

CHAPTER 7

DELIBERATIONS, CONCLUSIONS AND RECOMMENDATIONS

Introduction

- 1 Human stem cell research and the advances in cloning technology have emerged as key scientific developments of the end of the last century, holding out the promise of important new therapies and cures for a wide range of debilitating and presently incurable diseases.
- 2 At the same time, these rapid and fundamental advances have raised difficult and complex ethical issues which have to be addressed by society in order for the science and the new medical treatments arising from it, to proceed in a sustainable fashion.
- 3 On these fundamental questions, social norms, theological perspectives and philosophical persuasions shape the answers given by each society. Nonetheless, in any ethical discussion on the exploitation of science and technology, two broad guiding principles would probably be accepted by most responsible societies, that the results must be both just and sustainable. ‘Just’ refers to the obligation to respect the common good, that there must be fair sharing of the costs and benefits. ‘Sustainable’ refers to an obligation to respect the needs of generations yet unborn. The principles include the concepts of beneficence and nonmaleficence, that of encouraging the pursuit of social benefits while avoiding or ameliorating potential harm.
- 4 The BAC adopts these broad principles as a conceptual framework. In addition, in a multi-racial, multi-religious and pluralistic society like Singapore, public policy has to be based on a considered weighing and balancing of the spectrum of views held by various sectors. In turn, public policy would create the necessary foundation for laws and regulations. The BAC recognises that with its recommendations that aim to address the ethical

issues, other legal and regulatory issues would arise. However, any detailed legal or regulatory framework is beyond the ambit of this report.

Derivation and use of stem cells from adult tissues

- 5 Human biological materials, including cells collected in research projects, biopsy specimens obtained for diagnostic purposes, and organs and tissues removed during surgery, have long been used in research to increase knowledge about human diseases and to develop better means of preventing, diagnosing and treating these diseases. The collection and use of such biological materials is ethically well-accepted provided there is no adverse impact on the donor and adequate consent is obtained.
- 6 By extension, the BAC has no reservations about the derivation and use of AS cells, subject to informed consent sought from the donor. This view was validated in the consultation process. The local experts, religious and professional organisations, as well as members of the public strongly backed research with AS cells. AS cell research is also widely supported in many jurisdictions, including the UK and the US.

Recommendation 1: Research involving the derivation and use of stem cells from adult tissues is permissible, subject to the informed consent of the tissue donor.

Derivation and use of stem cells from foetal tissues

- 7 EG cells are derived from cadaveric foetal tissues. The ethical acceptability of deriving EG cells is closely tied to the ethical acceptability of abortion. In the main, the local experts, interest groups and the public are of the view that the derivation and use of EG cells should be permitted.
- 8 However, the BAC observes that abortion remains a contentious issue for certain sectors of society. The National Council of Churches of Singapore (representing the mainline Protestant denominations, other Christian organisations and member churches), The Catholic Medical Guild, and the Sikh Advisory Board countenance only the use of naturally aborted fetuses.

Implicitly, there were reservations about elective abortions. In this regard, the BAC notes that elective abortion is permitted and governed by the Termination of Pregnancies Act (Cap 324). Criminal sanctions apply to those who fail to comply with the Act, which provides safeguards in relation to the abortion process. It is not within the purview of the BAC to revisit this issue.

- 9 As with the case of donation of adult tissue for the derivation of AS cells, there must be informed consent from the donor of the foetal tissue. In addition, the decision to donate the cadaveric foetal tissue must be made independently from any decision to abort.

- 10 Again, the BAC believes its position is well supported by the positions taken by other countries. In the US, federal funding is allowed for research involving the derivation and use of human EG cells from cadaveric foetal tissue. Such research is seen to be analogous to the use of foetal tissue in transplantation. In the UK, the use of aborted foetal tissue is permissible, and the Polkinghorne Code of Practice provides guidance relating to the use of such material in teaching, research and therapy. In fact, in Singapore, the Medical (Therapy, Education and Research) Act (Cap 175) governs the donation of any part of a human body, including organs and tissues, upon death. This Act also applies to the donation of organs and tissues from stillborn infants and fetuses.

Recommendation 2: Research involving the derivation and use of stem cells from cadaveric foetal tissues is permissible, subject to the informed consent of the tissue donor. The decision to donate the cadaveric foetal tissue must be made independently from any decision to abort.

Derivation and use of stem cells from human embryos

- 11 Although promising research is currently being conducted with AS cells and EG cells, this does not replace the need for research using ES cells. ES cells have different properties from EG and AS cells. They are pluripotent, and currently appear to offer the greatest potential in their ability to give rise to almost any cell type. Scientists are largely in agreement that out of the three

types of human stem cells, research with ES cells has the best potential to deliver benefits to mankind. The use of ES cells derived from human embryos has heightened the tension between the commitments to cure diseases and to protect human life.

- 12 From the local feedback, there were different responses regarding the derivation of ES cells from human embryos, arising largely from divided views on the status of the human embryo. There were strong contentions that a *human* life begins at the moment of conception. This view was held by the National Council of Churches of Singapore, The Catholic Medical Guild of Singapore, the Sikh Advisory Committee and the Singapore Hospice Association. Others held the view that a human life did not begin until some time after conception (eg. four months, according to the Majlis Ugama Islam Singapura).
- 13 On one end of the scale, the use of any human embryo for research purposes is seen to be unethical and unacceptable on the grounds that an embryo should be accorded full human status from the moment of its conception. Equally, there are views that it would be ethically irresponsible to deny the progress of scientific research that would benefit mankind. For instance, the Buddhist Federation would support such research.
- 14 The BAC notes that disagreements about the status of the human embryo are not confined locally. Internationally, theologians and scholars, even those within the same faith, differ on the issue¹.

¹ See the National Bioethics Advisory Commission's report 'Ethical Issues in Human Stem Cell Research', at Appendix E – Summary of Presentations on Religious Perspectives Relating to Research Involving Human Stem Cells, page 100, where it was pointed out that although the restrictive 'official' position within the Roman Catholicism opposes EG and ES cell research, individual Catholics have differed in how to interpret the basic convictions in practice. In contrast to the restrictive view for instance, another Catholic might, with the aid of science, look to the reality of the early human embryo, and see that which is not yet an 'individualised human entity with the settled potential to become a human person'. Hence it is sometimes permissible to use it in research, though as human life it must always be accorded some respect. See also Chapter 4, page 50 and Appendix E pages 100-103, where the NBAC stated that other scholars from Protestant, Jewish and Islamic traditions noted that major strands of those traditions support a view of foetal development that does not assign full moral status to the early embryo.

- 15 The debate about the moral status of embryos has revolved around the question of whether the embryo should be treated as a person, or viewed as a potential life. From a strictly biological point of view, there is not a clear-cut point at which human life begins. Sperm and eggs are living things, and they fuse to form an embryo, which potentially grows into a living person.
- 16 There is continuous development from independent gametes all the way through to an independent human being. Attempting to define a point at which this new human being *begins* based on embryology is, the BAC concedes, arbitrary.
- 17 Taking into account the diversity of views on when *human* life begins, the BAC adopts the intermediate position that a human embryo has a special status as a potential human being, but is not of the same status as a living child or adult. Such respect is however, not absolute and may be weighed against the recognised benefits arising from the proposed research.
- 18 Therefore, the BAC supports ES cell research. However, ES cell research should take place only when there is very strong scientific merit in, and potential medical benefit from, such research. The BAC's other recommendations on the use of ES cells for research are as stated below.

ES cell lines

- 19 ES cells can be derived from three sources, namely, the existing ES cell lines, surplus embryos and embryos created specifically for research. Existing ES cell lines form a ready source of ES cells, without requiring any further sacrifice of embryos. The BAC recommends that should ES cells be required for research, they should, wherever possible, be drawn first from the existing ES cell lines. In the US, federal funding of research with ES cells derived from approved existing ES cell lines is allowed.

Surplus embryos

- 20 The BAC, however, also recognises the limitations that may be faced in research using only existing ES cell lines. For example, there are concerns

expressed by the scientific community regarding possible immunological rejections at the stage of clinical application, in view of the limited number of existing ES cell lines. Even at this stage, the scientific evidence points to the necessity for an alternative source of ES cells.

21 Surplus embryos are not created for the sole purpose of research, but for fertility treatment. Where such embryos are no longer required, the options are to let the embryos perish or to use them. In this scenario, to use them in research to pursue wider therapeutic benefits would be an act of greater respect for these embryos. As such, the BAC considers surplus embryos, which would be otherwise discarded, to be a suitable alternative source of ES cells.

22 The BAC's stance is supported by the positions in other jurisdictions. In the UK, the derivation of ES cells from surplus embryos is permitted. In particular, the Nuffield Council on Bioethics expressed the view that the removal and cultivation of cells from surplus embryos is analogous to tissue donation and concluded that such removal and cultivation of cells do not indicate a lack of respect for the embryos. Although federal funding of such research is not allowed in the US, the NBAC supported the federal funding of such research, and put forth this statement²:

‘Research that involves the destruction of embryos remaining after infertility treatment is permissible when there is good reason to believe that this destruction is necessary to develop cures for life-threatening or severely debilitating diseases and when appropriate protections and oversight are in place to prevent abuse.’

23 The BAC endorses such views. The BAC notes that in Singapore today, surplus embryos less than 14 days old can be used for research purposes provided they meet the stringent regulatory stipulations set out under the Guidelines for Private Healthcare Institutions Providing Assisted

² ‘Ethical Issues in Human Stem Cell Research’, at Chapter 4, page 52

Reproduction Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations (Cap 248, Rg 1). The BAC also observes that there is a fair amount of public acceptance of such research.

Creation of embryos

24 Next, research embryos may be created by IVF, SCNT or other cloning technology. For some, conducting research on embryos that were originally created for reproduction but which were subsequently not needed is easier to justify than is research conducted on embryos that were created for that very purpose. For others, it is difficult to distinguish between what one can do with an embryo created solely for research purposes, and what one can do with an embryo remaining from infertility treatments.

25 The BAC acknowledges that there is a valid distinction to be drawn between surplus embryos and research embryos. The distinction stems from the fact that the latter are created as a means to an end, for use as research material.

26 In the final analysis, concerning the creation of research embryos, the burden on the BAC is the same as in considering ES cell research on the whole - to weigh the need to protect the human embryo against the scientific value of research embryos and the potential benefits to be reaped from research.

27 As for the source of ES cells, there should be a sufficient supply from ES cell lines, followed by surplus embryos. It is unlikely that it would be necessary to create new embryos by IVF for human stem cell research. In the Chief Medical Officer's report in UK, entitled 'Stem Cell Research: Medical Progress with Responsibility', it was recognised that there are examples of research which could not be conducted using surplus embryos, such as to test the viability of sperm or eggs. However, the view was expressed that 'there should be a sufficient supply of spare embryos for such [human embryonic stem cell] research. It may therefore not be necessary to create new embryos by *in vitro* fertilisation for basic research on the extraction of stem cells.'

- 28 Unlike research embryos created by IVF, there is evidence that research embryos generated by cloning offers an opportunity to derive stem cells which are genetically compatible with the person being treated. Tissues repaired by such ES cells would be more likely to be immunologically compatible with the intended recipient, thereby avoiding the problems of rejection. Therapeutic cloning also enables scientists to learn about the mechanisms of reprogramming adult cells to behave like embryonic stem cells again. In the future, adult cells may be able to be reprogrammed to behave like stem cells, and potentially making it unnecessary to resort to using embryos as a source of stem cells.
- 29 Nevertheless, ES cell research today is developing at a fast pace, and the scientific evidence on the need for the use of research embryos is emerging day by day. In the UK, the Human Fertilisation and Embryology Act 1990 allows the creation and use of human embryos up to 14 days old for research purposes, subject to a license being issued for such research upon satisfaction of conditions. The regime allows for embryos to be created both by IVF and cloning techniques. Again, in 'Stem Cell Research: Medical Progress with Responsibility', it was stated that as at 1998, 118 embryos have been created for research by IVF. To date, the HFEA has not received any application to conduct research involving the creation of an embryo using cell nuclear replacement. Nonetheless, the regime is flexible enough to respond to advances in science in order to facilitate worthy research to proceed, and yet robust enough to prevent abuse of human embryos.
- 30 The BAC adopts the position that the creation of embryos for the specific purpose of research should only be permitted after the satisfaction of stringent conditions and guidelines as evaluated by a statutory body to be set up to license, audit and control human stem cell research. In other words, the BAC is of the view that research can adequately be carried out using the existing ES cell lines, and if proved to be required, surplus embryos. As long as there are sufficient and appropriately donated surplus embryos from fertility treatments available for use in research, there are no compelling reasons to allow

additional embryos to be created merely to increase the number of embryos that will be available for ES cell research or therapy.

31 Therefore, the creation of human embryos specifically for research can only be justified where there is strong scientific merit in, and potential medical benefit from, such research, no acceptable alternative exists, and on a highly selective, case-by-case basis, with specific approval from the proposed statutory body.

32 The BAC acknowledges that there is a further debate regarding the permissibility of creating embryos by cloning technology. The fear is that such research may well result in the cloning of a whole human being. The BAC considers that these fears can be allayed by the strict prohibition of any implantation of such an embryo into a womb.

Age of embryo

33 As an embryo develops, the BAC believes the level of respect and protection accorded must increase.

34 In embryology, before five days, the embryo is a mass of undifferentiated cells. Any cell is as likely to develop into the placenta as to be part of the embryo proper. At day 14, the primitive streak appears. This signals the onset of cell differentiation and organ formation, which includes the development of the nervous system³.

35 Hence, as a further measure of respect and protection for the human embryo, the BAC recommends that only embryos less than 14 days old should be used for the derivation of ES cells. In relation to the existing stem cell lines, only those where the original ES cells that were used to propagate ES cell lines were derived from embryos of less than 14 days old are to be used.

³ Since the nervous system is not in evidence before day 14, the qualities of pain and sentience in the sense normally understood would not exist before day 14.

36 The BAC notes that the Law Reform Committee of the Singapore Academy of Law has questioned whether pain is an appropriate measure of determining the cut-off period for use of human embryos, as pain is not a determinant in considering whether an offence has been committed against a person. The BAC emphasises that pain is but one factor in relying on the 14-day mark. A more important consideration, as stated above, is that in an embryo's development, before the 14-day mark, the cells of the embryo are as yet undifferentiated into tissues, in that there is no organised development. Taking into account the overall state of development of such an embryo, the BAC considers that the 14-day mark is still an appropriate limit.

Informed consent

37 Having dealt with the extent of the means and methods of deriving ES cells, the BAC moves on to consider the status of donors. There must be informed consent from the donors of surplus embryos, gametes and cells.

Recommendation 3: Research involving the derivation and use of ES cells is permissible only where there is strong scientific merit in, and potential medical benefit from, such research.

Recommendation 4: Where permitted, ES cells should be drawn from sources in the following order: (1) existing ES cell lines, originating from ES cells derived from embryos less than 14 days old; and (2) surplus human embryos created for fertility treatment less than 14 days old.

Recommendation 5: 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.

Recommendation 6: For the derivation and use of ES cells, there must be informed consent from the donors of surplus human embryos, gametes or cells.

Reproductive cloning

38 Since the birth of Dolly the sheep, the first cloned mammal in the UK in 1996, many sectors of society have expressed great apprehensions and reservations about this technology being used to clone human beings. The argument is that cloning violates respect and dignity of human life and poses safety problems for those born as a result of cloning technology. The UK, US, Germany and many other major countries have banned the reproductive cloning of humans.

39 There is consensus from all sectors in opposing reproductive cloning. The BAC is of the view that the implantation of a human embryo created by any cloning technology into a womb, known as reproductive cloning, or any other treatment of a human embryo intended to result in its development into a viable infant, should be prohibited. There are strong public policy reasons for this position. These include: (a) the view that human reproductive cloning goes against the moral idea that holds that a human being is not to be treated as a means to an end, but only as an end. This translates into the fear that a whole human being may be brought into existence for a utilitarian purpose; (b) that the social and legal implications of reproductive cloning are very serious, including issues of identity and responsibility; and (c) the fear that it will result in a reduction in biodiversity.

Recommendation 7: There should be a complete ban on the implantation of a human embryo created by the application of cloning technology into a womb, or any treatment of a human embryo intended to result in its development into a viable infant.

Comprehensive legislative framework and regulatory body

40 It is critical that human stem cell research be licensed, and subsequently monitored and assessed by an appropriate body, to establish whether the research is delivering the envisaged benefits, as well as to highlight any currently unforeseen concerns and issues which may arise. The professional organisations generally indicated the need for a well-established and effective framework for the control of such research in Singapore. The Singapore Medical Council stated the need to establish a system which may involve the

setting up of a body at a national level as an oversight committee, backed by legislation that provides stiff penalties for any breaches in the guidelines governing such research. This is to ensure that the researchers strictly adhere to the guidelines for stem cell research. The Biomedical Engineering Society (Singapore) proposed that a Register of Researchers in human stem cell research be set up to regulate the practice of research. The Singapore Society for Biochemistry and Molecular Biology noted that the scientific community in Singapore is small, and hence care should be taken to ensure that no conflict of interests arise from composition of the oversight body tasked to monitor the adherence to guidelines on human stem cell research.

41 Given the ethical issues involved in human stem cell research, the public must be assured that such research can be effectively and efficiently licensed, monitored and regulated, with sufficient attention given to the relevant ethical considerations. Strict oversight of human stem cell research is necessary to prevent abuse. This duty is incumbent on Singapore as a responsible nation in an international community. In the UK, research with human embryos is subject to a licence being issued by the Human Fertilisation and Embryology Authority. The BAC recommends that the UK model be used as a basic model, subject to such modifications as necessary for Singapore, as well as refinements found in regulatory systems in other countries.

42 The BAC recommends a regime as follows:

- (a) a statutory body be mandated or established with the functions to license, audit and monitor all human stem cell research in Singapore;
- (b) the management of the statutory body shall be vested in a board. The Chairman of the Board should not be a person who has been directly involved in stem cell research. The members of the board should be multidisciplinary, including members of the public;
- (c) the permissible areas of human stem cell research for which licences may be granted should be research that increases knowledge about the development of the embryo, serious diseases, or enables any such knowledge to be applied in developing treatments for serious diseases. In

- granting licences, the body must review the proposals for research, and its protocols, to ensure that they meet the requirements as stipulated above;
- (d) strict conditions should be attached to such licences, including conditions on derivation, storage and use of research materials;
 - (e) the body should be empowered to conduct regular checks and audits to determine whether the research is delivering the anticipated benefits and also to identify any concerns which may arise;
 - (f) the body should also be empowered to impose sanctions, including criminal sanctions, on those who fail to comply with the laws or regulations; and
 - (g) there should be provisions governing informed consent, commerce and sale of research materials and conscientious objections by individuals in such research.

Recommendation 8: There should be a statutory body to license, control and monitor all human stem cell research conducted in Singapore, together with a comprehensive legislative framework and guidelines.

Informed consent

- 43 The comprehensive legislative and regulatory framework must ensure that in all cases, potential donors for stem cell research must be able to make voluntary and informed choices on whether and how to dispose of biological materials. The informed consent must be obtained from donors of any adult tissues from which AS cells are derived, of foetal materials from which EG cells are obtained, of surplus embryos from which ES cells are derived, and of materials for creating embryos for research.
- 44 In the course of seeking consent, there should not be any financial, therapeutic or other benefits or inducements for the donors or any specified individual, or any coercion or undue influence for the donation. Although the donor is not to be induced to donate any materials, by any financial, therapeutic or other benefits, this does not preclude the donor from receiving treatments or therapies that may be subsequently developed. The extent of information to be provided to each donor in each specific situation will differ, depending on

the particular circumstances of the donation. A set of regulations or guidelines on obtaining informed consent from donors is necessary.

Recommendation 9: In obtaining consent from donors of cells, gametes, tissues, foetal materials and embryos, the information provided to the donors must be comprehensive, and there must not be any inducements, coercion or undue influence.

Commerce and sale

45 Just as the donors of tissues, cadaveric foetal tissues or surplus embryos are not permitted to receive any financial or other gains from the donation of such materials, similarly, researchers to whom such materials have been donated should not be permitted to trade in such donated materials. Nonetheless, researchers should not be prohibited from gaining commercially from the fruits and products of research, as well as treatments and therapies developed from donated materials.

Recommendation 10: The legislative and regulatory framework should prohibit the commerce and sale of donated materials, especially surplus embryos. Researchers should not be prohibited from gaining commercially from the products of research, as well as treatments and therapies developed from the donated materials.

Conscientious objection

46 With diverse views on the ethics of human stem cell research, it is envisaged that on moral or religious grounds, a segment of the research community and the public may not wish to be involved in such research or in a particular manner of such research. Such objections would be legitimate, given that Singapore is a multi-religious and pluralistic society. It is not the remit of the BAC to challenge or reconcile disagreements held from personal moral or religious convictions. As such, every individual should be allowed to make an informed choice on whether to participate in such research, given his or her beliefs. Hence, the legislative framework should provide for such a situation, in that no one should be under a duty to participate in any such research or

manner of research, which would be authorised or permitted by the law, to which he has a conscientious objection. In the UK, there is provision for this within the Human Fertilisation and Embryology Act 1990.

Recommendation 11: The legislative framework should provide that no one shall be under a duty to participate in any manner of research on human stem cells, which would be authorised or permitted by the law, to which he has a conscientious objection.

Conclusion

47 The BAC believes that the recommendations would lead to ‘just’ and ‘sustainable’ results. The results would be ‘just’, in that research with tremendous potential therapeutic benefits to mankind will proceed. The results would be ‘sustainable’ as such research has little biological or genetic impact on future generations, especially with the ban on the reproductive cloning.

48 The BAC also believes that the recommendations strike a proper balance between allowing research with tremendous potential therapeutic benefits to mankind to proceed while affording a measure of respect and level of protection to human embryos which takes into consideration the diversity of views on the status of the human embryo.

49 Finally, the BAC reiterates that the recommendations aim to address, in the main, the ethical issues of human stem cell research. The BAC recognises that other legal and regulatory issues would arise. However, any detailed consideration of all the potential legal and regulatory issues would be beyond the ambit of this report.