by whereby a somatic cell is converted into one that has the capacity of an unspecialized cell to develop into a living organism (totipotence) or differentiate into all types of cells (pluripotence). Understanding this process may lead to the possibility of achieving direct reprogramming, which does not involve the use of eggs of the need to create embryos." Have the recent announcements on IPS research already proven the case for direct reprogramming of somatic cells?

[22] Apparently some scientists at the leading edge of IPS research accept that there is still a need to push ahead with embryonic stem cell research. See Artificially Created Stem Cells Cure Sickle Cell in Mice. Dailytech, December 8 2007 at: http://www.dailytech.com/Artificially+Created+Stem+Cells+Cure+Sickle+Cell+in+Mice/article9937.htm. See also the AFP Report Nov 27 2007: Stem Cell Pioneer says Embryonic Research still Needed. http://afp.google.com/article/ALeqM5jIUGHePXLAdeS4Rc52rHOk7fHAAg. According to this report, Shinya Yamanaka who led the Japanese research team on IPS accepts that embryonic stem cell research is still needed. In particular it is noteworthy that Yamanaka is of the view that it will be a long time before researchers could treat stem cells from skin like those from embryos. Compare this with the article by Doyle, Promising Stem Cell Breakthrough is a Moral Milestone, say Catholic Ethicists, December 7, 2007 at: http://www.the-tidings.com/2007/120707/stemcell.htm.

jurisdictions may well take different views on this. For the purposes of this Comment, the author assumes that Singapore courts are likely to take a position that is similar to that taken in England.

To avoid battery, the general approach taken is to ask whether the patient has been informed in broad terms of the nature of the procedure and armed with that knowledge, gives consent.[23] Failure to explain risks and implications is generally regarded more as the concern of negligence.

To avoid negligence, the doctor must of course carry out the medical procedure with reasonable care. But, even before carrying out the procedure, he/she must provide the patient with sufficient information. How much information must be provided and the reference point for sufficiency (patient or doctor centric) is a matter of some controversy. Nevertheless, Professor Dworkin writing in 1987 states that Sidway "appears to have established a test loosely based upon what a reasonable doctor would tell the patient in the circumstances…" From this perspective, Professor Dworkin concludes that "…full rein is not given to the concept of patient autonomy and there is considerable scope for a patient's information to be limited, and, indeed, for the doctor in some cases deliberately to withhold information by using his therapeutic privilege…"[24]

Using the above framework as the starting point, two important issues arise in the context of egg donations. First, does consent validate all medical/research procedures as a matter of law? Second, whether a stricter approach should be taken in cases of non therapeutic research.

So far as the first issue is concerned, it is clear that the law does not permit all and any type of bodily intrusion under the cover of consent.[25] Thus in one well known English case, the fact that sadomasochistic acts of mutilation were consensual was no defence to a prosecution.[26] In the case of medical treatment or medical research, public policy of course allows and supports bodily intrusions but not without limits (especially in the case of medical research).

Where is the line to be drawn? Professor Dworkin with some force argues that "clinical research, within reason and subject to a reasonable risk/benefit ratio, is clearly not against public policy…" It follows that the greater the risk of harm to the patient/donor, the greater the importance of counterbalancing benefits. Where the risk of harm is high and where the consequences to the patient/donor are severe, it is difficult to see how the

---

[23] Chatterton v Gerson [1981] QB 432; Sidaway v Bethlem Royal Hospitals [1985] AC 871; Freeman v Home Office No.2 [1984] 1 All ER 1036. Cf Tan Keng Feng at (1987) 7 LS 149.

[24] Dworkin, Law and Medical Experimentation: Of Embryos, Children and Others with Limited Legal Capacity, MULAR Vol 13 189 at 193.

[25] Professor Dworkin ibid. notes at p.193 that in some countries, statute law prohibits tattooing of persons under 18 even though they have consented and that the common law, as a matter of public policy, will not allow a person to consent to be maimed unless there is some sound justification, such as medical treatment.

[26] R v Brown [1993] 2 All ER 75.

procedure could ever be justified under common law. Even where the expected benefit counterbalances the risk, the degree of risk must have an effect on the information to be disclosed to avoid a suit in negligence. Professor Dworkin rightly stresses that in the case of non therapeutic research, the therapeutic privilege has no application and that in Halushka v University of Saskatchewan[27] it was said that "the subject of medical experimentation is entitled to a full and frank disclosure of all the facts, probabilities and opinions which a reasonable man might be expected to consider before giving his consent." Professor Dworkin was of the view that "indeed, the law may be more demanding, in that a patient is entitled to information about all the facts which may be material to him, even though they may not be of significance in scientific terms."[28]

What then is the current position in Singapore on egg donation? I turn first to adequate consent.

At present, the Directive for Private Healthcare Institutions Providing Assisted Reproduction Services provides in paragraph 8.6 that in the case of prospective oocyte donors (patients who come primarily to donate oocyte for research and not as part of fertility treatment) that:

- There must be a review by a panel comprising a lay person and 2 medical practitioners one of whom is an authorized AR practitioner.

- The panel must be satisfied that the donor is of sound mind, has clear understanding of nature and consequences of the donation and has given explicit consent free of coercion or inducement before allowing the donation to proceed.

- In addition, the panel must take account of the public interest and community values when assessing the application. (One might query why there is no reference here to undue influence although it may be said that this is subsumed within the requirement of consent).

I am unable to comment on how this provision has actually worked in practice. In principle, the requirements are in general unobjectionable in the light of the legal framework outline above. Some points of clarification may however be helpful.

Clearly the donor must be of sound mind. Is there any need to protect vulnerable female donors such as teenagers? Is there a case for a provision that the donor must be over the age of 18 or indeed 21 or, that at the very least, consent of parents are also obtained? This may well be the practice: but if so will it be helpful to build this into an explicit

---

27 (1966) 53 DLR (2d) 436. See also Michael Jones, Medical Negligence, at 6-177.

28 Ibid at p.194. Note also that a difference may have to be drawn between consent by a competent adult and proxy consent for example on behalf of an infant. In the case of proxy consents (by parents for a female child under the age of majority), arguably a stricter view should be taken on the degree of acceptable risk. It is one thing to consent to a risky research procedure on one's own body: quite another to do so for another by way of proxy. In England, it seems that proxy consents for children are only justified where the risk is *minimal*.

affirmative requirement?[29] As a matter of principle, my view is that it is likely that the common law will permit a person under the age of 21 to consent to medical research provided he/she has sufficient maturity and understanding. But, as Professor Dworkin notes, the younger a person is or the more intrusive the research, the more difficult it will be to persuade the court that the child had capacity to consent.[30]

Clearly the donor must have an adequate understanding of the nature and consequences of the donation. But, is there a good understanding even amongst the medical profession as to what the nature and consequences are? To be sure, the nature of the medical procedure (use of hormones, anesthesia etc) and the associated medical risks must be disclosed in language that the donor understands. But what are the risks associated with ovarian stimulation etc? The Consultation Paper states that the risk in egg retrieval is relatively low. The Background Paper on the other hand appears more cautious recognizing that "some specialists in reproductive medicine are concerned that there is insufficient information about the long term effects of these drugs to encourage healthy volunteers to undergo such procedures when there is no reproductive benefit to balance against the risks."[31] Risks of infection are also mentioned as are psychological risk factors.

But supposing that all *the risks and uncertainties* (short term and long term) are explained: why shouldn't the donor be allowed to proceed? After all, drug trials on healthy patients, carry similar if not even greater risks. All pioneering medicine involves risks and uncertainties. Even if it is entirely uncertain as to how long it will be before successful treatments are developed for diseases such as Alzheimer's disease or spinal injury: the benefits if successful will be incalculable. What is under consideration is not stem cell research for the sake of eugenics or human vanity: it is stem cell research in the hope that it may lead to treatments for severe debilitating diseases and injuries. It seems to me that this hope is well worth encouraging: provided full information on the medical risks and uncertainties are explained to the donor.

---

[29] The age of majority in Singapore is 21. In the absence of statutory provisions, the position of minors and consent depends on the common law. In some cases consent by proxy (usually parental) will be necessary. In other cases, were the procedure is minor, the child may have capacity to consent if he/she is capable of understanding the treatment. Gillick v West Northfolk and Wiesbech Area Health Authority [1985] 3 All ER 402. Professor Dworkin, ibid. at p.196 states that the age and seriousness of the procedures are directly related: a child may have legal capacity to consent to a trivial medical procedure at an earlier age than to a more serious medical procedure. Egg donation procedure would appear to involve a serious medical procedure.

[30] Ibid at p.197. Assuming that parental proxy consent is needed, there remains the tricky question as to the criteria by reference to which the proxy consent is to be judged: best interest of the child, substituted judgment, not against interests of child etc. Professor Dworkin notes at p.202 (1987) that the English view was that a socially responsible parent might think that there was merit in taking social interest into account and contributing to medical research provided always that the risk to the child was minimal. Professor Dworkin also supports the case for legislative clarification of the power to give proxy consent for the purposes of research on children.

[31] Dr. Benjamin Capps at p.7 citing Pearson, H. 2006. Health Effects of egg Donation May Take Decades to Emerge, Nature 442: 607-608.

Would it be helpful in this context for the MOH to issue guidelines as to the medical information that should be explained to women considering becoming egg donors? In this regard, recognizing the importance of giving the prospective donor adequate time to reflect, should a minimum period of time be required to elapse between the explanation and her making of the decision or the carrying out of the procedure (a cooling off period as such and always allowing for a change of mind)?

Still on consent and the importance of explaining the nature and consequences of the donation: what about the non-medical consequences? Much research into stem cells is likely to take place with a view towards commercial application. Distinction between pure academic research and applied or industrial research is increasingly blurred: academics are now often partners with industry. New IPS or ES procedures may be patented. New drugs or treatment products such as "replacement neurons" may also be subject to patent claims of one form or another. The desire or need to protect the investment of the pharmaceutical/industrial arm of the research effort is understandable. Should this be made clear to the donor: for example, that the research may lead to valuable commercial applications and that under most legal systems, she as donor will have no share in any resulting intellectual property? This is quite apart from the inducement issue. Is it not fair and reasonable to make clear to a prospective donor, that the research may well result in downstream commercial applications.[32]

A connected point is whether as a matter of principle, the donor should be given information as to who is conducting the research and the use to which the eggs are to be put.[33] On this I note the earlier recommendations of the BAC in its 2002 Report on Human Tissue Research which touch on the question of human tissue banks.

That the consent must be explicit is understandable: perhaps this should be clarified to mean "written" consent. The requirement of "no coercion" is equally understandable although there must be some ambiguity as to what coercion refers to. The obvious case of threats will be easy to deal with. It is the less clear cases where perhaps greater clarity is needed. Experience in other countries actively pursuing stem cell research suggest that female members of research teams may be under subtle or sometimes not so subtle pressure to donate eggs. A person may be "unduly influenced" without being "coerced" as such. The mere fact that there is informed consent does not mean that there is no coercion or undue influence.[34]

---

[32] See Moore v Regents of the University of California 793 P2d 479.

[33] See Helsinki Declaration. Art 22: "In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail …" See http://www.wma.net/e/policy/b3.htm. Brazier, Medicine, Patients and the Law, 3rd ed. rightly underscores also the need to demonstrate volition. She asks the highly relevant question at 404: "Do medical students feel under compulsion to assist in drug trials mounted by their teachers? Do patients feel obliged to help their doctor if he asks them to participate in non-therapeutic research"? See also Michael Jones, Medical Negligence, 2003 at para 6-165 where it is argued that non disclosure of research objectives may well invalidate consent (for purposes of tort of battery). A similar view is taken by Kennedy & Grubb, Medical Law, at 1710.

[34] Professor Dworkin, ibid at p.204 whilst recognizing that students may be vulnerable, agrees that it does not follow that all financial inducements should destroy the voluntary nature of all responses.

Where the donor is in a vulnerable position (medical student, employee of research team etc) the institutional review panel should be under a positive duty to ensure that no undue influence has been brought to bear.[35] The medical researcher should bear the burden of establishing that no undue influence or coercion was used to obtain the consent.[36]

A more extreme (but simpler) position will be to exclude medical students, employees, members of research team or the institution concerned from volunteering as donors.[37] Is the latter realistic? Is there any reason why medical students and the like should not be allowed to give consent subject to the proviso that the researcher proves that no undue influence has been used and the donor given the opportunity to receive independent advice? Is there any consensus in Singapore on this? If patients seeking IVF/AR treatment are permitted to donate excess eggs for stem cell research, is there any reason to disallow medical students/members of research teams from volunteering always assuming that proper consent has been obtained. Both are vulnerable donors (in that they may be susceptible to influence). If a proactive requirement of ensuring independence in the consent procedure suffices for patients, why should it be any different for medical students and research team members?

Then what of the question of inducement? As currently framed, the consent must be free of any inducement.[38] Non-financial inducements are also caught. That said, in the majority of cases where this may be relevant, the inducement is likely to be in the form of money or money's worth such as priority medical treatment. For convenience these will be considered under a number of headings of increasing difficulty.

Reimbursement of costs/expenses

Reimbursement of costs/expenses incurred by the donor does not appear to run counter to the spirit of altruism that society seeks to encourage. If the donor could not be paid direct costs/expenses incurred then not only is she altruistic she is also in a real sense being asked to underwrite part of the research costs. Section 13(3) of HCPP does allow the payment of reimbursement for reasonable expenses incurred by a person in relation

---

On the other hand, the fact that the consents were fully informed is not conclusive on the question of volition.

35 Kennedy & Grubb, Medical Law at p.1722 where the issue of voluntariness is discussed in the context of persons who may volunteer for research because of some felt pressure.

36 See Professor Dworkin, ibid at p.204 where he argues that fiduciary principles can be relied on to impose an affirmative burden on the researcher. Professor Dworkin also stresses at p.205 that ethical research committees in deciding whether to approve the research must take account of the risk/benefit factor. In the case of proxy consent for non therapeutic research on children, it appears that England allows these where the risk to the child is minimal. The assessment of risks is bound to be controversial. Minimal risks (in the case of proxy consent) are said to be those where the probability and magnitude of physical and psychological harm are no greater than that encountered in daily lives or in routine medical or psychological examination of healthy children.

37 See generally also the discussion by Michael Jones, Medical Negligence, 2003 at 6-164.

38 Inducement in this sense vitiates consent. Threats can be a powerful form of inducement such as a threat to withhold treatment or to dismiss from service. Inducement can also take the form of offer of benefits. Either way, what the law is concerned with is the free will of the patient/donor.

to the supply of any human egg. This is not limited to the donor but includes any person in relation to the supply. So, if a donor incurs transportation fees to go to the clinic or has to buy creams or drugs to mitigate discomfort in connection with collection of her egg: reimbursement should be permitted. If a research team having extracted her eggs with her explicit informed consent (and complying with the necessary procedures) transfers the eggs to another research team in a different institution, they will not be allowed to charge a fee but may recover reasonable expenses incurred in respect of the collection, storage and transportation. From the perspective of the donor, how much "out of pocket" expense will she likely incur in undergoing the extraction procedure? It is unlikely in most cases to be substantial. If this is the sum total of her entitlement: then as Dr Capps points out, the donor may well be financially worse off as a result of the procedure.[39]

But, is there any reasonable alternative? Reimbursement of direct "out of pocket" expenses of the donor should not be regarded as a prohibited inducement. Whether there should be some other payment for loss of time and risks incurred is likely to be far more controversial.[40]

Compensation for loss of time

What then about the time expended by the donor? This is less clear and in any case the circumstances can vary considerably. The time lost may translate into lost wages or opportunity to work (if self employed). In other cases, the medical procedures may be conducted after working hours or at weekends etc. In some cases, the employer may have given permission to take paid leave to make the egg donation. In other cases, the donor may be unemployed and without any or any regular source of income. Loss of earnings may be considerable: it may also be non existent. If the donor has indeed suffered objective financial losses, such as lost wages, payment of compensation restores her to the financial position she would have been in but for the donation procedures. In this sense, the compensation whilst still a form of inducement, does not result in any "profit" for the donor. On the other hand, if the donor was out of work, any payment for the time expended will represent a very real financial gain. An inducement in the sense of compensation for actual financial losses may be less controversial than an inducement that is founded on financial benefit.

But, even in the case of compensation for loss of earnings: problems may arise. In the case of actual lost wages: objective assessment may be relatively easy: at least in some cases. Troublesome cases will not be hard to find. What if the medical procedures take place on her off days or after office hours or if the employer continues to pay her salary? What if she is self-employed and the time lost is loss of work opportunity?

---

[39] Background paper at p.12.

[40] Questions may arise as to how direct out of pocket expenses are calculated. Should these be subject to some overall requirement of reasonableness? How will the scheme deal with a foreign donor who claims the cost of air flight to Singapore etc to participate in an egg donation procedure? This may be dealt with either by having a cap on direct out of pocket expenses or by limiting participation to donors resident in Singapore and who are either citizens or permanent residents with a specific exclusion for donors who are merely on a social visit/work permit.

Should there in any case be a "cap" on the amount payable? As an alternative, is it preferable to have a fixed/standardized payment in recognition of the time spent and the general inconvenience of the medical procedure?

Payment of compensation for loss of time, wages or earning opportunity appears to be fraught with difficulties of assessment, proof and limits. Even in UK, Dr. Capp notes that compensation for loss of earnings is capped at £55.19 a day with an absolute limit within each cycle of oocyte donation of £250.[41] For some donors, this amount may not be of any financial significance. For others, the amount may be of considerable significance and may even attract cross border movement.

Benefits in Kind

The idea of payment by way of benefits in kind in return for contributions towards medical treatment is not new. Indeed, section 14(3) HOTA expressly recognizes any scheme introduced/ approved by the Government granting medical benefits or privileges to any organ or blood donor (or their families or nominees).

Where the donor is also seeking AR treatment it may, as Dr. Capp points out, be possible to provide subsidized IVF treatments in return for donation of excess eggs for research. This obviously is irrelevant where the donor is providing the eggs specifically for research and is not seeking AR treatment. My understanding is that the main thrust of the BAC Consultation Paper is concerned with the latter scenario. If so, then the provision of benefits in kind in the form of subsidized IVF does not address the problem. Even where the linkage is made between use of excess eggs and AR treatment, Dr. Capp rightly points out that problems of "abuse" may arise. Under such a scheme, there may be an "incentive" to induce as many eggs as possible with an eye to using the excess for stem cell research. The tensions that this creates between the goals of medical treatment and research are clear. It is understood that there are real health risks associated with the oocyte stimulation procedure. It must follow that from a pure AR or IVF perspective: the lesser drugs used and the lesser induced oocyte cycles the woman undergoes, the safer it will be for the woman's health.[42]

---

41 This is about 745 Singapore dollars.

42 I do not know how many excess eggs on average there are left after completion of AR treatment for a donor. Doubtless this is a matter for the scientific experts and medical profession to investigate. If subsidized IVF is considered for such donors, care must be taken to ensure that the best interests of the patient (and fetus assuming the IVF is successful) from the medical perspective has priority over any research objectives. To this end, strict compliance with the rule requiring the principal physician to be independent of the principal researcher must be adhered to. The MOH should consider whether a simple requirement that they are to be different persons is sufficient to ensure independence. They may be different persons but working in close cooperation! In the case of vulnerable donors, what is needed is a system to ensure that the donor has a reasonable opportunity to discuss the matter with persons independent of the research exercise.

Indemnity for adverse medical consequences

Leaving aside inducements, another issue that may be worth examining concerns the position of a donor (especially one who provides eggs specifically for research and not as a result of an AR or IVF program) who suffers ill effects from the procedure: the drugs used to induce ovulation, anesthesia, removal procedures etc. Granted, the BAC Consultation Paper indicates that few cases of adverse side effects have been reported. Nevertheless these may become more common and in any case it will presumably be a while before long term effects become clearer. The donor may not necessarily have any legal cause of action against the doctors, medical researchers and hospital. If proper consents have been obtained, and if the necessary information provided before the procedure and if due care is taken, an action for battery or negligence will be hard to maintain. A successful suit will be even more difficult where the adverse consequences only appear many years after the event. There must be some risk that the donor will find that she has to bear the consequences of her decision to donate. Some may say that medical risks are part and parcel of medical research and if a donor has decided (with the necessary information) to consent, that decision and risk is part and parcel of the altruism underlying the donation.

But can society do more in return to protect the interest of such a donor from adverse consequences? What is the position in respect of the costs of medical treatment in the event that some complication arises: whether short or long term? These could be substantial. What about compensation for pain and suffering and any loss of earnings arising from any disability? How significant will causation issues be: especially in the event of injuries or disabilities that only surface years after the event? This is a tricky issue that requires a considered response. In UK, one commentator notes that liability in tort (based on fault) may be hard to establish. For this reason it is said that:

> "… all modern guidelines or directives as to the management of research projects emphasize the importance of compulsory protection of subjects against the possibility of mishap. Thus the mandatory EC Directive states unequivocally that a clinical trial may be undertaken only if, inter alia, provision has been made for insurance or indemnity to cover the liability of an investigator and sponsor … while before approving a proposal, a REC in the UK must, currently be reassured as to insurance and indemnity arrangements for treatment and compensation in the event of injury, disability or death of a research participant attributable to participation in the research."[43]

The commentators continue by noting the uncertainty as to what amounts to sufficient reassurance. Recommendations of the Association of British Pharmaceutical Industry state that compensation should be paid when on the balance of probabilities the injury was attributable to the administration of the medicinal product under trial or any clinical intervention or procedure provided by the protocol that would not have occurred but for the inclusion of the patient in the trial. Two points may be worth

[43] Mason, McCall Smith and Laurie, Law and Medical Ethics, 6th ed.592. The authors explain that the provision on reassurance is found in Guidelines para. 9.15(1).

raising. First, this recommendation seems to be concerned only with medical risks arising from drug trials. What about risks associated with provision of tissues, ova and the like? Second, it is just a recommendation. To what extent is the recommendation followed in practice? How will the research team provide reassurance: insurance, industry funds?[44]

In principle, this commentator agrees that some scheme should be implemented (supported by law) to provide compensation for individuals injured in the name of non-therapeutic medical research. The scheme should not be limited to participants in drug trials but should extend to an include persons volunteering in human egg donation programmes.[45] If such a scheme is implemented, the question as to whether it is made applicable to both therapeutic and non-therapeutic research participants will also need consideration. If such a scheme is established, there is no reason why it should be seen as diluting the moral value of the donor's contribution. Such a scheme may go some way to reassure volunteers in all types of medical non-therapeutic research that society values and respects the risks they are undertaking.

Indeed, the issue of compensation for adverse consequences arising from drug trials is not new in Singapore. In 1999 Dr Woo wrote:

> "Singapore, the government has decided will be shaped and poised to become a hub for R&D of drugs. The government, through the Economic Development Board, will be investing and inviting companies locally as well as overseas, to commit and invest in Singapore as a regional hub in Asia for pharmaceutical R&D… There will be a greater need for more clinical trials … All clinical trials must be conducted in accordance with the Declaration of Helsinki"[46]

More recently, the National Medical Ethics Committee (NMEC) has issued updated recommendations on Phase 1 Clinical Trials.[47] The very early point underscored in its

---

44 See also Brazier, Medicine, Patients and the Law. 3rd ed at 412. The author notes that the English Pearson Committee recommended a no fault strict liability system. Writing in 2003, the author states that no change in the law had been effected. Instead, various ex-gratia schemes have been implemented by the pharmaceutical industry. She notes that "the case for no-fault compensation of persons injured in the course of research has long received wide support among doctors too. The burden of compensating those injured in the course of research to benefit us all should have a wide base. A fund could be financed from all bodies promoting research, from the medical profession, the pharmaceutical industry and the Department of Health".

45 This is without prejudice to the requirement that the research must be approved in the usual manner.

46 KT Woo, Conducting Clinical Trials in Singapore, Singapore Medical Journal 1999 Vol 40(04). http://www.sma.org.sg/smj/4004/articles/4004ra4.html. Dr Woo notes that it is the responsibility of the Medical Clinical Research Committee to, amongst other things, ensure the protection of the rights, safety and well being of human subjects involved in a trial. Dr Woo also stresses that Hospital Ethics Committees have the responsibility of reviewing the amount and method of payment to subjects to assure that neither presents problems of coercion or undue influence on the trial subjects. Issues of compensation available are also within their purview.

47 http://www.moh.gov.sg/mohcorp/uploadedFiles/Publications/Guidelines/NMEC_Guidelines/NMEC%20Compn%20Clin%20Trials_24%20May%2007_final_public_clean.pdf. Interestingly, the Recommendations note (in the context of clinical drug trials) the practice in Singapore that

Recommendations was that investigators should preserve and maintain the public's confidence in medical research by offering care and adequate compensation for adverse events arising from their studies. Specifically, the NMEC recommends that:

> "11 Institutions that allow non-physician investigators to do clinical studies should take out specific insurance cover for liabilities that these investigators may incur.
>
> 12. Research ethics committees should ensure that there are no gaps in responsibilities for providing compensation for relevant no medical costs and for medical bills that arise from adverse events …
>
> 13. Medical costs and relevant compensation should be awarded on a no-fault basis."

The NMEC rightly stresses that the UK Guidelines of the Association of British Pharmaceutical Industry are based on the assumption that the injured in the UK have access to free and continuing health care under the National Health Service. The position is different in Singapore. The NMEC stresses and this commentator agrees, that:

> "the individual's own medical insurance cover may not apply to injuries sustained in a clinical trial and even if it did it would not be right for sponsors of clinical research to draw upon this source of income of insurance for injuries due to their studies, nor should the participants suffer the recurring increase in annual premiums that would result there-from."[48]

If it is right and proper to require a no fault compensation scheme for adverse consequences arising from participation in clinical drug trials, this commentator can see no reason why a similar scheme should not be made available for human egg donors for non-therapeutic research (or indeed any person who participates in medical research where that research is for the public benefit).

---

participants are reimbursed at modest rates for time, transport and inconvenience. Free medical assessment and comfortable accommodation for overnight stays are sometimes offered. It is also said that the centres are guided by principles to avoid encouraging people to participate in trials for financial gain. This indicates support for the view that in the case human egg donations for non-therapeutic purposes: financial gain should not be the basis of the donation. Can any distinction be drawn between clinical drug trials and ES research using donated eggs?

[48] Interestingly, the NMEC accepted that payments for participation in trials should be commensurate to the burden of participation and that the remuneration and other benefits offered should not be such as to induce people to volunteer against their initial judgment. This suggests that NMEC is against payments by way of inducement and that remuneration should be limited to expenses of participation.

Assessment

TYPE	BENEFIT	FIVE YR SUCCESS	RISK PROBABILITY	SEVERITY	ETHICAL ISSUES
Blood donation	Clear (I)	High	Low	Low	Consent and vulnerable donors. Commodification
Kidney	Clear (I)	Good	Medium	High	Consent and vulnerable donors. Commodification
Drug trials	Clear (S)	High	Medium	High	Consent and vulnerable persons. Commodification
Participation Survey	Unclear	Unclear	None	None	Privacy issues
Oocyte Donation	Possible (potentially enormous)	Uncertain	Low/uncertain	Low but uncertain	Consent and vulnerable donors Commodification Pro-life issues

Before attempting to reach some conclusions to the questions raised by the BAC, a comparative assessment of different types of "medical" altruistic behaviour involving living healthy donors may be of some help. The above Table selects 5 such activities. There are of course many more activities that could be included but for convenience, these will suffice.

The assessments are entirely judgmental and based on current the understanding (or lack thereof) of the author. The Table and assessments are simply used to assist the author in reaching a view on the questions raised. They are in no way based on empirical research data. [49] "Benefit" refers to benefit to the recipient (I) and/or society (S) as a whole. "Five Years" success refers to the likelihood that after 5 years the benefit will be ongoing. "Risk Probability" refers to the likelihood of adverse health

[49] In particular, the author stresses that the difficulty in deciding the applicability/relevance of some of the factors was in itself a useful exercise. The author accepts that other commentators may single out other factors or come to a different view as to relevance and applicability of the factors referred to. The author apologies in advance if the risk assessments are off the mark.

consequences (primarily to the donor). These include short, medium and long term risks. "Severity" refers to the likely seriousness of the adverse consequences.[50] "Ethical issues" refers to the main ethical issues have arisen in respect of the donation in question.

Blood Donation. In the case of blood donations, the benefit to individual recipient is clear and obvious. My understanding is that whilst there are some alternatives such as "artificial blood" and saline solutions etc, the preferred choice will always be compatible human blood. The 5 year probability of success in the sense that the donor/recipient will still be alive and/or derive a benefit is high. The risk of adverse effects is understood to be low. For the donor: it is primarily risk of infection and some discomfort associated with the procedure. For recipient, it is also primarily risk of infection but this time from the blood itself. Overall, the severity of adverse effects to the donor is presumed to be low (although for the recipient it can be high as where the recipient receives HIV or Hepatitis B infected blood). What are probably more important to the BAC questions are the risks to the donor. It is likely that blood donation is now regarded as a "routine" medical procedure. Whether the medical risks are "minimal" or "negligible" it seems that in most cases the risk to the donor is very low. Ethical issues are also likely to be few and to primarily concern vulnerable donors, consent and commodification issues. By this, I refer mainly to the issue as to whether donor should be paid a sum over and above "out of pocket" expenses.

Kidney Donation. Again, the benefit to the recipient is clear and obvious (as also in many other living organ transplant cases such as donation of liver lobes). Alternatives do exist such as dialysis, artificial kidneys and trans-species transplants. The most common alternative I understand is dialysis. The long waiting list for human kidneys underscores the obvious point that the latter is much preferred. The 5 year success probability is likely to be good. The risk of adverse effects to the donor is medium. There are the risks inherent with the invasive medical procedure, infection and the use of associated drugs. Whilst many kidney transplants from living donors are successful, adverse health consequences can be high. For the donor, there must be some risk of death during the procedure and the fact remains that post operation, he/she will only have one kidney instead on two. I am not sure how high the risk is to the donor but this much is clear: kidney donations are not routine medical procedures and the risk of

[50] The author understands that in the United Kingdom the term "minimal risk" refers to those where the probability and magnitude of physical or psychological harm is the same as that encountered in routine medical or psychological examinations. See Dworkin ibid at 205. Dworkin also notes that in the USA, a minor increase over minimal risk for proxy consents refers to risks of harm or discomfort greater in probability of magnitude than those encountered in the normal life of children but not posing a significant threat to the child's well being. See also PJ Nicholson, Communicating Health Risk, Occup. Med. Vol. 49 No 4 253 at 255 where minimal risk is described as "1/100,000 – 1/1,000,000 eg railway accident." Nicholson refers to a classification that places being struck by lightning as a "negligible risk", death from playing soccer as "very low risk", death from influenza (low risk), death from smoking 10 cigarettes a day (moderate risk), transmission of measles as "high risk". Minimal risks are between negligible and very low risks. See also Kennedy & Grubb, Medical Law, 3rd ed at 1726. Minimal risks are said to be those where the risk of death is less than 1 in a million and risk of major complication less than 10 per million and risk of minor complication less than 1 per thousand.

adverse consequences must be quite a bit higher than in the case of blood donation. Ethical issues can arise. These concern commodification, integrity and even "sacredness" of the human body (donor is giving up a healthy organ). In some cases, the ethical dilemma may be far worse as in the case of alleged forced donations (for example from prisoners) and donations by vulnerable persons.

Drug Trials. The benefit of drug trial participation is also clear. This time the benefit is to society at large. Alternatives may exist in the form of animal studies and *in silica* testing. These are however unlikely to replace human drug trials and it is assumed that for the foreseeable future, drug trials will remain essential. The 5 year success probability is good in the sense that the knowledge obtained will still be of relevance and utility. The risks to the donor are likely to be medium and presumably largely concern unexpected adverse reactions. Long term risks may be even less predictable. Participation in drug trials is far from being routine and the risks may vary quite a lot depending on the nature of the drug. In some cases, it is presumed that the severity of adverse consequences can be high. Ethical issues largely concern commodification. In some cases, there may also be problems associated with forced or deceptive testing.

Participation in Survey Studies. By this, I refer to general research studies into the social/life style backgrounds that may have an impact on disease incidence. Whilst such studies can benefit society, it is probable that the benefit will not be as clear. That said, the risk probability is very low and ethical dilemmas largely concern the need to maintain confidentiality and privacy of the identity of the participants.

Donation of Oocytes. The immediate benefit to society is not as clear as in the case of participation in drug trials or blood or organ donation. The chances of success after 5 years (in the sense of a proven benefit), is also uncertain. Some suggest that it may be decades (if ever) that embryonic stem cell research will lead to new therapeutic treatments. Others are far more optimistic. If ES stem cell technology does succeed, the benefits however may be immense or incalculable. Organ transplantation (kidney, liver, heart, corneas etc) may cease to be a problem, spinal cord injuries corrected and the ravages of Alzheimer's and Parkinson's disease brought under control. But, the "if" remains significant. ES stem cell research lies somewhere near the start of the long "R&D" process behind new medical therapies. The further back or nearer the start of the R&D time-line: the greater must be the uncertainty of what and when practical benefits will arise. In the case of drug trials, the position is different. These typically are near the end of the R&D process. The drug has been researched and tested on animal models. Commercial release into the market may be just around the corner. Studies have been conducted and patents obtained. Whilst unexpected and sometimes disastrous adverse effects may arise (short term, medium or long term) drug trials are conducted with a real expectation of benefit in the immediate future.

But, the story behind many scientific/medical breakthroughs often begins with a "journey into the unknown". The potential benefits of ES research are enormous and broad based (multi- disease/injury). The risk of adverse consequences to the donor appears to be low (especially in the case of short term consequences). Long term risks

including increased incidence of ovarian cancer from the hyper-stimulation of the ovaries is less clear. Similar risks are undertaken by women undergoing IVF/AR procedures (although here the risk is balanced by the benefit of pregnancy).The consequences of ovarian cancer may be severe. But, it is likely that equally if not more severe risks may arise from participation in drug trials. Aside from rejecting stem cell research in its entirety, are there real alternatives to ES stem cell research? To be sure, there are some research paths that involve the use of adult stem cells or cord blood. It is understood however that these may not be as useful as ES stem cells: either because of lesser degree of pluripotency or because of problems associated with immune responses.

IPS technology may be different. Immunological problems will not arise but there may be problems associated with the use of oncogenes and viral vectors. Doubts remain as to whether IPS cells truly mimic ES cells. If the promise of IPS holds true, then it may well offer a viable: indeed better route to stem cell technology than the current dominant ES model. But, if there is a big technical "if" for ES stem cells, there appears to be an equally big "if" over IPS technologies. Supporters of ES may well argue that the "if" over IPS technology is greater: at least by reference to present knowledge.

The ethical issues with oocyte donation arise in a number of ways. First, there are pro-life arguments especially where the oocyte is fertilized during the process. Even if cloning technologies are used, some may question the status of the cloned embryo and whether such technologies should be permitted.

Second, some may raise the question of commodification and exploitation of women for benefit of human kind.

Third, there is the danger of risk to the health of the donor.

Fourth, there is the slippery slope argument: the same technology that is used to develop new medical therapies out of stem cell research may also lead to a brave new world of eugenics and supermen and superwomen. These are significant questions. But, to be fair, will IPS technology really be as ethically neutral as first appears. IPS technology appears to possess the same ability to open the door to brave new worlds. Even more difficult may be the status of the re-programmed undifferentiated somatic cell. Does this cell truly possess the ability to develop into a range of adult tissues including a fully viable new born? If so, does this mean science has the power to turn any cell in the adult body into an embryo? If so, what are the ethical considerations? A woman oocyte donor who is allowed a profit based payment will be receiving payment for her participation in a fairly intrusive physical procedure over several occasions and with some uncertain long term risks. The short term risks and discomfort appear to be low and largely manageable. The practical benefit to society in terms of if and when therapeutic treatments will develop is far less clear. The potential seems enormous: the uncertainty high and the impact likely to be reserved for generations down the line.

Who is most likely to donate blood and organs? Leaving aside post mortem donations, it seems probable that in most cases, it will be a relative or friend of the recipient in need. True, donations from complete strangers can arise: especially in the case of blood. But for organs (and quite often also for blood) it is assumed likely that bonds of friendship, love and affection underlie the act in question.

Who is most likely to participate in drug trials? This is different. I don't know of any studies into the profile of drug trial participants. It stands to reason that they will not necessarily be related to any loved one suffering from the disease or injury. They may well be ordinary members of the public who participate for a large variety of reasons.

Then, who is most likely to donate oocytes? At present, it seems that these by and large are women seeking AR treatment. It is assumed that very few (if any) women have been approached to make donations solely for the purpose of research in a non-therapeutic context. If these AR connected donations are inadequate to support ES research in Singapore, should Singapore adopt a system whereby women are encouraged to donate eggs purely for research purposes? Voluntary donation of eggs for approved research is as I understand it already permissible. Should an incentive scheme be supported? Who is likely to be attracted by such a scheme? Given the discomfort and invasiveness of the procedure and the uncertain long term risks and uncertain benefits: who is likely to participate? It may be that payment of a small incentive will only be attractive to those who are in dire financial straits or those who are already vulnerable to "persuasion". On the other hand, those who participate because of the "adventure of scientific discovery" are likely to do so in spite of that payment and not because of the payment. For these, recognition and coverage for any adverse consequences may be far more important.

Conclusion

The issues raised by the present BAC Consultation Paper are important and timely. Indeed, some of the points stretch beyond research on embryonic stem cells and human eggs to any type of medical non-therapeutic research such as drug trials and the like. It is hoped that the discussion set out above is of some assistance to the BAC. The writer accepts that expert evidence as to the degree of risks associated with human egg donation and possible benefits are critical to reach a proper conclusion of where the balance lies.
The balance is likely to be dynamic in the sense that it will need review from time to time in the light of new scientific knowledge and experience such as with IPS technology.

Given the matters discussed above the writer's views on the two questions raised by the BAC are as follows.

(i) Whether women should be allowed to donate eggs for research. Yes, I am of the view that women should (subject to proper approvals for the research proposal and proper consent) be allowed to donate eggs for research. I do

not see any distinction between donation of eggs surplus to AR treatment and eggs obtained solely for the purposes of research (non-therapeutic research).[51] However in the former case, I underscore the importance of ensuring that a clear line is drawn and maintained between the medical IVF/AR team and the research team. The system must clearly require independent taking of consent. I am also in favour of careful review of the scope of information that must be revealed to validate the consent. Such information should include not just information about the medical risks but also the research affiliations and commercial interests that may be involved.[52]Where the donor is a vulnerable person such as an employee or research assistant of the research team, the burden should be on the researcher to prove that the consent is truly voluntary and that the donor has been given reasonable opportunity to obtain independent advice. Special consideration should also be given to the case where a proxy consent is sought for a female child donor. Given the uncertain long term risks and the uncertain benefits, I am not in favour of parental proxy consent for minor females. At the very least, the consent of the minor female must be sought alongside parental consent. The minor female must of course be of sufficient maturity to understand what is being asked of her. Special consideration may also be needed to take account of any possible increase risk to young female donors from the procedure.

(ii) Whether any payment may be made to, or received by, the egg donor. Aside from payment of direct "out of pocket expenses" I am not at present in favour of any payment for the donation.[53] This is so whether the payment is in respect of loss of earnings during the medical procedures or for the time spent. I am also unconvinced that purely notional sums will have much impact in any case on the number of women volunteering. If the sum is more than notional, there may be adverse consequences such as women from poorer levels of society (within and from outside of Singapore) making donations: ostensibly altruistically but in reality for the payment being offered. Individual autonomy and freedom of choice must be balanced against interests of society as a whole. If a conservative approach has been

---

[51] Even if contrary to earlier discussions, Singapore does not currently permit oocyte donations purely for research (not connected with AR): there does not seem to be any good reason why this should not be allowed subject to proper consent and compliance with research regulations of the MOH. The fact that the benefit is uncertain has to be balanced against the possible benefits to society as a whole. Participation in drug trials also does not necessarily always confer an immediate benefit to the participant.

[52] By way of comparison, the Medicines (Clinical Trials) Regulations mention over 20 specific areas to be discussed and explained to the person considering participation in drug trials. These include: any compensation and treatment available to the subject in the event of injury arising from participation in the clinical trial. It is also noted that Reg 20 provides that the holder of a certificate or any person assisting him in a clinical trial or any subject in a clinical trial shall not directly or indirectly have any financial interest in the trial.

[53] I understand that South Korea in late 2007 amended its law to clarify that sale or purchase of ova is not allowed. http://www.koreatimes.co.kr/www/news/nation/2007/09/113_10900.html.

adopted in respect of payments for participation in clinical drug trials, why should the position be any different for human egg donation procedures?

Is it right that the health risks to the donor from egg donation are so "small" as compared to those associated with drug trials and organ donation, so that a policy against commodification has less relevance? But even if the health risks for the donor are relatively low, why should this lead to a more favourable view on commodification? How do we factor in the reality that long term risks are still uncertain? Is the argument in favour of payment better supported by the assertion that the potential benefits to society of successful human stem cell research are incalculable (albeit still unproven)? But if so, how is this any different from the societal benefits of individual participation in drug trials? Is the urgency driven by scientific need or commercial interests or both? These are tricky questions and different views are bound to arise. The fact that Singapore has invested in the life science industry in general and embryonic stem cell research in particular does not mean that the Government places commercial considerations ahead of all other concerns. The setting up of the BAC and its broad mandate clearly underscores the importance attached to ethical considerations.

On balance, given that there are emerging technologies (particularly IPS stem cell research) that *may* well lessen the need for ES stem cells and given the uncertain (particularly long term) risks arising from the egg donation procedures, the principle of altruism should remain underscored. Yes, the potential benefits of stem cell research to society are likely to be enormous. But, against this there remains the real danger of abuse of the technology. It is often said, and rightly so, that technological development always involves risks especially those arising from abuse. The present BAC Consultation Paper is not directly concerned with stem cell research and use of genetic information to treat disease or infirmity and the dangers of abuse (for example cloning of individuals beyond the 14 day limit). Indeed, I make no comments on the general question of ethics and research on human embryos.

The BAC Paper looks at the specific issue of the *source* of human stem cells and in particular, supply of eggs to advance permitted embryonic stem cell research.[54] Nevertheless, proper attention to ethical issues concerning the

[54] It is also noted that other approaches to stem cell research such as human/animal chimera (chimerids) involving insertion of human genome from somatic cells into animal ova may also be "promising" from a purely scientific point of view. But, even here, whilst no human embryo is involved as such, there will be hard issues of definition: what is it to be "human" and what is it to be an "embryo"! Behind these definitional issues, tough ethical questions will not be hard to find. Also there may be questions as to whether remnant animal DNA such as mitochondrial DNA has any impact on the harvested stem cells. The debate over chimerids has been fierce in UK with UK only accepting the creating of human/animal chimeras (for stem cell research) in late 2007. See http://www.publications.parliament.uk/pa/ld200607/ldhansrd/text/70503-0002.htm and also http://www.guardian.co.uk/science/2008/jan/01/science.review.2007.

supply of human eggs is an important first step that supports the development of an ethical stem cell research and development program. Payment, over and above direct out of pocket expenses, raises too many questions. Will this be acceptable to Singapore society?[55] What impact might this have on other forms of medical altruism? Given the globalised world and Singapore's increasing international status, is there a real and unacceptable danger that "poorer" donors from the region might come to Singapore to participate in egg donation payment schemes? How much payment over and above direct out of pocket expenses should be provided under a payment scheme? Should this be linked to lost earnings or capacity to earn? Should the payment simply be based on what the market is prepared to pay? Should there be a cap and if so how is this to be assessed? Is there any "international" consensus of what is an acceptable payment? If the payment is notional: does it serve any purpose? If more than notional, will this exacerbate the problem of "exploitation" of poorer donors whether within or from outside Singapore?

(iii) I am also strongly in favour of society providing some form of safety net for donors who suffer adverse health consequences as a result of the procedures. I agree that this should be done on a strict liability basis: either through insurance or some industry wide fund. I am unconvinced that an *ex gratia* system is sufficient. Some form of dispute resolution scheme might also be usefully developed to handle cases where problems do arise.

The current science suggests that there are a number of avenues to pursue the goal of human stem cell research. These include: use of adult stem cells, use of embryonic stem cells, induced pluripotent stem cells and possibly human/animal chimera methods. Whilst none of the approaches are entirely free of ethical considerations, it does seem that use of embryonic stem cells and possibly chimerids will be the most controversial and for some time yet to come. Stem cell research should have as its goal the benefit of human kind: new medical therapies with dignity and respect for life as a whole. The

[55] Indeed, experience in UK suggests that the taking of public opinion is by no means an easy task. Some have even queried whether participants in opinion surveys have the necessary scientific knowledge to properly grasp the issues that have arisen. For example, in the debate in the UK House of Lords on chimerids, some speakers queried whether 70% UK acceptability of embryonic stem cell research was reliable. See for example, the speeches by: Baroness Kennedy, Baroness O"Cathain and Lord Crisp. Baroness Kennedy (Chairperson of the Human Genetics Commission) lays great importance on public consultation as "good policy and progress in science are made in a context of public acceptance…Public engagement is essential to achieving that acceptance. From experience, what we have seen is that where science outpaces public acceptance, for example with genetically modified foods, it can lead to inhibition of research and of the benefits of that research." Nevertheless, Baroness Kennedy states that the consultations of the Human Genetics Commission (unsurprisingly) reveal a wide range of views on the ethics of stem cell research. If the taking of informed public opinion is hard in UK, it is likely to be no less difficult in Singapore and especially ASEAN as a whole. But, it does not follow that just because a wide range of views are likely (with no dominant or universal consensus) that the consultation exercise is pointless. Consultation and public engagement will at the very least result in better public understanding of the issues and should prove helpful to the policy makers.

different methods of stem cell research should not be seen as commercial competitors and research decisions should be made based on which line(s) offers the best hope of progress for humankind as a whole.

Addendum: Scenario Postulated by the BAC

Since the preparation of the comments, my attention has been drawn to a hypothetical scenario posted on behalf of the BAC and designed to help elicit focused responses. The scenario concerns a Parkinson's patient and possible donation of eggs by a number of individuals.

1. Do you think Abi, who is 35 years of age and a mother of three children, should be able to donate eggs to MMS for research?

    - Abi is the daughter of the patient.
    - She is of age and is legally competent.
    - This is a case of non therapeutic research.
    - Assuming Abi is informed of the health risks (including uncertainties) and understands the medical procedures involved, I would support her right to make the donation.
    - Abi should also be given information that the research may well lead to commercial applications and any questions that she may have on the research at MMS be fully answered.
    - Her identity as donor must be kept in strictest confidence.

2. If Abi needs to take time off from work, do you think she should be compensated either in full or part for the loss of income, inconvenience and risk involved?

    - Even assuming that she suffers provable loss of income, I am not in favour of Abi receiving compensation for that loss. Compensation in full or part raises too many problems and in any case goes against the supposed altruistic nature of the donation. Person's like Abi donate because they want to do so: because they feel it is the right thing to do.
    - Inconvenience and risk will be very hard to quantify. Any sum is likely to be notional. For individual's who might be persuaded by "financial inducements" the offer of a notional sum to compensate for inconvenience and risk is unlikely to make any difference. For those who might be persuaded by such payments, it is probable that they will come from highly disadvantaged sections of society. Some may even come from overseas.

3. If so, what type of compensation would be acceptable and not amount to inducement?

    - Generally I am not in favour of a "compensation" package for loss of time/inconvenience and risk.
    - Payment of direct out of pocket expenses is acceptable. This should include the costs of any consequential medical treatment and/or medicines.

- A no fault strict liability scheme should be established to compensate for any adverse effects of the donation procedure. Granted there may be some difficulties of proving causation especially where the adverse effect arises many years down the road: nevertheless as a matter of principle, this seems the right response for society.

4. Carol who is 21 years of age was inspired by her aunt Abi and she wants to donate her eggs to help advance the work of her research team. Do you think she should be allowed to do so?

    - Carol is of full age and is legally competent.
    - Nevertheless, as a member of the research team she may be regarded as a "vulnerable" person in that she may be subject to "contextual duress".
    - Whilst her expressed desire is said to be "inspired" by the altruism of Abi, it is important for society to ensure that she has not be subject to any undue influence arising from her position as member of the research team.
    - The burden must be on the research team to seek approval from the relevant IRB and to demonstrate that Carol's consent is truly independent. At the very least, Carol must have had an opportunity to obtain independent advice and given reasonable time to reconsider her decision.[56]
    - Carol must be given the same information as to risk and consequences as is given to any other non therapeutic donor.
    - Carol's identity as a donor must be kept in strictest confidence.

5. Do you think Carol should receive any payment for the time, inconvenience and risk?

    - No, her position should be the same as for Abi.

6. If Betty decides to donate her "spare" eggs to MMS, do you think she should be subsidized by MMS for the cost of her IVF treatment?

    - Betty is undergoing IVF/AR treatment. She should be allowed to donate her excess eggs subject to her consent being obtained based on provision of the same information as is provided to Abi.
    - Aside from the consent being informed, it is very important to dispel any "suggestion" of undue influence as she is a "vulnerable" donor.
    - The taking of her consent must be by individuals who are independent of the MMS research team. I am not sure that a bare requirement that the principal

[56] It will be important to discover what is the international practice and experience on donations from research team members. Leaving this aside for the moment, as a matter of principle even vulnerable donors should be capable as a matter of law of giving real consent. Vulnerability does not mean legal incompetence. What is essential is that a strong system be put in place to ensure that situational duress is not the reason for the donation. If the view of the medical profession is that it will be hard in practice to protect research team members from situational duress or to discover if the donor is affected by her situation, the egg donation should not proceed.

investigator must be a different person from the principal physician is sufficient.

- The IRB must be satisfied that the eggs are truly "excess" or "spare" and were taken in the first place for the purposes of IVF treatment. In short, the practice must not be allowed to develop where a deliberate "over supply" is obtained from the IVF patient so as to "create" an availability of spare eggs.
- I am not sure of a scheme that permits the cost of her IVF to be subsidized. Given that her wish is to become pregnant and given that pregnancy involves a new life, I would tend towards utmost caution.
- The health of the IVF patient and the prospective health of any implanted fetus are of the utmost importance. Whilst I do not understand the risks involved it seems probable that the less physical intrusion/stimulation of the ovaries, the safer it will be for mother and hopefully, the child that is desired. Having a link between IVF costs and donation of surplus eggs may create/exacerbate any tension between the IVF and Research Team. This is especially so where the decision to donate excess eggs is made prospectively (in advance of the IVF egg obtaining procedure). I am not sure what the position is for donation of blood. There, it may be that the blood donor receives priority or subsidized access to blood transfusions should he require these in the future. Arguably, the position is different. The blood donor is in essence getting back nothing more than what he/she has given. The taking of blood (presumably) involves a much lower health risk to the donor as compared with the far more invasive procedure of egg donation. The question of linkage between IVF costs and donation of surplus eggs is a matter on which I would prefer to express no concluded view.

A final point concerns confidentiality of the identity of egg donors. Confidentiality is always an important concern of medical patients and research subjects. In the case of embryonic stem cell research it is worth underscoring this point: not the least because of the important background debate over use of human embryos for research. I am not sure of the practicalities but would urge consideration of a system whereby even members of the research team are unaware of the identity/source of the eggs being used. If medical students/members of research teams are allowed to make egg donations, is it possible that these could be to a "central egg bank" controlled by a body independent of embryonic stem cell research teams? Any research team can then request release of eggs for embryonic stem cell research approved by the relevant IRB. Would this better protect the identity of donors and reduce any tension between the research team and female members who wish to contribute their own eggs for stem cell research? Human egg donation raises many hard policy driven issues. The controversy emanating from South Korea in 2005 will remain fresh in the public conscience for some time to come. What are the lessons to be drawn on egg donations and members of research teams? Is it enough/helpful that the research team is unaware of the identity of the donors? From one point of view, this may reduce the possibility of pressure on research team members to donate. But, is that enough? Is there a danger that research teams will be able to hide behind a veil of ignorance? Much will depend on the system

Singapore puts in place to handle human egg donations. If the donations are processed by each research team, donor anonymity will be hard to maintain and the research team should be under a positive duty to ensure informed voluntary consent has been obtained prior to obtaining the eggs. If the eggs come from some centralized authority, then it will be the duty of that authority to ensure that the research team's use has been authorized by the IRB and that the eggs in the bank are all covered by voluntary informed consent donations within the legal framework for the making of such donations. Under such a scheme, research teams in Singapore will not be allowed to use human eggs obtained otherwise than from the central authority. I am not sure how realistic such a procedure may work in practice and I do accept that donor anonymity should not excuse undue influence that has affected the volition of a donor/member of the research team. Whether there is a centralized system or whether individual hospitals/centres are allowed to collect eggs themselves, it is important that vulnerable donors including employees and students be protected from contextual duress.[57]

_____

[57] http://www.guardian.co.uk/korea/article/0,2763,1650066,00.html#article_continue. See this link for a short piece on the egg donation controversy in South Korea.

Comments from Associate Professor Allen Yeoh

Yong Loo Lin School of Medicine
National University of Singapore

9 January 2008

Paper is clear and not controversial. As a clinical translational researcher, I strongly feel that the current ethical regulations are unduly restrictive and stifle research without corresponding improvement of protection of subjects.

a) Reimbursement of expenses only is inadequate and requires an overly "altruistic" commitment from the donor who sees no immediate direct benefit of the cause.

b) Compensation of time and inconvenience is appropriate and should not be deemed excessive. Given the high average social income of Singaporeans, it is unlikely that donors are "coerced" into donation by the reasonable reimbursement. The guide should be similar to the reimbursement for drug trials of normal subjects. The suggested compensation of $760 per cycle by UK HFEA, in my opinion is inadequate while the US$5000 by American Society for Reproductive Medicine is probably excessive, given the easy accessibility in Singapore.

c) Provision of medical insurance cover of possible side-effects of ovarian hyper-stimulation and the harvesting procedure, as in any drug trial, is important. The authority responsible for the Donation of Human Eggs for Research should set up the guidelines of insurance coverage for such matter.

Comments from a member of the public (1)

Received via email on 8 November 2007

Dear Prof Lim Pin

I support the use of human eggs in research for the potential good it can bring.
I also fear the temptation to abuse it when it is allowed.
Therefore the following suggestions:

To encourage donors to come forward, it should just only be a vague general sense of altruism. The donors are encouraged to feel more involved; their contribution more purposeful, effort more directed and meaningful.

1. Donors are educated on what current ongoing or future research works are about both the difficulties and promise they hold. This can be done before and/or after donation.

2. Donors are encouraged or can choose to allocate some of the eggs (the rest can be set aside for a 'general pool') to specific cause or project/s they feel strongly for. E.g. Miss A may come forward and want to donate some of her eggs towards works on Parkinsonism after reading the plight of actor Michael J. Fox or his foundation. Madam B may volunteer her eggs for studies on cancer after knowing a friend/relation who has been diagnosed with a malignancy.

3. Donors can choose to be updated regularly on the general progress of whichever areas/studies they feel strongly affiliated to. With the periodic updates, reminders on by what new portals there are that they can also urge other fellow friends or colleagues to step forward to donate too.

   Rewards should comprise both the intangibles and the more concrete. More so if it involves some discomfort, time and maybe medications e.g. Drugs to stimulate eggs release.

4. Any monetary rewards should be accredited into medisave/medishield. The donor can choose the account holder to be any of her family members and herself. Or she can choose to donate it any charity of her wish, preferably one with IPC status. This is to reward like with like.
   a) This will help avoid cases in some developing countries where the poor and deprived are coerced to donate blood/kidney for immediate money and food, neglecting efforts to correct the underlying poverty.
   b) This will help avoid situations in many developed countries where recruitment for human trials always attract a disproportionate number of drugs addicts and

gamblers who readily spend this perceived 'easy $' on drugs, sexual workers and gambles.

5. Any benefit that derives the outcome of the particular research can be shared with the donors involved in various form.
   a) It can monetary.
   b) Or subsided therapy if the donor or any person named by the donor --does develop the condition or disease.

6. To encourage repeat donations, for each year or each additional batch of eggs donated, a new nominee can be named as beneficiary.

My grandmother-in-law has just passed away. After cremation, my wife asked me how would I like my body to be dealt with.

Me: “Please donate my cornea, kidneys, heart/lung, bone, skin and whatever it's useful"
Wife, not surprised, pressed on:"what about the rest, they don't need everything"
Me:" Donate it to medical school" (wonder if they still need it now that's computed aided visual teaching
And by then my body will have missing anatomical parts)
Wife....silence.....:"but they will cut you up, gulp"

If some of the above suggestions are workable, please also consider it for bold donation and organ transplant.

I am not involved in any research work and have no vested interest.

Comments from a member of the public (2)

Received via email on 25 March 2008

Healthy women should be allowed to voluntarily donate eggs for medical research, provided legal safeguards including the following are in place:

1. Exclude women who are unsuitable as egg donors or have higher risks of ovarian hyperstimulation e.g. Women with PCOS, menstrual disorders, reproductive structural defects, allergies to drugs used in the procedures, family history of ovarian, uterine, cervical or breast cancers, low BMI, women intending to conceive in future.

2. Exclude tourists & foreigners on short term visits.

3. Informed consent to be properly taken.

4. Donors to be allowed voluntary withdrawal at any time without penalty.

5. Procedure to be done free of charge in MOH approved institutions only, which should be subject to regular audits by MOH.

6. Free medical examinations to be performed to assess risk & suitability after informed consent are given.

7. Donors to be allowed to opt for either donation via ovarian stimulation or without stimulation (i.e. collection via natural ovulation) if the latter is feasible.

8. OHSS or other complications/adverse reactions arising from the procedure to be managed free of charge.

9. Donors to be adequately treated & compensated if harmed in the procedure through medical negligence or improper techniques.

10. No monetary or other forms of compensation other than transport reimbursement based on cab fares or mileage & parking claims.

11. Donated eggs are to be used locally for medical research and not sold or exported.

Wrt to points 8 & 9, institutions performing the procedure may wish to provide free insurance to donors against medical problems arising from the procedure.

Summary of Responses from REACH Online Discussion Forum and e-Consultation

On 7 November 2007, members of the public were invited via a press conference and subsequent media reports and announcements to provide feedback on the BAC's Consultation Paper on Donation of Human Eggs for Research. To facilitate public deliberation on the issues presented in the Consultation Paper, the following scenario was posted on a discussion forum (called "discussion corner") managed by REACH [1], to specifically seek views on:

- whether healthy women, not undergoing fertility treatment should be allowed to donate eggs for research and if so, under what conditions; and
- whether compensation of egg donors amounts to inducement.

Scenario

Abi's father suffers from Parkinson's disease. Since his late 40s, her father started to experience muscle rigidity, tremors, memory loss and a slowing of movement. The family is concerned that he may lose physical mobility in a few years. From what she has been told, Parkinson's disease affects the nerve cells in a part of the brain that controls muscle movement. The exact cause is not known and there is also no cure for it.

Abi learnt that her niece, Carol, is part of a research team at Merlion Medical School (MMS) that is conducting embryonic stem cell research that could lead to a cure for the disease in the long run. However, the research is proceeding slowly due to a shortage of human eggs. Abi feels that she should donate her eggs to help advance the research even though the procedures involved are invasive and carries some health risk. While a cure may not be found quickly enough to help her father, future generations may benefit from the research.

Abi discussed her intention with her older cousin, Betty, who will be undergoing *in vitro* fertilisation (IVF) at Merlion Hospital. IVF is a clinical and laboratory procedure whereby the eggs and sperm from a couple are extracted and fertilised outside their bodies. Such a procedure is a kind of assisted reproduction aimed at increasing the chances of a couple conceiving a baby. After speaking with Abi, Betty is also thinking of contributing some of her eggs not used in her fertility treatment to MMS.

[1] REACH (Reaching Everyone for Active Citizenry http://www.reach.gov.sg/) is an agency set up by the Singapore Government to engage and connect with its citizens.

Questions:

(i) Do you think Abi, who is 35 years of age and a mother of three children, should be able to donate eggs to MMS for research? If Abi needs to take time off from her work so that she could donate her eggs, do you think she should be compensated (either fully or in part) for the loss of her income, inconvenience and risk involved? If so, what type of compensation would be acceptable and not amount to an inducement?

(ii) Carol, who is 21 years of age, was inspired by her aunt Abi and she wants to donate her eggs to help advance the work of her research team. Do you think she should be allowed to do so? If she is, do you think she should receive any payment for the time, inconvenience and risk involved? Carol is a graduate student at MMS and does not receive an income.

(iii) IVF is an expensive procedure, and even then, the couple undergoing the treatment may not be successful in conceiving a child. Eggs that are leftover from the treatment may be kept for future use, donated to other infertile couples, donated for research or destroyed. If Betty decides to donate her "spare" eggs to MMS for research, do you think she should be subsidised by MMS for the cost of her IVF treatment?

Summary of Responses

1. From 7 November 2007 to 7 January 2008, a total of 47 entries were received on REACH's Discussion Corner and 10 responses through the e-Consultation. These 57 responses were from at least 44 individuals.

2. Many respondents indicated that healthy women should be allowed to donate eggs for research because women should be able to decide on how to use their eggs so long as such decision is made voluntarily and on a fully informed basis.

3. The reasons given by those opposed to allowing healthy women to donate eggs for research are:
   a. religious concerns;
   b. associated health risks; and
   c. possible exploitation of women.

4. A number of respondents expressed the view that advancement of science is a public good. Thus, some compensation is considered appropriate because donors have contributed to the public good.

5. Support for the provision of subsidy to women who contribute "spare eggs" from fertility treatment for research was also based on the idea of public good.

6. Respondents who opposed the provision of compensation or subsidy were generally against any form of commercialisation of the human body.

7. Even where respondents expressed support for the provision of compensation or subsidy to donors, they were generally of the view that donation of materials for research should remain altruistic.

8. Only a handful of respondents appeared to be supportive of outright commercialisation although some respondents considered this to be necessary for the advancement of science or for long term societal benefit.

9. Concerns that were emphasised include:

   a. Duress and inducement, and the need to ensure the voluntary nature of informed consent;

   b. Safeguard against the commercialisation of the human body (although some respondents considered this to be necessary for the advancement of science or for long term societal benefit);

   c. Privacy of donors and the confidentiality of their information;

   d. Proper information to be provided to donors and in a manner that is effective in facilitating understanding;

   e. Availability of medical care for short-term and long-term adverse health consequences arising from the egg donation procedure; and

   f. Exploitation of women, especially from poor countries.

Background Papers

1. Oocyte Donation — Clinical and Scientific Aspects
   - *Professor Ng Soon Chye*
   Director, O & G Partners Fertility Centre, Gleneagles Hospital, Singapore

2. Oocyte Procurement for Research
   - *Dr Benjamin Capps*
   Centre for Biomedical Ethics, National University of Singapore; and Centre for Ethics in Medicine, University of Bristol, UK

Oocyte Donation – Clinical and Scientific Aspects

This paper has been prepared for the Bioethics Advisory Committee as background information on oocyte donation for research.

June 2007

Professor Ng Soon Chye
Director, O & G Partners Fertility Centre
Gleneagles Hospital
Singapore

Introduction

Oocytes for fertility treatment

Oocytes (eggs) can be donated for the treatment of infertility or for research. The donation of oocytes for the treatment of infertility is an established method of assisted reproduction and has been used in patients with ovarian failure, increased risk of serious genetic disorders, or multiple failed *in vitro* fertilization (IVF) attempts. Older women are more often recipients of donated oocytes for fertility treatment as they are more likely to suffer conditions for which such treatment is needed. Those who donate oocytes for the treatment of infertility may be women undergoing infertility treatment and who are willing to share their oocytes with another infertile woman; or they may be healthy women who donate their oocytes altruistically.

Oocytes for research

Oocytes for research may come from a wider range of sources:

(a) Women undergoing infertility treatment. Oocytes from such women could be surplus to their fertility treatment, or they could be immature oocytes that are unsuitable for fertilisation or have failed to fertilise following IVF;

(b) Women undergoing medical procedures such as the removal of ovaries. These procedures may yield immature oocytes that can be used for research;

(c) Women not undergoing any form of medical treatment i.e. healthy women who undergo ovarian stimulation in order to provide oocytes specifically for research;

(d) Cadavers and aborted foetuses, which may provide immature oocytes for research; and

(e) Oocytes created from stem cells. It has been shown that it is possible to create mouse oocytes from mouse embryonic stem cells. If this could be achieved using human embryonic stem cells, these created human oocytes could then be used for research. A team of researchers in the UK have demonstrated that human embryonic stem cells display a capacity to generate immature gametes. However, research on creating human oocytes from human embryonic stem cells are in the preliminary stages.

Recently, the demand for human oocytes for research purposes has led to concerns regarding the risks of the procedures involved in obtaining the oocytes. To understand these concerns, one has to understand how oocytes are normally produced, the hormone therapy that a woman has to undergo to produce the additional oocytes required for infertility treatment or for research, and the procedures involved in the retrieval of these oocytes.

How Oocytes are Normally Produced

Oocytes are produced in the ovaries. The number of oocytes in a woman's ovaries is fixed before birth and diminishes with age. At birth, a baby girl has approximately one to two million oocytes. At puberty, the number has reduced to 300,000 to 400,000, of which usually one will fully mature each month and about 1000 will die at various stages of maturity. This continues till menopause, when the number of functional oocytes will have been exhausted.

Before puberty, the oocytes are in the resting stage and each of them is surrounded by cells that protect it and support its development, forming structures called primordial follicles. Each month, about 10-20 primordial follicles mature and can be detected by ultrasound scans. These follicles will compete for growth-inducing follicle-stimulating hormone (FSH) resulting usually in the development of only one follicle, termed the dominant follicle. Under the influence of luteinising hormone (LH), the dominant follicle will release a mature oocyte at ovulation (a term used for the time mid-way in the menstrual cycle when the mature oocyte is released).

Ovarian Stimulation and Retrieval of Oocytes

Normally only one follicle will fully mature and release an oocyte in each monthly cycle. However, in the presence of sufficient FSH, or other drugs with a similar action, more follicles can mature. In assisted reproduction, FSH is used to stimulate these follicles so that more oocytes would be available for use. In the standard therapy, the hormone is given daily for 10-12 days by injections. To prevent premature release of the oocytes, injections of another hormone are also given.

During ovarian stimulation, the physician will closely monitor the patient for signs and symptoms of adverse effects of the drugs used, as well as the maturation of the follicles through serial ultrasound scans and blood tests. When the ultrasound scans show that the follicles have reached the appropriate stage of maturity, another hormone, human

Chorionic Gonadotrophin, is given by injection to induce the release of oocytes at 36-40 hours. However, in practice, the oocytes are collected before they are released, via a special needle attached to an ultrasound vaginal probe and with the woman under anaesthesia. Figure 1 shows how oocytes are produced via normal ovulation and via ovarian stimulation.

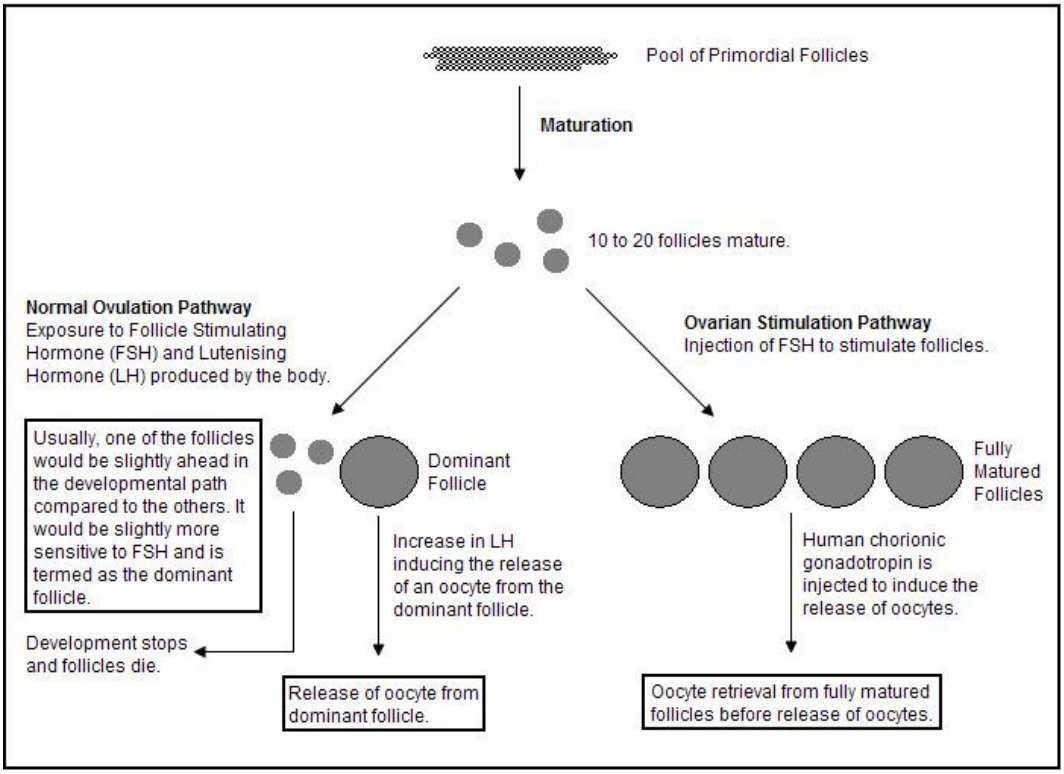


Figure 1: How oocytes are produced in the ovaries

Medical Risks of Ovarian Stimulation and the Retrieval of Oocytes

Ovarian stimulation may give rise to ovarian hyperstimulation syndrome (OHSS), in which there is accumulation of fluids in the abdominal cavity. The symptoms of OHSS are nausea, vomiting, diarrhoea, lower abdominal discomfort or distension, usually occurring soon (less than 10 days) after ovulation or oocyte retrieval and resolving spontaneously within several days. These symptoms are caused primarily by an increased permeability of blood vessels. Clinical experience suggests symptoms of mild OHSS are a common side effect in up to 20-30% of patients undergoing assisted reproductive technology (ART) procedures. The moderate form of OHSS is of greater concern and occurs in 1-10% of such patients. It can be minimised with careful use of FSH in the ovarian stimulation.

Severe OHSS occurs in less than 1% of IVF patients, usually when large numbers of oocytes (more than 30) are produced as a result of high sensitivity to the standard dose of FSH. The symptoms usually appear after seven days of oocyte collection and include hypotension and decreased urine output, reflecting gross accumulation of fluid in various parts of the body, such as the abdominal and lung cavities. Life-threatening complications include kidney failure, respiratory failure, bleeding from ovarian rupture and thromboembolism (obstructive blood clots). OHSS is more often seen in patients who become pregnant. OHSS can be avoided by the judicious use of hormones and careful pre-treatment assessment and monitoring of the patients. Women less than 30 years old and those with polycystic ovaries are at increased risk. For oocyte donors, careful use of low doses of FSH prevents OHSS.

As oocyte retrieval involves a minor surgical procedure, done under mild anaesthesia, there is a risk, although very low, of haemorrhage and infection and adverse effects of the anaesthesia.

It is not known if there are adverse long-term consequences of ovarian stimulation. The possibility of the potential risk of cancers of the breast, ovary and uterus, which are hormone related, has been investigated. The results so far have suggested at worst some low risk of ovarian cancer, but more research over a longer time span is required to determine if there are definite undesirable long-term or very long-term effects of ovarian stimulation. Although there are no clearly documented proofs of adverse long term effects of ovarian stimulation, the American Society for Reproductive Medicine's view is that "it would be prudent to consider limiting the number of stimulated cycles for a given oocyte donor to approximately six" because of the possible health risks.

Oocytes for Research

Oocytes donated for research can be used in many experimental situations. They can be fertilised to create embryos, from which stem cells can be derived or they can be used as they are, without being fertilised, for example in preclinical safety or feasibility studies of new technologies. Examples would be oocyte preservation or *in vitro* maturation, or somatic cell nuclear transfer (SCNT), also known as therapeutic cloning. Oocytes can also be activated to produce an entity called a 'parthenote', from which stem cells could be derived. Human oocytes are particularly required for studies of nuclear re-programming.

Nuclear reprogramming is the process whereby a mature somatic cell is transformed into one that has the characteristics of an embryonic cell, which may be totipotent (able to develop into all types of tissues) or pluripotent (able to develop into all types of tissues except the placenta). Various strategies have been used to induce the pluripotent embryonic state, such as SCNT, cellular fusion, the use of cell extracts and culture-induced reprogramming.

Currently, nuclear reprogramming is not well understood. Much more research is required in this area, which could be applied in the treatment of many presently

incurable diseases. There is the possibility of deriving patient-specific stem cells, which could prevent tissue rejection, deriving disease-specific stem cell lines to study the cause, progression, diagnoses and treatment of diseases as well as the possibility of generating tissues and organs to replace diseased ones.

The oocytes presently available for research are mainly those that have failed to fertilise following IVF. However, fresh oocytes are preferred to oocytes that have failed to fertilise following IVF, as they are believed to improve the efficiency of SCNT. Oocytes that have failed to fertilise after IVF are less effective as they have been shown to have limited developmental potential. Scientists have indicated that increased availability of suitable oocytes would enhance stem cell research. Hence, such oocytes are in considerable demand for research.

Oocyte Sharing

Oocytes from a woman undergoing infertility treatment can be "shared" with other patients or with a research programme. In return the woman receives help to bear the cost of the infertility treatment. The advantage for research is that the oocytes will be fresh and mature, and thus the chance of successful nuclear reprogramming will be higher than with oocytes that are matured in-vitro. The disadvantage is the possibility that women may be induced to "share" and inducement is considered undesirable. Heng et al. have suggested that compensated oocyte sharing is the best means of securing oocytes for therapeutic cloning research.

Current Guidelines on Oocyte Donation for Research in Singapore

In Singapore, all research involving human oocytes must be approved by a research ethics committee or an institutional review board (IRB) as well as the Ministry of Health (MOH).

Explicit consent must be obtained from the oocyte donor and there must be no inducement, coercion or any undue influence. Potential oocyte donors, who are not part of an ART programme, must be interviewed by a special panel, which has to be satisfied that the prospective donor is of sound mind, has fully understood the procedures and implications of the donation and that she has given her consent voluntarily.

In cases where the potential donor is a patient undergoing infertility treatment, the principal physician and embryologist in charge of the patient's treatment should not be the principal investigator of the research team using this patient's oocytes.

Specific Issues in Oocyte Donation

There are a number of ethical issues raised in oocyte donation and the use of oocytes for research, which overlap with, but are not the same as, the issues raised in infertility treatment. The essential difference is that in infertility treatment, a child will hopefully

result from the process, and the interests of the child add a further dimension to consideration of ethical issues. In research, on the other hand, there is no child and no direct benefit to the donor, and the ethical considerations primarily relate to the need for consent, the risks to the donors and the avoidance of coercion and exploitation.

Ethical issues are not covered in detail in this paper, but a number of special considerations are considered below:

a) ***Beneficence*:** It is a basic principle of medicine that benefits should outweigh risks/harm, and the proportionality principle should apply, i.e. higher risks must be minimised and where unavoidable, justified by greater benefits (Pennings et al, 2007; Mertes & Pennings, 2007). In the case where oocytes are to be used in research, the benefits are general, not specific to the donor, and the obligation is for careful selection of promising experiments likely to yield useful research findings with minimal risk to the oocyte donor.

b) ***Payment*:** In general one can distinguish three positions with respect to payment for oocytes – re-imbursement of reasonable expenses only, limited payments for time, trouble and effort, and outright sale regulated by supply and demand. The Human Cloning and Other Prohibited Practices Act 2004, Singapore, (HCOPP Act) states that reasonable expenses incurred by oocyte donation are allowed. The intention is to avoid commodification of oocytes and to maintain oocyte donation as an altruistic act done without inducement. There has been some debate on whether that should be relaxed. Heng et al., for example, proposed that subsidy be made to compensate patients undergoing IVF in exchange for oocytes donated for research (Heng et al., 2006). Mertes & Pennings (2007) suggested that any payment be based on effort and discomfort rather than on the number of oocytes retrieved, that there should be limits on payments, and that they should be made directly to the donor and not through middlemen or clinics.

c) ***Import & export of oocytes*:** For a number of countries such as Australia and the UK, the import and export of oocytes are regulated because of the concern that women, especially those who are financially vulnerable, may be exploited. Ethical concerns arising from the import or export of oocytes should be seriously considered.

d) ***Compensation for complications*:** Complications during ovarian stimulation and oocyte retrieval may occur; the risk of OHSS is higher when there are more follicles developing. This is an accepted risk during infertility treatment. However, for volunteers who donate oocytes, the question of compensation has to be addressed. In clinical drug trials the principle is accepted that healthy volunteers need to be insured by the institution against possible adverse consequences arising from their participation. Whether a similar requirement could be required in research involving the donation of oocytes is open to doubt, as insurance companies do not as a rule offer such policies and research grant agencies are also not likely to allow

such costs to be built in. A lack of insurance cover might, however, be a major disincentive to healthy volunteers.

e) ***Collection only in licensed ART centres:*** As the process of obtaining oocytes involves careful monitoring and specialised procedures, it should be conducted by suitably qualified physicians and in licensed ART centres. In Singapore, research using oocytes can be carried out only in ART laboratories which are licensed by the MOH.

Guidelines for the Procurement of Oocytes for Research

Subsequent to the news of unethical procurement of human oocytes by South Korean stem cell researchers, there is an increasing interest on this subject. Several ethics and professional bodies worldwide have issued new guidelines or revised their existing guidelines on obtaining oocytes for research.

International Society for Stem Cell Research (ISSCR)

In December 2006, the ISSCR finalised its Guidelines for the Conduct of Human Embryonic Stem Cell Research. Section 11 deals with the provision of oocytes for research. The guidelines include recommendations along the following lines:

1. Monitoring of recruitment practices should be done to ensure that women from vulnerable populations are not exploited;

2. When reimbursement is allowed, the research proposal should be reviewed rigorously so that any reimbursement or financial compensation does not constitute undue inducement;

3. No payment should be made based on the number or quality of the oocytes;

4. Oocyte procurement be done by experienced physicians, and the ovarian stimulation protocol used should be such that the risk of OHSS is reduced;

5. There should be a limited number of cycles of ovarian stimulation that a woman is allowed to be exposed to (for both research and for treatment); the number to be determined by an oversight committee based on review of latest available scientific information;

6. The cost for medical care required "as a direct and proximate result of the woman's provision of oocytes for research" should be provided;

7. "Researchers may not request that members of the infertility treatment team generate more oocytes than necessary for the optimal chance of reproductive success" (paragraph 11.5a); and

8. "An infertility clinic or other third party responsible for obtaining consent or collecting materials should not be paid specifically for the material obtained, but rather for specifically defined cost-based reimbursements and payments for professional services" (paragraph 11.5.b.vii).

European Society for Human Reproduction and Embryology (ESHRE)

In 2007, the ESHRE Task Force on Ethics and Law published its recommendations on Oocyte Donation for non-reproductive purposes (Pennings et al, 2007). It adopted the position that "women who donate oocytes for research should be treated similarly to research participants in clinical trials" (page 1210) and that the donation should primarily be altruistic, and thus recommended along the following lines:

1. Minimising the risks for the donor by ensuring that the research is based on ethical principles and that the ovarian stimulation protocols are such that the risk of OHSS is reduced;

2. Careful selection of research projects to avoid wastage of oocytes;

3. Sharing of research data in order to avoid unnecessary duplication of experiments;

4. Oocyte donors must give free and voluntary consent. They should be counselled, provided with relevant information and given time to think the matter through before making the decision;

5. Oocyte donors should be reimbursed for the cost of all procedures, whether direct or indirect, as well as be compensated for the time lost and inconvenience suffered during the treatment;

6. To prevent undue inducement and disproportional recruitment among vulnerable groups, illiterate and poor women should be excluded as donors;

7. Prohibition or at least a very cautious attitude towards import of oocytes;

8. Research centres are responsible for obtaining oocytes ethically;

9. Donors from abroad should not be accepted; and

10. Encourage more research using alternatives sources of oocytes.

UK Human Fertilisation and Embryology Authority (HFEA)

In 2006, the Human Fertilisation and Embryology Authority (HFEA), UK, carried out a public consultation on donation of oocytes for research. In February 2007, it issued a statement allowing women to donate oocytes either specifically for research or in

conjunction with their infertility treatment, provided "there are strong safeguards in place to ensure the women are properly informed of the risks of the procedure and are properly protected from coercion." In addition, the HFEA launched its new 7th Edition of the Code of Practice in May 2007, which includes detailed guidelines for the procurement, storage and use of oocytes for research.

Conclusion

Oocytes are important for the progress of basic science research as well as stem cell and ART research. The donation of oocytes is associated with medical risks and donors have to be fully informed of the procedures and risks, and given sufficient time and information before making the decision to donate. It is also important that there are safeguards to protect oocyte donors and ensure that there is no coercion or undue influence on their decision to donate.

As science and technology advances, there may be a possibility that human oocytes may not be required for research and alternatives such as cybrids and stem-cell derived oocytes may be used instead. Generally there appears to be a consensus world-wide on the need for oocytes for research, and that donors should be compensated for the risk and the time involved.

References

Aflatoonian B and Moore H. "Germ cells from mouse and human embryo embryonic stem cells". *Reproduction*. 132 (2006): 669-707.

American Society for Reproductive Medicine, Practice Committee Opinion. "Repetitive oocyte donation". *Fertility and Sterility*. 86 Suppl 4 (2006): S216-217.

Check E. "Ethicists and biologists ponder the price of eggs". *Nature*. 442 (2006): 606-607.

Editorial. "Safeguards for donors". *Nature*. 442 (2006): 601.

Heng BC, et al. "The egg-sharing model for human therapeutic cloning research: managing donor selection criteria, the proportion of shared oocytes allocated to research, and amount of financial subsidy given to the donor". *Med Hypotheses*. 66 (2006): 1022-1024.

Human Fertilisation and Embryology Authority. *Donating eggs for research: safe-guarding donors*. UK, 2006.
http://www.hfea.gov.uk/docs/donating_eggs_for_research_safeguarding_donors_consultation_FINAL.pdf

Human Fertilisation and Embryology Authority. *Code of Practice, 7th Edition*. UK, 2007.
http://cop.hfea.gov.uk/cop/pdf/COP.pdf

Hübner K, et al. "Derivation of Oocytes from Mouse Embryonic Stem Cells". *Science*. 300 (2003): 1251-1256.

Hyun I. "Fair payment or undue inducement?" *Nature*. 442 (2006): 629-630.

International Society for Stem Cell Research, Task Force. *Guidelines for the Conduct of Human Embryonic Stem Cell Research*. 2006.
http://www.isscr.org/guidelines/ISSCRhESCguidelines2006.pdf

Lavoir MC et al. "Poor development of human nuclear transfer embryos using failed fertilized oocytes". *Reproductive Biomedicine Online*. 11 (2005):740-744.

Marchant J. "Human eggs supply 'ethical' stem cells". *Nature*. 441 (2006): 1038.

Mathews DJH et al. "Integrity in International Stem Cell Research Collaborations". *Science*. 313 (2006): 921-922.

McLaren A. "Free-Range Eggs?" *Science*. 316 (2007): 339.

Mertes H and Pennings G. "Oocyte donation for stem cell research". *Human Reproduction.* 22 (2007): 629-634.

Pearson H. "Health effects of egg donation may take decades to emerge". *Nature*. 442 (2006): 607-608.

Pennings G, et al. "ESHRE Task Force on Ethics and Law 12: Oocyte donation for non-reproductive purposes". *Human Reproduction*. 22 (2007): 1210-1213.

Sauer MV. "Defining the incidence of serious complications experienced by oocyte donors: A review of 1000 cases". *American Journal of Obstetrics & Gynecology*. 184 (2001): 277-278.

Vogel G. "Ethical oocytes: available for a price". *Science*. 313 (2006): 155.

Oocyte Procurement for Research

A Background Paper for the Bioethics Advisory Committee of Singapore

April 2007

Dr. Benjamin Capps
Centre for Biomedical Ethics, National University of Singapore, Singapore & Centre for Ethics in Medicine, University of Bristol, UK.

Summary

The purpose of this Background Paper is to describe the main ethical issues that arise in regard to procuring oocytes for research. These issues are part of a current debate informed by recent controversies surrounding the conditions of oocyte donation from women, the market in oocytes in some jurisdictions, and the scarcity of oocytes specifically for stem cell research.

In Part One, I discuss the reasons why oocytes are needed for research at this current time, and describe the potential sources of oocytes for these purposes. In Part Two, I focus on the immediate concerns of sourcing oocytes for research purposes from consenting donors, which are issues of payment, compensation, and incentives. To illustrate the various jurisprudential strategies that have developed in this regard, I look at a number of current legislative frameworks. In Part Three, I discuss in detail three ethical issues that have come to the fore in oocyte procurement debates: payment and compensation, commodification, and autonomy and risk. I close this section – and conclude overall – that various interpretations of the 'public interest' are central to understanding this present debate.

Introduction

In 2006, investigations into alleged scientific fraud by the South Korean stem cell scientist, Woo Suk Hwang, revealed that there were, among other concerns, contentious circumstances surrounding procurement of oocytes for research.[1] Specifically, in the attempt to be the first to successfully clone a human embryo, Hwang had obtained oocytes from paid donors and junior members of his own research team, and he had lied about the conditions under which the oocytes had been obtained.[2] This controversy emphasised the ethical concerns surrounding the degree to which incentives may be a

1 Cyranoski, D. 2006. Blow Follows Blow for Stem-Cell Work. Nature 439: 8.

2 Steinbrook, R. 2006. Egg Donation and Human Embryonic Stem-Cell Research. New England Journal of Medicine 354: 324-326.

part in the procurement of oocytes. While this apparently isolated incident was alleged by some to be a result of economic and political influences upon scientific independence and integrity,[3] the case for inducements or incentives for consensual donation of cells, tissues and organs from healthy 'donors' remains a challenging ethical problem.

The issue has again come to the fore because of the claims that there may not be enough human oocytes to facilitate the advance of embryonic stem cell research. In response to this, various jurisdictions are considering whether it is ethically (and to what degree) appropriate to obtain oocytes from human donors and non-human sources. In this Paper, commissioned by the Bioethics Advisory Committee of Singapore, I will outline the main ethical issues that arise as a consequence of this pressure to obtain oocytes for research. The Paper is in three parts. Part One looks at the scientific background of oocyte procurement. Part Two discusses various legislative strategies that have been employed to regulate the procurement of oocytes. In Part Three, I discuss some of the main ethical issues that arise from oocyte procurement for research. The purpose is to provide a background for future policy discussions.

PART ONE: THE SCIENTIFIC BACKGROUND

I. Why Are Oocytes Needed for Research?

One of the outcomes of biotechnological progress is that human cells, tissues and organs have become valuable as commodities which can be bought and sold. For this reason, when certain human body parts become desirable – and by their nature are normally of limited availability – there are market pressures that turn them into (potential – if policy will allow it) premium commodities.

Human oocytes are valuable, because they are necessary for human reproduction – and therefore can become a commodity in the reproductive 'business', which is currently driven by higher levels of infertility and women choosing to have children later in life – but they are also valuable as a research resource. These dual demands, plus other issues such as health risks in donation and the removal of donor anonymity, mean that oocytes are in short supply. The two main areas of research that require oocytes are fertility-related research[4] and stem cell (SC) research. It is the latter research – driven by both hype and hope – that will predictably create the greatest demand for oocytes in research.

---

[3] Editorial. 2006. Ethics and Fraud. Nature 439: 117-118.

[4] Embryonic and developmental research are important in light of continued low success rates for IVF pregnancies, the potential for harm occurring as a result of current clinical practice, and reports of ill health in IVF children. Barri, P. 2005. Multiple Pregnancies: A Plea for Informed Caution. Human Reproduction Update 11:1-2; Klemetti, R., Sevón, T., Gissler, M. and Hemminki, E. 2006. Health of Children Born as a Result of In Vitro Fertilization. PEDIATRICS 118: 1819-1827.

SCs provide an intriguing and potentially promising solution to many avenues of medical enquiry. These include questions of basic developmental science, the repair of *in situ* tissues and organs – which are often untreatable, either because of unattainable internal access or cellular and aetiological complexity – and the generation of whole organs *in vitro*, addressing problems of organ shortage and immunological rejection.[5] Results in animal models have encouraged optimistic speculation about early human clinical applications in advanced generation and regeneration of organs and tissues.[6] However, no SC applications of this type have entered clinical trial stages at the current time, and most believe that such therapeutic applications, if possible at all, are some years ahead.[7]

Much of the ethical debate about SCs to date has been concerned with the moral status of the embryo and the contested merits of alternative SC sources.[8] While most jurisdictions are no closer to resolving the former question, there is general scientific agreement that progress does depend on isolating human embryonic stem (ES) cells from embryos, and that currently postulated (uncontroversial) alternatives – such as somatic SCs – have not reduced this need.[9]

ES cell research requires a source of oocytes to produce the embryos needed; and while animal models and animal oocytes have been employed in basic science and proof-of-theory research, human oocyte-derived embryos will inevitably be required for the transition into human clinical applications.[10] Alleged solutions to the *embryo research*

---

5 Solter, D., Beyleveld, D., Friele, M.., Hołówka, J., Lilie, H., Lovell-Badge, R., Mandla, C., Martin, U. and Pardo Avellaneda, R. 2003. Embryo Research in Pluralistic Europe. Berlin Heidelberg. Springer-Verlag.

6 SC from cord blood have been used for some time in the treatment of childhood blood disorders; however, the 'advanced SC therapies' which are envisaged take the science to a new level of medical-biotechnological innovation; see: Sousa, P., Galea, G., and Turner, M. 2006. The Road to Providing Human Embryo Stem Cells for Therapeutic Use: The UK Experience. Reproduction 132: 681-689; European Parliament-Committee on the Environment, Public Health and Food Safety ('Mikolášk' Report). 2006. Draft Report on the Proposal for a Regulation of the European Parliament and the Council on Advanced Therapy Medicinal Products [short title]. Provisional 2005/0227(COD) November. Strasbourg. available at: http://www.europarl.europa.eu/meetdocs/2004_2009/documents/pr/636/636826/636826en.pdf

7 Thomson, J. 2001. Human Embryonic Stem Cells. In: Holland, S., Lebacqz, K. and Zoloth, L. eds. The Human Embryonic Stem Cell Debate: Science, Ethics, and Public Policy. Cambridge, Massachusetts. Massachusetts Institute of Technology. pp. 15-26.

8 Capps, B. 2007. Bioethics and Misrepresentation in the Stem Cell Debate. In: Gunning, J. and Holm, S. eds. Ethics, Law and Society, Volume 3. Aldershot. Ashgate Publishing Ltd.

9 House of Lords Select Committee. 2002. Stem Cell Research. HL Paper 83(i) London. HMSO.

10 For example, most SC lines are currently grown on animal feeder layers, raising concerns of cross-species viral contamination if used in humans. Furthermore, there are important biological and chemical differences between the characteristics of SCs from human and other animal species; Bishop, A., Buttery, L. and Polak, J. 2002. Embryonic Stem Cells. Journal of Pathology 197: 424-429; Evans, M. and Hunter, S. 2002. Source and Nature of Embryonic Stem Cells. C. R. Biologies 325: 1-5; Reubinoff, B., Pera, M., Fong, C., Trounson, A. and Bongso, A. 2000. Embryonic Stem Cell Lines from Human Blastocysts: Somatic Differentiation In Vitro. Nature Biotechnology 18: 399-404; and Rossant, J. 2001. Stem Cells from the Mammalian Blastocyst. Stem Cells 19: 477-482.

debate – such as the creation of 'embryo-like artefacts'[11] and parthenotes[12] – will not alleviate the demand for human oocytes because they are dependent on a source of eggs to be 'genetically-altered' or 'activated'.[13]

One of the predicted advantages of ES cell therapies is that it may be possible to immunogenetically-tailor cells, tissues and organs to the patient by using Cell Nuclear Replacement (CNR) techniques.[14] The pressure to embark on CNR strategies may increase if alternative sources of genetically-matched SCs do not yield expected results;[15] and it is well known that CNR is currently inefficient and wasteful, requiring large numbers of oocytes for successful animal cloning techniques.[16] In the future, SC banks may become valuable resources of immunologically-matched SCs which can be used in regenerative medicine, without resorting to CNR; but establishing such collections is a long-term effort, and probably will require large-scale regional collaboration (e.g. European or Asian) to be a clinically useful representation of a given population.

A major factor influencing the demand for oocytes will be whether national regulation allows the creation of human embryos specifically for research, either by IVF or CNR techniques. If the creation of research embryos is permitted, then oocytes – either human or animal – will become a necessary component of this type of research. Thus it is likely that the expansion of national and international SC research efforts,[17] paired with the growing trend towards liberalising embryo research laws to allow the creation

---

11 Embryo-like artifacts are bioengineered 'entities' that can produce pluripotent SCs, but without having the biological potential to develop into a foetus; Hurlbut, W. 2005. Altered Nuclear Transfer: A Way Forward for Embryonic Stem Cell Research. Stem Cell Reviews 1: 293-300. So-called 'dead' embryos are considered as those which are not suitable for IVF treatment because they stop dividing spontaneously. The selection of criteria for death in an embryo with none of the characteristics that would indicate normal death is clearly controversial.

12 Parthenogenesis is a reproductive mechanism that is common in lower organisms and produces a live birth from an oocyte activated in the absence of sperm. Human parthenogenetic embryos have been shown to develop to the blastocyst stage and so can speculatively serve as a source of ES cells. This mechanism for generating SCs (it is alleged) has the ethical advantage of not involving the destruction of viable embryos. Moreover, the SCs do not involve the union of male and female and so genetic material will be derived exclusively from the female oocyte donor (with the attendant potential immunological advantages); Cibelli, J., Cunniff, K. and Vrana, K. 2006. Embryonic Stem Cells from Parthenotes. Methods in Enzymology 418:117-35.

13 Murray, T. 2005. Will New Ways of Creating Stem Cells Dodge the Objections? Hastings Center Report 35: 8-9.

14 Colman, A. and Kind, A. 2000. Therapeutic Cloning: Concepts and Practicalities. Trends in Biotechnology 18: 192-153.

15 Mertes, H., Pennings, G. and Van Steirteghem, A. 2006. An Ethical Analysis of Alternative Methods to Obtain Pluripotent Stem Cells Without Destroying Embryos. Human Reproduction 11: 2749-2755; Schulman, A. 2005. The Search for Alternative Sources of Human Pluripotent Stem Cells. Stem Cell Review 4: 291-292.

16 Hall, V., Stojkovic, P. and Stojkovic, M. 2006. Using Therapeutic Cloning to Fight Human Disease: A Conundrum or Reality? Stem Cells 24: 1628-1637.

17 Capps, B. 2005. The Human Embryo, Stem Cell Research, and the European Union. In: Bender, W., Hauskeller, C. and Manzei A. eds. Crossing Borders: Cultural, Religious, and Political Differences Concerning Stem Cell Research: A Global Approach. Münster. Agenda Verlag. pp. 435-467.

of embryos specifically for research,[18] will have the inevitable effect of increasing the demand for human oocytes.

II. Sources of Oocytes for Research

Various types of donors may be identified as sources of oocytes for research: (1) IVF patients; (2) healthy providers (who volunteer to donate or are paid to provide oocytes specifically for research); (3) women applying for specific gynaecological interventions; (4) women applying for an experimental reproductive technology for their own benefit; (5) posthumous donors; (6) aborted foetal gonadal tissue; (7) non-human animal sources; and (8) SC-derived gametes. I will discuss these in turn, concentrating on the scientific and procedural implications.

(1) In Vito Fertilisation Treatment Patients

Along with (2), the procurement of oocytes from IVF patients offers the most immediate solution to the shortage of oocytes for research,[19] although it is unlikely that this strategy alone will provide enough oocytes for clinically effective research. Within the clinical context there may be leftover oocytes after treatment which may be donated for research;[20] but the failure of many IVF cycles, the burdens of time and inconvenience, and the risks to health, will mean that many patients will prefer to go through as few cycles of controlled ovarian hyperstimulation (COH) as possible, and therefore store oocytes and IVF embryos for future personal use, thus taking many oocytes out of circulation.

One of the main issues with regard to oocyte procurement from living providers is the risk involved in COH and oocyte retrieval procedures involving the insertion of a needle through the vagina. Stimulating the ovaries in COH to produce more than the usual single monthly egg is an invasive procedure, requiring drug treatment. Ovarian hyperstimulation in IVF treatment is not without risks, and may cause ovarian

---

18 Capps, B. 2002. The European Union and Stem Cell Research: A Turnaround on Policy Regarding Human Embryo Research? Legal Ethics. 5: 18-23.

19 The numbers of women donating oocytes from (3), (5) and (6) are likely to remain small in comparison. Oocyte nuclear replacement therapy (4) is experimental at this stage, and therefore itself is a drain on available oocytes; Mayor, S. 2005. UK Team Hopes to Create a Human Embryo from Three Donors. BMJ 331: 359.

20 These oocytes may also be donated for therapy to women who are seeking to become pregnant and are unable to produce their own oocytes. However, it is reported that in countries where there are strict controls on payment for gametes, such as the UK and Singapore, there are currently insufficient oocytes to meet clinical needs because demand currently far outstrips supply. Further options are therefore for the women to participate in egg sharing schemes (the 'donor' shares her eggs for subsidised IVF treatment), payment to healthy donors, or, where payment is prohibited, to seek treatment abroad where they can pay for oocytes; Murray, C. and Golombok, S. 2000. Oocyte and Semen Donation: A Survey of UK Licensed Centres. Human Reproduction 15: 2133-2139; Ahuja, K., Mostyn, B. and Simons, E. 1997. Egg Sharing and Egg Donation: Attitudes of British Egg Donors and Recipients. Human Reproduction 12: 2845-2852.

hyperstimulation syndrome (OHSS) in some women.[21] This is a sudden and severe iatrogenic disorder which can result in morbidity. Fatalities linked to the syndrome have been reported.[22] There appear to be differences between women with regard to the risk of developing OHSS.[23] Short-term heath risks of needle aspiration include bleeding, infection, and the risks associated with anaesthesia.[24] Pain and psychological problems have also been studied.[25] There are also limited data to suggest that COH affects the woman's future health, such as a lifetime risk of ovarian and non-gynecologic tumours and malignancies, as well as other health conditions.[26]

(2) Healthy Providers

Previously, scientists have relied on women already undergoing fertility treatment donating their extra eggs for research; but, as noted above, this supply is limited by clinical need, and relies on the donation of oocytes by patients who are likely to have reproductive reasons to withhold them from research. Researchers have therefore started to consider the opportunities for healthy women to donate (altruistically) or provide (a 'vendor' or 'broker' where a fee is offered) oocytes for research. Increasingly, financial rewards and incentives are claimed to be the best means to deal with the demand for research oocytes.

---

21 Three categories of OHSS have been determined by clinicians: mild, moderate and severe. Estimates vary widely as to the incidence of OHSS in all its forms, but it has been stated that up to 10% of all cycles result in some form of OHSS. Severe forms (0.2–1.0%) often require hospitalisation to avert potentially lethal effects, and many moderate cases are also hospitalized; Aboulghar, R. and Mansour, M. 2003. Ovarian Hyperstimulation Syndrome: Classifications and Critical Analysis of Preventive Measures. Human Reproduction Update 9: 275-289; Fauser, B., Devroey, P., Yen, S., Gosden, R., Crowley Jr., W., Baird, D. and Bouchard, P. 1999. Minimal Ovarian Stimulation for IVF: Appraisal of Potential Benefits and Drawbacks. Human Reproduction 14: 2681-2686.

22 Lazar, K. 1999. Wonder Drug for Men Alleged to Cause Harm in Women. Boston Herald, August 22.

23 The aetiology of OHSS remains unknown and no strategy has yet been shown to completely prevent occurrence of severe OHSS, short of cancelling the cycle. There are certain molecular markers associated with the onset of OHSS and these may be predictive of the syndrome; Chen, D., Burmeister, L., Goldschlag, D., and Rosenwaks, Z. 2003. Ovarian Hyperstimulation Syndrome: Strategies for Prevention. Reproductive Biomedicine Online 7: 43-49; Shanbhag, S. and Bhattacharya, S. 2002. Current Management of Ovarian Hyperstimulation Syndrome. Hospital Medicine 63: 528-532; Orvieto, R. 2005. Can We Eliminate Severe Ovarian Hyperstimulation Syndrome? Human Reproduction 20: 320-322. There is some evidence that certain genes may provide important predicative information about individual responses to the drugs used; Greb, R., Behre, H. and Simoni, M. 2005. Pharmacogenetics in Ovarian Stimulation. Reproductive Biomedicine Online 11: 589-600.

24 Sauer, M. 2001. Egg Donor Solicitation: Problems Exist, but do Abuses? American Journal of Obstetrics and Gynecology 1: 1-2.

25 Jordan, C., Belar, C. and Williams, R. 2004. Anonymous Oocyte Donation: A Follow-up Analysis of Donors' Experiences. Journal of Psychomotor Obstetrics and Gynecology 25: 145-151.

26 Brinton, L., Moghissi, K., Scoccia, B., Westhoff, C. and Lamb, E. 2005. Ovulation Induction and Cancer Risk. Cancer Cause Control 12: 875-880; Healy, D. 1998. Ovarian Cancer, Infertility and Infertility Therapy. In Kempers, R., Cohen, J., Haney, A. and Younger, J. eds. Fertility and Reproductive Medicine. New York. Elsevier Science. pp. 1-14.

In healthy providers (i.e. woman undergoing COH to provide oocytes only and not as part of IVF treatment), there is a reported lower incidence of OHSS.[27] However, they are exposed to the same risks with regard to the drugs used;[28] and some specialists in reproductive medicine are concerned that there is insufficient information about the long-term effects of these drugs to encourage healthy volunteers to undergo such procedures when there is no reproductive benefit to balance against the risks.[29] A major concern for healthy donors is that oocyte aspiration may lead to infection, and infertility. There are also particular psychological concerns for the healthy provider;[30] and they are also at risk of unintended pregnancy, because hormonal contraceptives must be discontinued.

(3) Donation in Relation to Specific Gynaecological Interventions

Ovarian tissue can be donated after surgery involved in sterilisation and hysterectomy.[31] (It is unlikely that it will be possible for the woman to sell the tissue due to laws prohibiting the sale of organs and tissues.) The existing literature tends to focus on the ethics of donating such tissue for reproductive purposes (i.e. the resulting child's relationship to the donor).

An issue that may be considered in the context of this Paper is the question of whether tissue removed after surgery is considered as 'waste', and as such the property of the hospital to be used in research. This argument has been deployed in the context of cord blood (CB) collected during birth.[32] Previously, placental tissues and CB have been routinely destroyed, unless specific instructions had been given for it to be donated for

---

27 This is linked to the hormones released as a result of the implantation of IVF embryos; Sauer, M., Paulson, R. and Lobo, R. 1996. Rare Occurrence of Ovarian Hyperstimulation Syndrome in Oocyte Donors. International Journal of Obstetrics and Gynecology 52: 259-262.

28 The full extent of the damage to the health of the Korean women who provided the eggs used by Dr. Hwang is not known, but it is apparent that a coalition of 35 women's groups is suing the South Korean government on behalf of women who have been harmed in the process of egg extraction. Reports are that about 20 percent of the donors have experienced side-effects; Hwa-young, T. 2006. Ova Donors Demand Compensation from Government. AsiaNews.it. 2 July; available at: www.asianews.it/view_p.php?1=en&art=5322. Assessed March 2007.

29 Pearson, H. 2006. Health Effects of Egg Donation May Take Decades to Emerge. Nature 442: 607-608.

30 The possible psychological and medical stress for the oocyte broker was vividly captured by the traumas of an American Ivy League student. She described how after invasive probing of her persona, the recipient couple rejected her as an egg donor because of, as she described it, the perceived inadequacies in her gene pool; Sunday Telegraph (London), 5 January 2003. A (limited) study of women providing oocytes for research reported that they felt like and were treated like a commodity; '[t]hey used terms like "prostitute" and "livestock" to describe how they felt, and they described the medical care as cold and impersonal. Specific actions such as being referred to by a number or pseudonym rather than their names, being segregated into a separate waiting room, and being instructed not to speak to other patients contributed to this feeling'; Kalfoglou, A. 2001. Navigating Conflict of Interest in Oocyte Donation. American Journal of Bioethics 1: W1-W2.

31 Bromwich, P. 1990. Oocyte donation. British Medical Journal 300: 1671-1672.

32 Zhao Y, Mazzone T. 2006. Turning 'Waste" into Gold: Identification of Novel Stem Cells from Human Umbilical Cord Blood. Discovery Medicine 6: 87-89.

research, and in the case of CB, in treatment for childhood blood disorders.[33] However, a sudden increase in value of the latter has now been confirmed because of its SC content, and thus potential use in research.[34] In the context of oocyte procurement, the following issues arise: (a) informing the patient of the option to donate cells for research; (b) avoiding commitments to collect the cells in the event of clinical difficulties; and (c) obtaining consent to use this important resource, rather than routinely discarding it. In the UK, these issues have been brought into sharp relief by the controversy over retained organs without consent.[35]

(4) Donors in Experimental Reproductive Technology

A parallel development to regenerative SC medicine has been the possibility of oocyte nuclear replacement (ONR) to 'repair' oocytes by replacing damaged mitochondria residing in the oocyte cytoplasm. The use of ONR technology – which is technically similar to CNR – may provide the solution to many mitochondrial-associated diseases.[36] It is possible that oocytes collected for ONR research and therapy may be donated to other research projects. However, as well as the ethical dilemmas, societal concerns, and recent controversies regarding 'therapeutic cloning',[37] there are issues of participation in experimental clinical research (discussed further, below) and germ line genetic modification.[38] In the current context, it is important to consider whether the need for oocytes for SC research (which in this case is a subsidiary intention in regard to the reproductive-clinical research in treating mitochondrial disease) will detrimentally affect the normal rules of research participation. For example, whether withdrawing from an ONR project also entitles a woman to recall her oocytes, if they are being used in research elsewhere.

---

33 Hows, J. 2001. Status of Umbilical Cord Blood Transplantation in the Year 2001. Journal of Clinical Pathology 54: 428-434.

34 Wagner, J. and Verfaillie, C. 2004. Ex Vivo Expansion of Umbilical Cord Blood Hemopoietic Stem and Progenitor Cells. Experimental Hematology 32: 412-413. Future therapy is increasingly considered as an option via CB banks offering (questionable) autologious (self) treatments; Kmietowicz, Z. 2001. Doctors Object to Companies Offering to Store Cord Blood. British Medical Journal 323: 1203.

35 In the context of CB, see: Armson, B. 2005. Umbilical Cord Blood Banking: Implications for Perinatal Care Providers. Canadian Journal of Obstetrics and Gynecology 27: 673. Regarding the issue of retained organs, see: Campbell, A. V. and Willis, M. 2006. They Stole My Baby's Sole: Narratives of Embodiment and Loss. In The Self in Health and Illness: patients, Professionals and the Narrative Identity. Rapport, F and Wainwright, P. eds. Oxford. Radcliffe. pp. 123-129.

36 Hall, V., Stojkovic, P. and Stojkovic, M. 2006. Using Therapeutic Cloning to Fight Human Disease: A Conundrum or Reality? Stem Cells 24: 1628-1637.

37 The theoretical treatment in this case is oocyte nuclear replacement, which differs from the 'Dolly' technique (CNR) in that an oocyte, rather than a somatic cell, is used as the recipient of donor nuclear DNA.

38 Department of Health 2000. Stem Cell Research: Medical Progress with Responsibility - A Report from the Chief Medical Officer's Expert Group Reviewing the Potential of Developments in Stem Cell research and Cell Nuclear Replacement to Benefit Human Health. London. DoH.

(5) Posthumous Donation

The issues regarding posthumous donation involve the importance of the opportunity to specify personal wishes regarding the removal of specific organs, and in this particular case, reproductive tissue, which may have special symbolic and procreative status.[39] This raises many issues regarding organ donation in general, but with reproductive tissues there are the complexities of potentially creating new life from a deceased donor (and the possible implications for the familial relationships between living relatives). The important issue with regard to research however, are the pre-stated wishes of the person to involve her oocytes in research after her death, and the means to obtain consent though specific research pro-active policies.

(6) Aborted Foetal Tissue

Using eggs from aborted foetuses is possible due to advances in *in vitro* ovarian maturation and cryopreservation techniques. Some of the arguments against using foetal tissue in research reflect anti-abortion arguments, which are outside the scope of this paper.

One objection to the use of foetal tissue is that this demand will lead to coercion, devious pressures and financial incentives to terminate pregnancies. The common solution to such arguments is to separate the choice to have an abortion, the carrying out of the abortion, and any subsequent use of the tissue from the abortus. It is argued that the researcher should not have any influence on the clinical needs and decisions of women undergoing a termination of pregnancy, and consent for the use foetal tissue in research should be sought only after a woman has given her consent to the termination.[40] However, concerns about using oocytes or ovarian tissue from aborted female foetuses may also reflect more nuanced arguments regarding the relationships between the person undergoing an abortion and the researcher.

There is an argument that excluding clinical investigators from the clinical care of women undergoing termination codifies distrust of clinicians who undertake research, and so, according to the Royal College of Obstetricians and Gynaecologists (UK), inhibits the progress of research.[41] A second argument concerns the conditions of consent. In most jurisdictions, a woman's consent to the use of the foetus in research is general: she is not given the opportunity to specify how her foetal tissue may or may not be used. However, the use of non-specific consent is suggested to be ‘increasingly

---

39 Mizukami, A., Peterson, M.., Huang, I., Cook, C., Boyack, L., Emery, B. and Carrell, D. 2005. The Acceptability of Posthumous Human Ovarian Tissue Donation in Utah. Human Reproduction 20: 3560-3565.

40 Polkinghorne, J. 1989. Review of the Guidance on the Research Use of Fetuses and Fetal Material. London. HMSO.

41 Royal College of Obstetricians and Gynaecologists. 2004. Response to MRC Consultation on the Code of Practice for the Use of Human Stem Cell Lines. www.rcog.org.uk. Accessed June 2005.

out of step with modern expectations';[42] thus, for example, making decisions on an *informed* basis may require details of the *purpose* of the intended research and feedback on whether the oocytes have been used at all. Others have argued that we should do away with considerations of research-specific consent, and instead allow blanket consent to free up the purposes of research.[43] Finally, there is an argument that clinical practice and research need not be in conflict. Therefore it may be ethically acceptable to modify the termination procedure according to the needs of the latter (to ensure that the foetal reproductive tissue is collected with due care, indicating its future use in research), without this being to the detriment of the woman's health.[44]

(7) Non-Human Sources

In the future, the use of animal oocytes to create human-animal chimeras for research may significantly relieve the demand for oocytes (if permitted in regulations). Using animal oocytes as a 'shell' for human nuclear DNA for the purpose of creating genetically human SCs for research is a possible solution to the scarcity of human oocytes and the ethical concerns linked to some human sources.[45] However, this may not be a long term solution, unless (controversially) the use of animal oocytes in *therapy* is also permitted.[46] The ethics of 'Stem Cell Research and Interspecies Fusion' has been discussed in detail in a separate Background Paper prepared for the Bioethics Advisory Committee.[47]

(8) Stem Cell-Derived Oocytes

A further possible (and promising) solution to the demand for oocytes in research is the creation of female gametes directly from SCs. This proposal raises few new ethical concerns with regard to *research* (but may be controversial with regard to reproduction), but it is still at the experimental stage, and research will continue to require a source of conventionally created embryos using sourced oocytes to pursue this possibility.[48]

---

42 Department of Health. 2002. Human Bodies, Human Choices: The Law on Human Organs and Tissue in England and Wales. A Consultation Report. London. DoH. sec 15.13.

43 Burley, J. 2005. Stem Cells and Translational Medicine: Ethics, Law and Policy. In Bongso, A. and Lee E. H. eds. Stem Cells: From Bench to Bedside. Singapore. World Scientific. pp. 186-211.

44 Department of Health, op. cit. note 42, sec. 15.9-15.11.

45 Robert, J. 2006. The Science and Ethics of Making Part-Human Animals in Stem Cell Biology. The Journal of the Federation of the American Societies for Experimental Biology FASEB J 20: 838-845.

46 The creation of chimeras is possible in some countries, such as (currently) in the UK, for research purposes only; Karpowicz, P., Cohen, C. and Van der Kooy, D. 2005. Developing Human-Nonhuman Chimeras in Human Stem Cell Research: Ethical Issues and Boundaries. Kennedy Institute of Ethics Journal 15: 107-134.

47 By Nuyen, A.T. Department of Philosophy, National University of Singapore. 2006.

48 Master, Z. 2006. Embryonic Stem-Cell Gametes: The New Frontier in Human Reproduction. Human Reproduction 21:857-863.

PART TWO: CURRENT LEGISLATIVE FRAMEWORKS REGARDING MONETARY EXCHANGE AND OOCYTE PROVISION FOR RESEARCH

In this section and subsequent sections I will concentrate solely on the issues arising out of monetary exchanges when sourcing oocytes for *research purposes* from consenting women is permitted.[49] Other legal issues to consider, but which (due to space) cannot be discussed in this Paper, are those concerning contractual arrangements, including those of medical obligation (for example in the provision of treatment and negligence in cases of OHSS).

(1) Payment for Human Oocytes

It is widely established in jurisprudential regions,[50] though more disputed in the ethics literature,[51] that direct payments should prohibited with regard to human tissues and organs. Therefore, it is unlikely that this restriction would be (legally) challenged with regard to the donation of ovarian tissue in (3), (4), (5) and (6), above. Many countries also expressly prohibit the purchase of human oocytes.[52]

However, in the USA a market in oocytes is not illegal, since gametes are excluded from Federal law prohibiting the sale of organs. Interestingly, there are some States which permit payment for oocyte providers if the purpose is IVF treatment, but prohibit payment if the eggs are to be used in research. In States such as Massachusetts and California, compensation for reasonable expenses is permitted only.[53] (This may be an 'ethical' response to the large amounts of money invested in SC research and the continuing political requirement for public support.)

Strictly speaking, the US federal policy is one of laissez faire, rather than a deliberate decision to authorise an oocyte market. It probably developed out of the concurrent demand for IVF treatment and means of storing ones own oocytes for own use. This led

---

49 See, for example: Gunning, J. 1997. Oocyte Donation: The Legislative Framework in Western Europe. Bioethics 11: 98-102.

50 E.g. see the World Health Organisation's Resolution WHA57.18 on Human Organ and Tissue Transplantation; Fifty-Seventh World Health Assembly 22 May 2004. WHO. Geneva. For example, Singapore, the UK and the USA are fairly typical in prohibiting payment for organs through specific legislation; all three allow reimbursement for expenses associated with the donation; Human Organ Transplant Act 1987 (Singapore); Human Tissue Act 2004 (UK); and National Organ Transplant Act, 98-507 (1984) (USA).

51 Friedman, A. 2006. Payment for Living Organ Donation Should be Legalised. British Medical Journal 333: 746-748; Savulescu, J. 2003. Is the Sale of Body Parts Wrong? Journal of Medical Ethics 29: 138-139; Benatar, S. 2004. Blinkered Bioethics. Journal of Medical Ethics 20: 291-292; Campbell, A. V. In press. Why the Body Matters: Reflections on John Harris's Account of Organ Procurement. In Holm, S., Hayry, M., and Takala, T. eds. Life of Value. Amsterdam and New York. Rodopi.

52 E.g. Ministry of Health (Singapore), 1990; 6th Update 2006. Directives for Private Healthcare Institutions Providing Assisted Reproduction Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations (CAP 248, REG 1), sec. 4.11.2; Human Fertilisation and Embryology Act 1990 (UK), sec. 12(i).

53 Spar, D. 2007. The Egg Trade – Making Sense of the Market for Human Oocytes. New England Journal of Medicine 356: 1289-1291.

to raising payment to the level of what the market will bear.[54] Thus, demand for oocytes determines whether, and how much, 'donors' are paid,[55] with some clinics offering up to $10,000 and more for oocyte provision.[56] (Online and media advertisements can offer significantly more.)[57] The payment of 'private egg brokers' is seen by many as 'compensation for time and trouble'.[58] The rationale given for this is that in addition to the risks assumed by the provider, oocyte procurement is a significant burden for women in terms of time. The American Society for Reproductive Medicine (ASRM) cites an estimate that egg providers spend '56 hours in the medical setting, undergoing interviews, counseling, and medical procedures related to the process'.[59]

(2) Compensation for Living Oocyte Providers

Strict Compensation

Different levels of compensation exist in various countries. The least beneficial to personal profit – in terms of financial reward – is strict compensation, as found in Singapore. Here, the current position is that oocyte donation for research is permitted both for IVF patients and for healthy volunteers not undergoing fertility treatment. However, no inducement, financial or otherwise, is allowed under the *Human Cloning and Other Prohibited Practices Act 2004*,[60] although payment of 'reasonable expenses' is permitted for direct 'out-of-pocket' monetary loss.[61] In this model, it is possible that the donor will be financially worse off, if, for example, she has to take time away from work to participate in the donation or because of illness linked to the COH procedure.

Cost Neutral Compensation

The cost neutral model, adopted by a number of counties, prevents providers from making any profit from the donation, but also attempts to ensure that they are not financially worse off. As of early 2007, women in the UK are able to donate their eggs to research projects.[62] Women had previously been able to donate only spare eggs

---

54 Sauer, op. cit. note 24.

55 Sapr, D. 2006. The Baby Business: How Money, Science and Politics Drive the Commerce of Conception. Massachusetts. Harvard Business School Press.

56 Ethics Committee of the ASRM. 2000. Financial Incentives in Recruitment of Oocyte Donors. Fertility and Sterility 74: 216-220.

57 Kolata, G. 1999. $50,000 Offer For Egg Donor Sharpens the Debate. New York Times, 3 March. p. A10

58 Ethics Committee of ASRM, op. cit. note 56; ASRM. 2000. Financial Incentives in Recruitment of Oocyte Donors. Fertility and Sterility 74: 216-220.

59 Ethics Committee of ASRM. 2004. Financial Incentives in Recruitment of Oocyte Donors. Fertility and Sterility 82 Suppl. 1: S240-S244.

60 Chapter 131B; sec. 13; also see: Ministry of Health, op. cit. note 52.

61 Ibid. sec. (5)(a).

62 HFEA Statement on Donating Eggs for Research. 21 February 2007. Available at: http://www.hfea.gov.uk/cps/rde/xchg/SID-3F57D79B-9CF63D2F/hfea/hs.xsl/1491.html. Accessed March 2007; HFEA. 2006. Donating Eggs for Research: Safeguarding Donors – Consultation Document. London. HFEA. p. 9.

produced through IVF or in connection with gynaecological treatment such as sterilisation. Limited expenses can be provided to gamete donors as 'reimbursement' for any 'out-of-pocket' costs incurred *and* loss of earnings;[63] these are considered as reasonable expenses only if they are incurred within UK in direct connection with the donation.[64] Informal 'payment' may also be given to oocyte donors at the discretion of fertility clinics.[65] Compensation is therefore 'expense neutral', and the donor is left no worse off as a result of providing her oocytes.[66] It is not clear whether 'loss of wages' would include time away from work as a result of illness directly associated to the procedure.

Fixed Compensation

Some countries allow for fixed pecuniary compensation. This is set by policy rather than by market forces or the evidence of actual expenditure (as in the previous two schemes). The level of compensation may take into account any costs of the donor, but since it is a fixed amount, it does not specify what these 'costs' may be for each potential donor (i.e. direct costs, time, risk or loss of earnings). Thus the amount may constitute a positive benefit to the donor, since what is only reimbursement for one woman, may constitute payment for another.[67]

(3) Benefits in Kind

In addition to the 'cost neutral' compensation available in the UK, there are no legal restrictions on the value of *other benefits* which may be given to the donor. However,

---

63 Capped at £55.19 a day, but with an absolute limit for each cycle of oocyte donation of £250; HFEA. 2006. Directions Given Under the Human Fertilisation and Embryology Act 1990: Giving and Receiving Money or Other Benefits in Respect of Any Supply of Gametes or Embryos. Ref. D.2006/1. London. HFEA.

64 To dissuade 'fully funded' visits from abroad; HFEA. 2005. SEED Report: A Report on the Human Fertilisation and Embryology Authority's Review of Sperm, Egg and Embryo Donation in the United Kingdom. London. HFEA. (hereafter SEED). sec. 4.5.

65 Capped at fifteen pounds plus expenses, this is permitted as an incentive to recruit donors for IVF treatment; HFEA. 2003. Code of Practice 6th Edition. London. HFEA. sec. 4.26. Although it has previously been considered whether any payment at all is ethical; see: HFEA. 1998. Consultation on the Implementation of Withdrawal of Payments to Donors. London. HFEA. The current payment is set at a level which does not '…induce research participants to take risks that they would otherwise take, or to volunteer more frequently than is advisable or against their better interests or judgments'; quoted in: HFEA. 2006, op. cit. note 62, p. 23.

66 SEED, op. cit. note 64, sec. 4.

67 The danger is that poor countries will be the targets for donation, because compensation in one country may amount to payment in another. In reference to Romanians in particular donating in the UK, an HFEA spokesperson stated: 'We have to ask why there appear to be so many more altruistic donors in other countries'; Derbyshire, D. 2004. Law on Anonymity Drives Would-Be Parents Abroad. Daily Telegraph (UK), 3 July. Available at: http://www.telegraph.co.uk/news/main.jhtml?xml=/news/2004/07/03/nivf03.xml. Accessed April 2007.

the only ones which may be offered for this purpose are 'treatment services', and so, in practice, this means subsidised IVF treatment.[68]

A justification for such schemes is that OHSS and other risks may be acceptable for successful IVF outcomes (and which are not altered by the donation of spare oocytes for research),[69] but not for healthy volunteers involved in research only. Therefore, since patients are already exposed to these drugs, there is no need to differentiate the subsequent use of oocytes; and if there are spare oocytes remaining after treatment they may be donated for research (I will return to this issue, below).

A further issue is that this scheme exposes the tension (and blurring of boundaries) between IVF-clinical goals[70] and the drive for research progress. On the one hand, a policy of collecting large numbers of oocytes driven by clinical need may result in spare oocytes which can be donated for research. On the other hand, there is the view that lower numbers of oocytes – and therefore lower levels of drugs which may decisively reduce clinical complications –[71] may provide an equal probability of successful pregnancy.[72] Obviously, fewer oocytes will thereby be available for research. It is also not clear what the contractual consequences are, if no oocytes are available for donation for research subsequent to treatment.

(4) Other Conditions for Oocyte Donation

There are countries which allow the donation of oocytes only from those undergoing IVF treatment, and in South Korea, since the Hwang scandal, egg donors cannot receive any financial reward or personal benefit. However, where oocyte donation from healthy woman is permitted by regulations, there are some common provisions associated with any recompense.[73]

---

68 HFEA, op cit. note 63, para. 5. This clause relates to a Direction, issued in 1992, in which the HFEA permitted the provision of 'treatment services and sterilization in exchange for ovum donation' or 'egg sharing'; see: Blyth, E. 2002. Subsidized IVF: The Development of 'Egg Sharing' in the United Kingdom. Human Reproduction 17: 3254-3259.

69 This is partly driven by a policy in many clinics to obtain a large number of eggs which can be frozen and retained for later use by the clients if the initial round of treatment fails. However, others have cautioned against the unchecked drive for achieving a successful pregnancy; see: Abramov, Y., Elchalal, U. and Schenker, J. 1999. Severe OHSS: An 'Epidemic' Of Severe OHSS: A Price We Have To Pay? Human Reproduction 14: 2181–2183; Emperaire, J. and Edwards, R. 2004. Time to Revolutionize the Triggering of Ovulation. Reproductive BioMedicine Online 9: 480–483.

70 Ferber, S. 2007. As Sure As Eggs? Responses to an Ethical Question Posed by Abramov, Elchalal, and Schenker. Journal of Clinical Ethics 18: 35-48.

71 Aboulghar, R. and Mansour, M. 2003. Ovarian Hyperstimulation Syndrome: Classifications and Critical Analysis of Preventive Measures. Human Reproduction Update 9: 275–289.

72 Inge, G., Brinsden, P. and Elder, K. 2005. Oocyte Number Per Live Birth in IVF: Were Steptoe and Edwards Less Wasteful? Human Reproduction 20: 588–592; Edwards, R., Lobo, R. and Bouchard, P. 1996. Time to Revolutionize Ovarian Stimulation. Human Reproduction 11: 917–919.

73 For example, some countries, such as Denmark, allow donation of oocytes for IVF treatment from IVF patients only; Andersen A., Larsen J., Hornnes P., Starup J., Andersen C., Westergaard L., Rasmussen P., Ingerslev H. and Maigaard, S. 1993. Ovum donation: A Review

Underlying much of the justification for allowing women to provide oocytes for research are measures to ensure that information is openly and freely made available regarding the risks and that she is well aware of the consequences of her decision.[74] Importantly, any compensation or payment should not cloud her judgment. However, there are some reports that the full implications of the risks of oocyte donation are not always made available to donors.[75] To avoid this occurring, a detailed procedure to ensure proper information and to look for evidence of coercion (financial or emotional) is needed. In Singapore, for example, a scheme operated by the Ministry of Health includes provisions for the review of all prospective healthy donors by a panel to ensure that consent for donation is informed and voluntary.[76] In assessing each donation, the panel must give additional consideration to the 'public interest' and 'community values'.[77] Furthermore, often donors are screened in general medical evaluations, and specific screening for sexually transmitted diseases, genetic screening and a psychological assessment.[78] (Often these are more relevant to oocyte donation for reproductive purposes.)

(5) The International Demand for in Oocytes

The wide range of national policies on oocyte provision means that the international aspects of human body markets are significant; and the globalization of medicine has a

---

of and a Suggestion to Unified Guidelines for Treatment at Public Fertility Clinics in Denmark. Ugeskr Laeger 155: 2515-2519. Most countries have research ethics frameworks to establish the ethical and scientific credibility of research projects involving human participants. In this regard, such committees will probably want to ensure that the condition of oocyte procurement (consent and justified incentives) are in line with local regulations and ethical norms.

74 Ethics Committee of the ASRM, op. cit. note 56. The implications for future heath and risks for an IVF patient as a result of ovarian hyperstimulation are quite different from a healthy donor, and IVF patients go through no unnecessary or unrelated treatment to procure oocytes should they decide to donate them for research.

75 Magnus, D. and Cho, M. 2005. Issues in Oocyte Donation for Stem Cell Research. Science 308: 1747-1748.

76 Ministry of Health, op. cit. note 52; see section 8 on 'Research'.

77 Ibid. sec. 8.6. 'Public interest' lacks a concise definition in many legislatures. In Singapore, for example, Justice VK Rajah stated: '…it is also pertinent to reiterate that public interest is not a static concept fossilized by time or space, but rather a dynamic one, shaped and coloured by the circumstances and mores of a particular society'; Public Prosecutor v Law Aik Meng [2007] SGHC 33. I will return to this question later in the paper. 'Community values' may indicate the recognition of the plurality of established cultural norms in Singapore; Heng, B. 2006. Alternative Solutions to the Current Situation of Oocyte Donation in Singapore. Reproductive BioMedicine Online 12: 286–291.

78 It should also be noted that often the health and medical information required from the potential donor are significant, including health history, microbiological testing, genetic information and data on lifestyle choices. This is often not trivial information, and requires careful management on behalf of the donor by the collector, repository, and the researcher, and which must be consented to by the donor. Furthermore, rules on traceability are likely to become more significant, as the EU Tissue Directive demonstrates; Sousa et al., op. cit. note 6. See: ASRM. 2002. Guidelines for Oocyte Donation. Fertility and Sterility 77: S6–S8; ASRM. 2002. Psychological Assessment of Gamete Donors and Recipients. Fertility and Sterility 77: S11–S12. However, the problem in the USA is that the ASRM's recommendations are optional and therefore (evidently) ineffectual.

significant impact on market positive arguments. One of the arguments offered to support markets is that they prevent potential providers from heading overseas, and so limit the incentive for overseas providers to leave their country.[79] Erin and Harris claim that an open market in body parts can be ethical if it is regionally specific.[80] However, while creating more convenient and rewarding ways to procure oocytes may reduce the demand for overseas oocytes, it will not eliminate the demand as long as those overseas oocytes remain significantly cheaper to procure than home based ones. Controlling an 'ethical' market on the lines described by Erin and Harris would require a well defined and regulatory advanced region; but it is unlikely that such a state could ever be achieved without strict policing, and this raises its own concerns.[81] In Europe, where there is a developed regulatory framework in the procurement of organs, tissues and cells at the Community and Member State level, 'medical tourism' to procure various clinical services is evident; and it is clear that potential donors are willing to travel to receive payment for their oocytes.[82] With regard to SC science this raises a specific concern for the 'invisible donor':[83] the purchase of oocytes from brokers in de-regulated havens where there is no traceability, or evidence of, for example, informed consent.[84]

PART THREE: ETHICAL ISSUES

As stated at the outset of this Paper, current patterns in research will probably increase the demand on human oocytes. As a consequence there is likely to be an increased use of incentives or rewards to recruit potential donors and the possible emergence of a 'black market' in oocytes. In the following sections, I will address three issues that are at the forefront of the current debate regarding oocyte procurement from women able to consent. It will become clear that a theme to this debate is the actual choice which potential donors have when possible coercion and undue incentives are in the background. Reaching an ethical solution to the scarcity of human oocytes in public policy will therefore require an assessment of public interest as a guide to balancing altruistic and incentive-driven motivations.

---

79 Sauer, M. 1997. Reproductive Prohibition: Restricting Donor Payment will lead to Medical Tourism. Human Reproduction 12: 1844-1845; the stories of two British students who traveled to the USA to donate their eggs for financial reward can be found in: Sunday Times (London), 24 November 2002.

80 Erin, C. and Harris, J. 2003. An Ethical Market in Human Organs. Journal of Medical Ethics 29: 137-138.

81 Pennings, G. 2002. Reproductive Tourism as Moral Pluralism in Motion. Journal of Medical Ethics 28: 337-341.

82 It is alleged that a large number of Romanian women donate to UK and USA clinics, where 'reasonable expenses' of 100-250 Euros (or 6,400 Euros by one US company) provide a significant income for them in their home country; Daily Telegraph (London), 14th June 2005.

83 Delmonico, F. and Dew, M. 2007. Living Donor Kidney Transplantation in a Global Environment. Kidney International advance online publication, 7th February. doi: 10.1038/sj.ki.5002125.

84 Aldhous, P. 2000. Panacea, or Pandora's Box? Nature 408: 897-898.

I. Payment and Compensation

It is often pointed out that the problem of oocyte availability (and for that matter, organ availability) is comparatively less in countries where commercialisation is tolerated.[85] Therefore, it is argued that governmental restraints placed on payment may restrict woman from providing oocytes either for IVF treatment or for research.[86] Many see an appeal to healthy providers as a solution to the shortage of oocytes for research; but how one makes altruistic donation an attractive choice, or failing that, persuades women to donate oocytes, are crucial questions. It is argued that women are unlikely to donate oocytes for research when there is little, if any, direct benefit for them. Thus, payment is claimed to be a justified incentive to attract potential providers. However, others argue that this will merely lead to an uncontrollable market in oocytes, and once this happens, commodification and exploitation are significant risks (discussed in the next section). Thus, they believe that research must rely on altruistic and limited incentive-driven donation.

Proponents of oocyte payment schemes often question even the possibility of truly altruistic donation; some argue that, with the risks and inconvenience set so high, a culture of altruistic donation will never be achieved.[87] Thus, many turn to consistency arguments to allow universal payment for 'donors'. Presently, payment for organ donation is generally prohibited, but payment *is* permitted for participation in clinical research, where volunteers are recompensed for their time and effort, as well as for expenses incurred.[88] Often, risks are also factored into the amount paid.[89] It is argued that 'financially positive' compensation, whether it is for research, organ or oocyte donation, constitutes a fair recognition of the contribution of the individual. It is further claimed that this in no way diminishes altruistic motives or the generosity of the donor, rather that it is an appropriate gesture of thanks for the time spent and inconvenience (willingly) experienced.[90] Payment or comprehensive compensation for living donors should therefore be made ethically consistent, and exploitation and equitable treatment of donor and recipient can be managed through a controlled market, so it is argued.[91]

---

85 Sidebotham, M. 2003. Egg and Sperm Donation: An Issue for Health Care Professionals? Journal of Family Health Care 13: 134-136.

86 The other possibility is that the lack of regulation in the USA (for example) disproportionately encourages oocyte donation; Sauer, M. 2005. Further HFEA Restrictions on Egg Donation in the UK: Two Strikes and You're Out. Reproductive BioMedicine Online 10: 431-433.

87 Ironically, prior to the Hwang controversy, it was commented that: 'South Korea has a culture of egg donation for research, which enabled the scientists to obtain good-quality eggs'; Cookson, C. 2005. The Cloning Connections. In: The Future of Stem Cells. Financial Times & Scientific American Special Report. p. A11.

88 Woo, K. 1999. Conducting Clinical Trials in Singapore. Singapore Medical Journal 40: no page number (Singapore); General Medical Council (GMC). 2002. Research: The Role and Responsibility of Doctors. London. GMC (UK); and National Institutes of Health. Modification of GCRC Guidelines Regarding Payment to Research Subjects; June 2002. Available at: http://www.ncrr.nih.gov/clinical/crguide2001/gcrcguidelinemodify062002.pdf (USA).

89 The distinction between payment for donating for profit in IVF and compensation for donation for research in some US states is likewise criticised ; Spar, op. cit. note 51.

90 Ethics Committee of ASRM, op. cit. note 56.

91 Friedman, op. cit. note 51.

Others emphasise the difference between the donation of different body parts. Objection to the sale of parts like kidneys, they claim, 'lacks punch in the case of gametes, which are replaceable, and non-essential to health'.[92] So, the degree of risk for oocyte donors does not warrant the same paternalistic protection; and oocytes, since they lack characteristics that confer 'interests' (or a 'dignity' status, discussed below), can be bought and sold as property.[93]

In light of the concerns about markets in human body parts, policies have evolved that attempt to provide incentives without leading to direct payment to the donor. As we saw above, one solution, preferred in the UK, is to make the proposition of donation attractive to a limited population by offering 'benefits in kind' to IVF patients. Proponents of this scheme point out that, working with donors who are using ovulation-stimulating drugs anyway, avoids exposing otherwise healthy women to any risks associated with them.[94] The most recent study concerning egg-sharing in IVF exchanges provided evidence that such practices do not affect the success of IVF treatment;[95] therefore, it is possible that donating oocytes for research *as part of the IVF treatment* would also not affect the clinical outcome. Furthermore, it is argued, subsidised IVF treatment services do not represent payment in monetary terms. These 'other benefits' reflect services which cannot normally be measured in money. (One can pay for a service, but the service itself – once used – has no monetary value).[96] However, in addition to a number of clinical concerns of clinical practice to be arising,[97] some critics view subsidised IVF treatment as essentially a commodity exchange – redefining the interaction to avoid any reference to payment –, and so perilously close to a financial inducement.[98]

Compensation for expenses is therefore the most common incentive for oocyte donation. But even here there are concerns. Since the primary motivation of having a child is no longer present, any incentive treads very close to what may be considered as

---

92 Burley, op. cit. note 43, p. 193.

93 Ibid. p. 194.

94 Ahuja, K., Simons, E., Rimington, M., Nair, S., Gill, A., Evbuomwan, I. and Bowen-Simpkins, P. 2000. One Hundred and Three Concurrent IVF Successes for Donors and Recipients Who Shared Eggs: Ethical and Practical Benefits of Egg Sharing to Society. Reproductive Biomedicine Online 1: 101-105.

95 Thum, M., Gafar, A., Wren, M., Faris, R., Ogunyemi, B., Korea, L., Scott, L. and Abdalla, H. 2003. Does Egg-Sharing Compromise the Chance of Donors or Recipients Achieving a Live Birth? Human Reproduction 18: 2363-2367.

96 SEED, op. cit. note 64, sec. 10.

97 There are a number of established rules that should be followed surrounding the separation of the clinician and research, so as to ensure that, for example, there is no risk of over-stimulation to produce more oocytes for treatment and research. A problem is that pressure to donate by IVF patients is inherent in any subsidy agreement, since without the arrangement, the woman in under no pressure to donate. Furthermore, what should happen if the woman withdraws her consent to donate embryos while undergoing treatment?

98 Johnson, M. 1997. Payments to Gamete Donors: Position of the Human Fertilisation and Embryology Authority. Human Reproduction 12: 1839-1846.

'undue', especially if the decision to participate rests solely on monetary recompense.[99] If incentives are undue, it is normally to the detriment of the individual's ability to provide free and voluntary consent.[100] Therefore, compensation schemes, however they are presented, do provide an incentive which selectively attracts a certain – often financially less well off – person; and for some, this amounts to little more than subtle coercion and exploitation.

The fundamental question is where the point lies at which compensation becomes an undue incentive or reward, since a sum that will be merely compensation for one woman could be enticement for another. The recent drug trials in the UK and the recent research-related deaths in the USA illustrate the significant risks of harm in some classes of medical research.[101] This had lead to questions regarding the appropriateness of incentives in inherently risky clinical research, and indeed all activities in which the 'donor' exposes herself to significant risk.[102] If consistency is a criterion for regulating risky practices, then it might be argued that what is permitted for volunteers in one area should be applicable to all forms of volunteering, such as oocyte and organ donation. But the argument can cut the other way: perhaps the stricter controls on the latter should be applied to the former. This would mean that many current aspects of clinical research participation by healthy volunteers may be exposed as coercive. (How many would have participated – and what 'payment' would have been reasonable – in the TeGenero trial if they knew of the risks?).

II. Commodification

Commodification is the transformation of what is normally a non-commodity into a commodity, or, in other words, to assign monetary value. Once something has a value,

---

99 Tishler, C. and Bartholomae, S. 2002. The Recruitment of Normal Healthy Volunteers: A Review of the Literature on the Use of Financial Incentives. Journal of Clinical Pharmacology 42: 365-375.

100 Macklin, R. 1981. On Paying Money to Research Subjects: 'Due' and 'Undue' Inducements. IRB 3: 1-6. There are numerous concerns regarding consent in this specific context, for example, the comprehension of present risk and future health implications (such as healthy donors who are pre-motherhood and potential infertility through COH), especially in the present uncertainty and the paucity of meaningful statistics. In attaining consent, the oocyte collectors have the concern of the non-disclosure of information if incentives are too high. This not only risks the health of the patient, but also may invalidate research; Bentley, J. and Thacker, P. 2004. The Influence of Risk and Monetary Payment on the Research Participation Decision Making Process. Journal of Medical Ethics 30: 293-298.

101 Steinbrook, R. 2002. Protecting Research Subjects: The Crisis at Johns Hopkins. New England Journal of Medicine. 346: 716-720.

102 Indeed, oocyte donors have been classified as 'research donors' to distinguish them from research participants, while acknowledging that they are part of a wider research – rather than therapy – programme; Magnus, D. and Cho, M. 2005. Issues in Oocyte Donation for Stem Cell Research. Science 308: 1747-1748. That is not to say that all human research is as risky as giving up a kidney or going through ovarian hyperstimulation, but there may be cases in which 'special scrutiny' of certain types of research is needed; Levine, C., Faden, R., Grady, C., Hammerschmidt, D., Eckenwiler, L., Sugarman J. and Consortium to Examine Clinical Research Ethics. 2004. 'Special Scrutiny': A Targeted Form of Research Protocol Review. Annals of Internal Medicine 140: 220-224.

it can be bought and sold, and for some, this betrays the 'dignity' status of human beings.[103] For others, commodification leads to processes through which social relations are reduced to an exchange relation; thus the interests, health, wellbeing, and 'worth' of the individual come second to monetary interests, and there is an inevitable disregard of human rights and the encouragement of exploitive practices. In practical terms, commodification in human body parts leads to the inducement for economically vulnerable people to sell their organs, tissues and cells, since they are the only ones who stand to benefit by addressing financial burdens in this way. Therefore, a common argument against payment for human parts focuses on the concept of 'gift'.[104] It is argued that receiving 'valuable consideration' or 'money's worth' in exchange for organs contradicts the normal understanding of a gift as something that is given without the expectation of payment or reward; and by emphasising the altruistic nature of giving human parts, one is better able to avoid the risks of an open market.

A problem here is that donors may 'gift' their oocytes to research, but the relationship is really one of exploitation: 'If donors believe they are demonstrating altruism, but biotechnology firms and researchers use the discourse of commodity and profit, we have not 'incomplete commodification' but complete commodification with a plausibly human face'.[105] Solving this problem, according to some, would require making the transaction transparent – and therefore making it subject to *public* payment. Choice therefore becomes paramount; but we are left with the familiar problem that ''choice' appeals to those who have options, but it is relatively meaningless to those who do not, it is politically divisive'.[106] The European Parliament (of the European Union) therefore conclude that any trade – public or not – should be prohibited, and that 'egg cell donation, like organ donation generally, [should be] strictly regulated in order to protect both donors and recipients and to tackle all forms of human exploitation; [and] …any woman forced to sell any part of her body, including reproductive cells, becomes prey to organised crime networks that traffic in people and organs'.[107]

Another way to avoid commodification, so it is argued, is to prohibit payment altogether, and this is justified on the grounds that while there is some form of rights over the control of one's body parts (i.e. to be able to donate oocytes regardless of the risks),[108] there are no rights to exploit the commercial value of the same. This is similar

---

103 See: Brownsword, R. 2003. Bioethics Today, Bioethics Tomorrow: Stem Cell Research and the 'Dignitarian Alliance'. Notre Dame Journal of Law, Ethics and Public Policy 17: 15-57.

104 Titmuss, R. 1970. The Gift Relationship. London. Allen and Unwin.

105 Dickenson, D. 2002. Commodification of Human Tissue: Implications for Feminist and Development Ethics. Developing World Bioethics 2: 55-63, p. 62.

106 Fried, G. 2005. The Politics of Abortion and Reproductive Justice: Strategies for a Stronger Movement'. In: DIFFERENTAKES Series of the Hampshire College Population and Development Programme. No. 38, Fall. Available at: http://popdev.hampshire.edu/projects/dt/dt38.php.

107 European Parliament. 2005. Resolution on the Trade in Human Egg Cells. P6_TA(2005)0074 Thursday, 10 March. Strasbourg.

108 This point is similar to that made by Andrew Grubb, in which 'English law has developed …to provide significant protection to individuals' self-determination by recognizing a 'right to bodily integrity'' Grubb, A. 1998. 'I, Me, Mine': Bodies, Parts and Property. Medical Law International 3: 299-317.

to Ronald Dworkin's argument that a right, by definition, must trump *some* collective goal, but it does not follow that it must trump *all* such goals.[109] Thus, the deployment of individual rights may be limited by exceptions which uphold the rights and freedoms of others in general or of a specific group. I will discuss this further regarding public interest, below.

III. Autonomy and Risk

Those who support paid oocyte donation focus upon the desirable ends of SC therapies, and justify the solution to the current shortage of oocytes by openly paying for them. Taking this argument further, some maintain that it is ethically imperative for human oocytes to be readily available for SC research so that progress is not held up. The solution is therefore to protect individuals in the process of provision of oocytes, and to avoid the (not inevitable) pitfalls of 'black markets'. The key, some have argued, is to strengthen the rights of vulnerable individuals and populations by improving autonomy through consent procedures; as long as women give their free and informed consent, it is up to them to take the risks of egg donation. Others have called for a more cautious – but permissive – approach which may permit such donation, but requires the monitoring of all women who undergo COH either for research or therapy.[110] However, the concern here is that the future health problems for COH are currently unknown, and therefore consent is not truly informed, and donors may appear as research subjects in finding out the long-term effects.[111]

The possible future health risks have led some to reject entirely the suitability of healthy woman as oocyte donors for research. This is driven by the concern that research has not yet produced results which are convincing enough to justify the risks to some donors. They additionally point out that the reported 'emergency' in the lack of human oocytes for research may be unfounded or at least overblown, since currently there are relatively few SC research projects involving human oocytes or embryos;[112] and in the UK, careful oversight and control of 'compensated' and 'benefits in kind' donations in a recent project has achieved the requisite numbers of oocytes necessary.[113] SC research is barely past basic scientific scrutiny; and cloning

---

109 Dworkin, R. 2004. Taking Rights Seriously (New Impression). London. Duckworth. pp. 184-205.

110 Mertes, H. and Pennings, G. 2007. Oocyte Donation for Stem Cell Research. Human Reproduction 22: 629-634. The Royal College of Obstetrics and Gynecology (UK) endorse the establishment of an oversight committee to monitor the health of oocyte donors; RCOG Statement on HFEA's Discussions on Altruistic Human Egg Donations for Research. 21st February 2007.

111 Capps, B. and Campbell, A. V. 2007. Why (only some) Compensation for Oocyte Donation for Research Makes Ethical Sense. Journal of International Biotechnology Law 4: 89-102.

112 In the UK, as of March 2007, there were 34 current projects licenced by the HFEA, involving 25 UK Centres. Available at: http://www.hfea.gov.uk/en/374.html. We were unable to find a record of research using human embryos in the Singapore or the USA.

113 But with certain caveats; see: Choudhary, M., Nesbitt, M., Leary, C. and Murdoch, A. 2006. Donation of Fresh Oocytes for Nuclear Transfer Research – A New Approach. Reproductive Medicine Online 13: 301-302.

experiments, which seem to make the most demands of oocyte donation, have yet to pass animal-research stages, so that clinical applications are necessarily hypothetical.[114]

IV. The Public Interest and Policies of Oocyte Procurement

This current debate, I believe, can be better understood through the concept of public interest. The 'public interest' is a fundamental criterion in many medical and reproductive policies, placing constraints upon individual rights,[115] and in this regard it has an important role in determining the nature of national and global policies.[116] However, the careless deployment of the concept has created a number of confusions and has tended to mask differences in national policies. With such different opinions on the acceptability of a market in oocytes, clearly there must be more than one concept of 'the public interest' at work;[117] one which promotes autonomous self-interest – and therefore payment –, and another that values altruism as conducive to communitarianism. These are two common, but quite different accounts of the concept which are evident in oocyte procurement policies:

(1) The Public Interest as the Sum of Individual Interests

Market models, such as that found in the USA, consider the donation of oocytes from the perspective of meeting market demands. Since oocytes are in short supply, it is not unreasonable, the argument goes, for carefully controlled but positive incentives to persuade IVF patients and healthy individuals to donate oocytes by 'rewarding' their

---

114 Snyder, E. and Loring, J. 2006. Beyond Fraud: Stem-Cell Research Continues. New England Journal of Medicine 354: 321-324.

115 For example, it is implicit in case law; for the UK, see: Beyleveld, D. 1995. The Concept of a Human Right and Incorporation of the European Convention on Human Rights. Public Law Winter: 577-598; for USA, see: Dworkin, op. cit. note 109; and Sorauf, F. 1957. The Public Interest Reconsidered. Journal of Politics 19: 616-639. Indeed, arguably public interest is integral to any jurisdiction whose jurisprudential underpinnings rely on human rights; see: Rawls, J. 2005. Political Liberalism (Expanded Edition). New York. Columbia University Press; Gewirth, A. 1978. Reason and Morality. Chicago. Chicago University Press. In Singapore, where there is no human rights legislation, the public interest is expressly mentioned; supra. note 77.

116 The European Convention of Human Rights 1950 (which is incorporated into UK domestic law by the Human Rights Act 1998) construes public interest in 'health' (in Articles 8, 9, 10, & 11) as the '…interference by a public authority …as is in accordance with the law and is necessary in a democratic society in the interests of national security, public safety or the economic well-being of the country, for the prevention of disorder or crime, for the protection of health or morals, or for the protection of the rights and freedoms of others' (from Article 8 Right to Respect of Private and Family Life, but is similarly stated in the subsequent Articles).
In the US, the importance of the public interest can be inferred from case law. For example, the payment for organs was described as '…clearly repulsive to public policy and federal law'; Opinion by Judge Crabtree, Wilson v. Adkins. Court of Appeals of Arkansas, Division 1 941 S.W.2d 440 (Ark. Ct. App. 1997), quoted in Menikoff, J. 2001. Law and Bioethics: An Introduction. Washington, D.C. Georgetown University Press. p. 484.

117 McHarg, A. 1999. Reconciling Human Rights and the Public Interests: Conceptual Problems and the Doctrinal Uncertainty in the Jurisprudence of the European Court of Human Rights. Modern Law Review 62: 671-696.

altruistic actions.[118] Notwithstanding the public interest in procreation, medical, and specifically SC research represents benefits which are 'long-term' and reflect a 'relative value' that 'benefit many people within society'.[119] This defence of oocyte procurement therefore depends on the evaluation that current research can appeal to the public interest (i.e. it is not in the public's interest to stop this kind of compensated or paid oocyte provision).[120]

Market models built upon this idea promote the liberty interests or autonomy of donors and recipients on the grounds that most of our free choices presuppose some control over our own bodies – implying that people may sell parts of their body, while also benefiting others in society.[121] Indeed, some writers question whether we should even *allow*, let alone *encourage*, non-patient volunteers to donate eggs as an altruistic act.[122] Thus the US model reflects (in theory) a balance between empowering self-determination, providing fair incentives, and dissuading undue inducements, which could lead donors to discount risks and make ill-considered judgments.

The problem with this interpretation of the 'sum-of-particular interests' is that it restricts central (government) politics to only those goals held unanimously by members of society, such as the almost universal political condemnation and resulting prohibition of reproductive cloning. Moreover, many of these private interests are specific 'special' interests, leaving us with no way of assessing the advantage that gives *this* interest a prior claim to support in public policy.[123] Therefore, it has little moral depth, and so, according to Gunn, it is easy to criticize this position as a subjective collection of individual interests that '…do not 'add up''.[124] In the context of oocyte donation, many are quick to point out the implication of diminished, rather than augmented good, for vulnerable populations. Therefore, a decentralised market in oocyte procurement, of the kind evident in the USA, cannot produce collective outcomes and cannot protect vulnerable members of society from instrumentalism, or even enslavement and impoverishment. Regulations that minimally ensure that the potential donor is informed of the risks, and that no inducement or coercion is evident, primarily protect those well able to look after their own interests already. Therefore, it

---

118 Ethics Committee of the ASRM, op. cit. note 56, p. 218.

119 HFEA. 2006, op. cit. note 62, p. 9.

120 There remain questions as to how far reproductive autonomy can be permitted to go, and some acts should regardless be outright banned. Likewise, compensation for the physical inconvenience and risks may encourage some people to donate without thinking sufficiently about the consequences; payment therefore risks coercion and undue incentives which places undesirable burdens on women; SEED op. cit. note 64, sec. 5.9.

121 Resnik, D. 2001. Regulating the Market for Human Eggs. Bioethics 15: 1-26.

122 Lockwood, G. 1997. Donating Life: Practical and Ethical Issues in Gamete Donation. In: Shenfield, F. and Sureau, C. eds. Ethical Dilemmas in Assisted Reproduction. New York. Parthenon Publishing Group. pp. 23-30.

123 Sorauf, op. cit. note 115, pp. 620-621.

124 Gunn, J. 1968. Jeremy Bentham and the Public Interest. Canadian Journal of Political Science 1: 398-413, p. 398.

is argued, aggregating interest is bound to fail some members of the community when the 'sum' of conflicting interests represents no common unity.[125]

(2) The Public Interest as Sharing Agreed Goals

The 'common-interest theory' of public interests focuses on what sort of society we want to live in, and how best we can achieve these shared social goals. By considering these questions, it is possible to create a picture of a community in which every individual is equally recognised as a cooperative and social entity.[126] Therefore, the public interest supports ethical standards which apply to every member of the community as collective goals, benefiting all members of society. Public interest values can be distinguished from something which is advantageous to one person but disadvantageous to another.[127]

If public interest is viewed in this way, it is possible to direct attention towards often ignored interests, such as equal treatment, avoidance of exploitation and the fostering of opportunity, thus emphasising the importance of private achievements that contribute to the 'public' experience. This version of the public interest lends support to policies of altruism (as implicitly expressed in expense reimbursement only policies). In this sense, public interest equates to a justifiably paternalistic attitude which aims to protect certain worthwhile values of the *community*.[128] Without such protections and limits on individual autonomy, the concern is that community cohesiveness would be eroded. Ensuring that oocytes are donated for the benefit of others in the community and not for personal profit and that vulnerable populations are protected from potentially unscrupulous buyers are the priorities for this version of the public interest.

The common counter-argument here is that this approach removes part of our 'reproductive autonomy',[129] and which leads one back to public interest as the sum of individual interest. Provided that such choices are entirely free from coercion – and *regardless* of the possibility of intentional and foreseeable harm – why shouldn't women choose – and be paid as for any other legal public service – to use their oocytes to achieve their own, or someone else's pregnancy, or to donate them for research?

Conclusion

This Paper was commissioned by the Bioethics Advisory Committee of Singapore and completed in the period between January and April 2007. In this Paper, I do not offer

125 Lyons, D. 1994. Utility and Rights. In Waldron, J. ed. Theories of Rights. Oxford. Oxford University Press. pp. 110-136.

126 Rawls, J. 1973. A Theory of Justice. Oxford. Oxford University Press. pp. 522-525.

127 Cassinelli, C. 1958. Some Reflections on the Concept of the Public Interests. Ethics 69: 48-61.

128 Capps, B., Campbell, A. and ter Meulen, R. Forthcoming, 2007. Access to the UK Biobank Resource: Concepts of the Public Interest and the Public Good. Commissioned paper for the UK Biobank Ethics and Governance Council.

129 For a discussion on this, see: O'Neill, O. Autonomy and Trust in Bioethics. Cambridge. Cambridge University Press. pp. 55-72.

an opinion or support to any particular policy, and instead I offer an overview of the arguments offered for various strategies to procure oocytes for research.

The issues that arise in oocyte procurement are part of a current debate informed by recent controversies surrounding the conditions of oocyte donation from women, the market in oocytes in some jurisdictions, and the scarcity of oocytes specifically for stem cell research. In this Paper I have identified three ethical issues which should be considered in any future ethical policy on oocyte procurement: payment and compensation, commodification, and autonomy and risk. These issues are predominated by the demand for oocytes in stem cell research, and the available and potential alternative sources of oocytes. Resolving these issues requires a debate regarding the definition of 'public interest' in oocyte procurement policies, and the balance that one wishes to set between self-interest and communitarian ethics. Central to this balance is the degree to which consensual donation of human parts should be incentivised – to encourage the self-interested to donate oocytes – or predominantly motivated by altruism.

The 'politics' of egg donation is not merely a question of identifying and mitigating risks to donors' health, it is also an issue of scientific 'promise', society's interest in bio-medical progress, and protecting the vulnerable in our community.

Acknowledgements

My thanks to Charles Lim Aeng Cheng for guiding me through aspects of Singaporean Law; and Alastair V. Campbell for his many helpful and insightful comments on earlier drafts. During the completion of this Paper I was on secondment at the Centre for Biomedical Ethics, National University of Singapore, and I am grateful for the advice and support given during this time. Needless to say, the responsibility for any mistakes remains with the Author.