STEM CELL POLICIES AND REGULATIONS IN JAPAN

Deliberation over the ethical and legal implications of human embryonic stem cell research commenced at a national level in 1998. In recognition that an embryo has an ethical status as "Germ of Human Life", legislation was introduced in 2000 to prohibit reproductive cloning and non-binding guidelines authorised research on human embryonic stem cells ("hESC") with surplus embryos. Therapeutic cloning, a prospective technique for avoiding adverse immunological effects in regenerative medicine, was initially prohibited. However, with regulatory experience and promising advancement of hESC research, this prohibition has been lifted. Meanwhile, a tremendous breakthrough has recently taken place in induced pluripotent stem cell technology. A new regulatory framework is being introduced to enable the therapeutic application of human stem cell research. This article provides an overview of the policy and regulatory changes that have taken place in Japan. The rationale and motivations behind these changes are also considered.

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I. Introduction

1 This article discusses the development of Japan's policies and laws on stem cell research, including stem cells that are produced through induced pluripotent stem cell ("iPSC") technology.[1] Currently the Ministry of Education, Culture, Sport, Science and Technology ("MEXT") is working with the Ministry of Health, Labour and Welfare ("MHLW") in realising the clinical potential of stem cell technology, particularly in regenerative medicine. Research on either embryonic stem ("ES") cells or iPS cells has so far been conducted as basic research. However, as there have been considerable developments in research on embryonic stem cells and iPS cells are considered to be more amenable

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1 For a general overview, see <http://www.dnapolicy.org/policy.international.php?action=detail&laws_id=28> (accessed 15 October 2010). For a useful but somewhat dated paper on the regulatory situation in Japan (until September 2004), see <http://ukinjapan.fco.gov.uk/resources/en/pdf/5606907/5610028/36060X.pdf> (accessed 15 October 2010).

for clinical use on patients, the focus has shifted from basic research to therapy.

2 In Japan, biomedical research is divided into basic and clinical research, the former being regulated by the MEXT and the latter by the MHLW. The MEXT is developing an integrated research project for the realisation of regenerative medicine with four main areas of activities:

> (a) The derivation of human pluripotent cells through iPSC technology or from human embryos. Research will be extended to search for a process to create a safer iPS cell line, without the use of retroviruses as vectors to introduce genes into a somatic cell, and for a more efficient and certain process for the derivation of ES cells.
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> (b) Handling of stem cells and their development. Research will focus on (i) a more efficient differentiation of ES cells to cells available for transplantation, particularly cardiac muscle cells and liver cells, and (ii) technological development for the creation of target cells to be used for regenerative medicine.
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> (c) Application of stem cells for therapeutic purposes. Research for advancing medical technology for regenerative medicine, particularly in the application of cells and tissues differentiated from human iPS cells and ES cells in a preclinical study in anticipation of a clinical trial in humans to follow.
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> (d) Stem cell banking for research, comprising collections of stem cells, namely, (i) iPS cells and ES cells, (ii) disease specific iPS cells and (iii) somatic stem cells from cord blood. This area is of growing importance, as researchers and medical doctors do not think it is necessary to create patient specific stem cells for treatment.[2] Stem cells derived from human embryos or through iPSC technology could potentially be applied in therapy if there is autoimmune compatibility (established through typing of human leukocyte antigen or HLA Typing) with the intended patient.

II. Chronology of regulatory developments

3 Japan started its own bioethical consideration at the national level in 1998 when the Government established its Bioethics Committee ("BC") under the Prime Minister.[3] Since then, it has considered the

2 Juan Carlos Izpisúa Belmonte, James Ellis, Konrad Hochedlinger & Shinya Yamanaka, "Induced pluripotent stem cells and reprogramming: seeing the science through the hype" *Nature Reviews Genetics* 2009 (December); 10(12): 878–883.

3 The Bioethics Committee was established in the Council of Science and Technology ("CST") as an advisory body to the Prime Minister in 1998. However,

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bioethical implications of cutting edge work in the life sciences and technologies, such as human cloning, genomics or genetic research, and human ES cells ("hESC"). The BC presented two reports consecutively in 1999 and in 2000, one on human cloning and the other on hESC research. In 2000, following an advice of the BC, a law was enacted to regulate the application of cloning technology to human beings.[4] Under this legislation, reproductive cloning is prohibited so that a violation of this provision could lead to a sanction of ten years imprisonment or a ¥10m fine. Therapeutic cloning is not prohibited by the law. Nevertheless, it was in fact not permitted immediately as the law requires the establishment of the relevant guidelines to be set out by the MEXT.

4 Further developments followed from this legislative response at two levels. At one level, the guidelines on research on certain kinds of embryos were promulgated by the MEXT, under which nine categories of artificial embryos are enumerated.[5] However, human therapeutic cloning was not permitted for a duration because of the prematurity of Japanese scientific work and bioethical consideration. Hence, permission for carrying out therapeutic cloning could not be obtained until the guidelines were subsequently revised in 2009. At another level, a set of guidelines on derivation and use of hESCs was issued.[6] These guidelines allowed Japanese researchers to conduct research involving the derivation of hESCs from embryos. The first three hESC lines were successfully derived in 2003.[7] In 2003, with more than three years of experience and development in hESC research, the Expert Panel on Bioethics of the Council for Science and Technology Policy ("CSTP"), which replaced the former Bioethics Committee,

as a consequence of the reform of governmental institutions in 2001, a new organ, named "Cabinet Office", was established for planning and drafting important policies headed by the Prime Minister. With this reform, the CST was replaced by the Council for Science and Technology Policy ("CSTP"), which was created in the Cabinet Office to take charge of policy planning for science and technology. The Expert Panel on Bioethics was set up in the CSTP, replacing the Bioethics Committee but with slightly weaker standing. Bioethics is thus deemed as part of science and technology policy.

4 Act on Regulation of Human Cloning Techniques (Act No 146 of 2000). See <http://www.cas.go.jp/jp/seisaku/hourei/data/htc.pdf> (accessed 15 October 2010).

5 Ministry of Education, Culture, Sports, Science and Technology, Japan, *Guidelines for Handling of a Specified Embryo* (2001).

6 Ministry of Education, Culture, Sports, Science and Technology, Japan, *Guidelines for Derivation and Utilization of Human Embryonic Stem Cells* (2001). See <http://www.lifescience.mext.go.jp/files/pdf/n503_02.pdf> (accessed 15 October 2010).

7 In Japan, five human embryonic stem cell ("hESC") lines have been created at Kyoto University. The first three hESC lines were derived from about 20 donated embryos. The source of the two other hESC lines is unclear.

issued a report on "Basic Conception on Handling Human Embryo".[8] It was proposed in this report that therapeutic cloning be permitted on the condition that appropriate guidelines should be established. Currently, only chimeric embryos created through the introduction of human cells into animal embryos and therapeutic cloning are permitted.

5 In 2006, the MHLW issued its ethical guidelines on the use of human adult stem cells in clinical trials, but the use of hESCs was not permitted.[9] After almost ten years of experience with regulating human embryonic stem cell research (since 2000) and also with the development of iPSC by Professor Yamanaka at Kyoto University, the Government adopted a more active stance towards further promoting regenerative medicine as a leading objective of its science and technology policy.[10] In May 2009, the MEXT issued a set of revised guidelines for research on certain kinds of embryos that permitted therapeutic cloning, and in August 2009, it also revised the existing guidelines on ES cells as two separate sets of guidelines; one on derivation and distribution of hESCs, which included derivation of hESCs from therapeutic cloning, and the other on utilisation of such cells. A year later, in May 2010, the MEXT issued guidelines for research involving the creation of gametes from human iPSCs and hESCs. At the same time, also in May 2010, the two sets of August 2009 guidelines were again revised so as to permit research for gametes differentiated from hESCs. More recently, the MHLW issued its revised ethical guidelines on clinical trials using human stem cells (including iPSCs and hESCs) in August 2010.[11]

6 It may be useful to consider the way in which Japanese ethical policies regarding stem cell research have developed. As the BC was discontinued since 2004, the Expert Panel on Bioethics of the CSTP of the Japanese Cabinet is the supreme decision-making body for science and technology policy, which includes bioethics. Some other ministries, acting under the political direction of the Cabinet, have their own committees that deal with bioethics issues, namely, the MEXT, the MHLW and the Ministry of Agriculture, Forestry and Fisheries ("MAFF") as well as the Ministry of International Trade and Industry

8 For more information on the Expert Panel on Bioethics and the Council for Science and Technology Policy, see: <http://www8.cao.go.jp/cstp> (accessed 15 October 2010).

9 Ministry of Health, Labour and Welfare, Japan, *Ethical Guidelines on Clinical trials using Human Stem Cells* (2006).

10 Kazutoshi Takahashi & Shinya Yamanaka, "Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors" Cell 2006 (August); 126(4): 663–676.

11 Unfortunately, English translation is given only for the guidelines on the derivation and utilisation of human embryonic stem cell ("hESCs") (2001) and for the guidelines on the utilisation of hESCs (2009).

("MITI"). Bioethical decisions should theoretically be made at the national level by the Expert Panel, and so by the CSTP. However, only the MEXT has observed such a structural flow in decision-making, whereas the other ministries take the decisions of their bioethical bodies as final. As basic research relating to regenerative medicine comes mainly within the purview of the MEXT, the Expert Panel has been influential on the ethical direction in this field as the MEXT has consistently referred their activities, in particular their guidelines and reports, to the Expert Panel for review. In contrast, the MHLW has not sought the advice of the Expert Panel for its guidelines on clinical medical activities. Consequently, there has not been a coherent development of ethical policies and standards on stem cell research between the two ministries.

III. Ethical issues concerning hESCs, including therapeutic cloning

7 It is pertinent here to present first of all the Japanese conception of the ethical status of a human embryo.[12] The report of the BC in 2000 on the subject determined the Japanese position on this matter.[13] It recognised a human embryo as the first stage of human life, or "Germ of Human Life". Hence, the embryo was attributed a dignity that is derived from that of a human being, and would require proper handling with special respect if applied in research. Consequently, the general policy in Japan is that any human embryo should not be created for any purpose except for human reproduction. It was also on this basis that the BC permits the utilisation of a human embryo only for human reproductive medicine or embryological science. The only exception is that surplus embryos from fertility treatment may be used for research in regenerative medicine. This is based on the rationale that since surplus embryos are destined to "lose their lives," their use in research should be allowed for saving the patients suffering from difficult diseases. Also for this reason, hESC research for regenerative medicine is permitted.

8 The first guidelines on hESCs covered both derivation and utilisation of hESCs. Taking into account the ethical gravity in the derivation process of hESCs, *ie*, destruction of a germ of human life, the process of deriving and the using of hESCs have been under strict control. The main aspects of the restrictions are:

12 Basic conception of ethical values in Japan may be found in the following articles presented by the author: Ryuichi Ida, "Ethical and Legal Aspects of Biotechnology" in *Cross Cultural Biotechnology* (M C Brannigan ed) (Rowman & Littlefield, 2004).

13 National Bioethics Committee, Japan, *Basic Conceptions of Human Embryo Research Focusing on the Human Embryonic Stem Cells* (2000). See <http://www.mext.go.jp/english/news/2000/02/s000202.htm> (accessed 15 October 2010).

(a) an appropriate informed consent procedure for the donation of embryos;

(b) assurance of the ethical consciousness and technological capacity of the researcher involved;

(c) prohibition of creation of human beings and gametes with hESCs, the latter being permitted since the 2009 revised guidelines;

(d) capability of the institution and of its equipment for implementing the conditions set out in the guidelines, and

(e) a double ethical review system, *ie*, review by an institutional review board and by the national expert committee on ES cell research in the MEXT.

9 There are three especially salient points that should be mentioned. First, there are particular requirements on the donation of embryos. Donation of supernumerary embryos should be done with appropriate procedures to obtain informed consent. As consent may only be obtained from *de jure* married couples, surplus embryos may only be donated for research after assisted pregnancy is achieved, *ie*, after the success or abandonment of IVF treatment.[14] The reason for this requirement is to prevent the creation of a large number of embryos by people who are not married. Full explanation and information should be given to the donor couple concerning the objectives of the research, the process of derivation and the significance of the research. In particular, it should be explained that, on one hand, a human embryo is a germ of human life and the derivation of hESCs is an act equivalent to the destruction of an entity which should have been a human life if born, and that, on the other hand, hESCs would bring new medical cures and treatments, *ie*, regenerative medicine, for currently incurable diseases.

14 There is no legislation on assisted reproduction. Existing guidelines are promulgated by the Japanese Association of Obstetricians and Gynecologists. Reproductive choice does not fall within the purview of the Ministry of Education, Culture, Sport, Science and Technology. As fertilisation, and therefore infertility, is not regarded as a healthcare problem, assisted reproduction does not fall within the purview of the Ministry of Health, Labour and Welfare. Assisted reproduction and handling of human embryos is regulated by the Guidelines of the Japanese Association of Obstetricians and Gynecologists, a professional body for assisted reproduction. In addition, human embryos should be destroyed through incineration under prescribed techniques and processes. There are more than 20,000 embryos in over 400 assisted reproduction clinics in Japan. It is true that ART embryos should be destroyed using appropriate techniques or processes. One or two years ago, the media reported that a clinic threw out embryos and aborted foetuses into the garbage, which created some controversy.

10 A double consent system is entailed. Consent should be obtained for the first time from both parents for the use of surplus embryos in research. Once this consent is obtained, a second consent is to be taken only after 30 days have lapsed. The second consent will be the final consent. This interval of 30 days gives the couple time for reflection as to whether they would "really and definitively" like to donate their embryos for hESC research. Hence, only frozen embryos are used in research, and not "fresh" ones.

11 The guidelines further authorise importation of hESCs, subject to two conditions:

(a) the embryo is clearly proven to be supernumerary; and

(b) the donors' consent is obtained.

12 Only two conditions apply as it is considered to be unreasonable to impose every detailed condition required in the guidelines to hESCs derived in foreign countries, which have different cultural backgrounds and ethical standards concerning human embryos.

13 There is also a concern with the use of "totipotent" cells as these could give rise to a human being or differentiated into gametes that could then be used for reproductive purposes. Hence, there is a ban on use of such cells for human reproduction or for the creation of human-animal chimeras.

14 Second, as hESCs have a special status but not other human or animal cells, human embryos and hESCs "shall be handled carefully and consciously without violating human dignity".[15] More precisely, research institutions involved in hESC research should provide equipment and facilities specifically assigned for human embryos or ES cells and separated from those for animal cells or tissues. In addition, researchers dealing with human embryos or ES cells should be skilled, which entails having ample experience with animal ES cells. Otherwise, less skilled researchers should not deal directly with human embryos or ES cells.

15 Finally, the guidelines establish a two-tiered ethical review system. The first tier of ethics review is conducted by the ethics committee of each institution (or "IRB") for research involving either the derivation or utilisation of hESCs. The IRB must itself fulfil

15 Ministry of Education, Culture, Sports, Science and Technology, Japan, *Guidelines for Derivation and Utilization of Human Embryonic Stem Cells* (2001) Art 3. This provision remains as Art 3 in each of the subsequent revised guidelines on derivation and utilisation of human embryonic stem cell ("hESCs") (2007 and 2009) and on derivation and distribution of hESCs (2009). The latest version is the *Guidelines for Derivation and Distribution of Human Embryonic Stem Cells* (2010).

the requirements provided for in the guidelines, namely, multi-disciplinarity, independence and taking into account gender considerations. In particular, an IRB should be composed of at least two female members. This requirement is indispensable because the embryo donation process is inevitably invasive of the female body. It is particularly important in an ethics review for the physical and psychological conditions of the mother to be considered.

16 The second tier relates to a review at the national level. The Experts Committee of Research on hESCs and Specified Embryos was established for this purpose in 2001.[16] A research protocol that has been approved by an IRB is examined in detail at this level. Even the discussions of the IRB are subject to review *in extenso*, as is the quality (and composition) of the IRB. This "double-checking" approach is a means to promote and enhance the ethical awareness of researchers, as well as of the public at large.

17 Ethics reviews carried out by the Expert Committee have been very rigorous. On a number of occasions, the Expert Committee has called into question the ethics approval of an IRB, and has called upon the IRB to re-examine the ethical provisions of the researcher or of the research institution, and even those of the IRB itself. The Expert Committee has also pointed out inadequacies with regard to meeting the regulatory standards in the research design, including provisions for equipment and installations. The examination process of the Experts Committee makes it clear that ethical requirements should be strictly observed. With the accelerated development of research using hESCs, and with the benefit of accumulated ethical and regulatory experiences, regulatory control over the utilisation of hESCs has been relaxed, so that by 2009, research involving the utilisation of hESCs need not undergo the two-tier review process. Instead, the research protocol need only be registered with the MEXT.

18 Where hESCs are to be applied to a patient, adverse immunological reaction is a key concern. Clinically applied hESCs are derived through therapeutic cloning (or somatic cell nuclear transfer, "SCNT" in brief), where genetic material from the patient is transferred into an enucleated egg in order to create an SCNT embryo. It is from this SCNT embryo that immunologically compatible stem cells are derived for implantation into the patient. However, there are several grave ethical concerns that arise from therapeutic cloning, apart from the legislative prohibition of reproductive cloning. The important ethical concerns are:

16 The latter category of "Specified Embryos" is provided for in the law concerning the limitation of the application of the cloning technique to human beings.

(a) limiting therapeutic cloning research to the sole objective of searching for effective treatment for grave or so far incurable diseases;

(b) procurement of unfertilised oocytes;

(c) appropriate informed consent procedure;

(d) procurement of somatic cells;

(e) requirements to be observed by research institutions conducting therapeutic cloning research; and

(f) prohibition of voluntary donation of oocytes.

19 Among these concerns, the most important arise from the procurement of unfertilised oocytes for therapeutic cloning.

20 The MEXT revised the *Guidelines for Handling of a Specified Embryo* in 2009 to permit therapeutic cloning thus far banned. To address the ethical concerns, the guidelines attempt to safeguard the physical and psychological well-being of women as donors, by limiting the sources of oocytes to those obtained through surgery, oocytes that are not used in assisted reproduction, disused frozen oocytes, and frozen oocytes left over after the death of the woman concerned. Voluntary donation of oocytes by healthy individuals is so far strictly prohibited.[17] In addition, the guidelines set precise conditions and measures for handling of an SCNT embryo and limit the research only to regenerative medicine.

21 As for hESCs from therapeutic cloning, its derivation and use are not particularly different from those derived from ordinary embryo. So, although the two sets of Guidelines on hESCs mentioned above have provisions applicable to each of these two kinds of embryos, the only significant difference relates to the process of therapeutic cloning itself and not of derivation *per se*. The guidelines on derivation similarly contain provisions relating to the above mentioned ethical concerns. Overall regulatory control is achieved with legal prohibition of

17 There is currently no regulation on oocyte donation from one couple to another. According to the Japanese Association of Obstetricians and Gynecologists, it should not be permitted, although sperm donation is permitted. One committee of experts in the Ministry of Health, Labour and Welfare reported that oocyte donation should be permitted on the condition that a child born from the donation should have the right to know the identity of his or her biological parents. Guidelines are being developed but not yet released. As it stands, oocyte donation is still not permitted. On the recommendation of the professional body, surrogacy is also not permitted. Recently, a famous couple went to the US to conceive a child through surrogacy but this was not recognised by the Ministry of Justice. They are required to go through the adoption process.

reproductive cloning, guidelines relating to the use of certain embryos and guidelines on the use of hESCs so derived.

IV. Ethical issues regarding iPSCs

22 While iPSCs could overcome ethical concerns over the ethical status of an embryo, ethical concerns remain in at least two respects:

(a) scientific concerns over the safety and efficacy of iPSCs, since iPSCs are so far generated using vector virus and through gene insertion; and

(b) potentially controversial use of iPSCs that are differentiated as gametes and brain cells.

23 On the first concern, it is often said that "bad science" is also "bad ethics". Hence, safety and efficacy concerns, which are primarily scientific issues, should also be given ethical consideration. In terms of moral considerations, the process of deriving iPSCs is less contentious as the issue of the moral status of an embryo does not arise. Although there is ongoing research on the derivation of iPSCs that do not use genes for reprogramming, the current method depends on the insertion of genes using vector virus. There is concern that either gene insertion or the process of insertion would give rise to adverse and possibly fatal effects that are so far unknown, especially if pluripotent stem cells obtained through iPSC technology are applied for therapeutic purposes. While the process of obtaining pluripotent cells from SCNT embryos is morally contentious, there are less safety and efficacy concerns should such cells be applied therapeutically.

24 The second set of ethical concerns arises at the point of differentiation, such as the differentiation of pluripotent cells into brain cells or gametes. Although concerns over the differentiation of stem cells into brain cells may not be as pressing at the moment, it should be asked to what extent cells, tissues or organs of a human person may be replaced by foreign sources or those artificially generated. The same issues arise from research involving humanoids or cyborgs.

25 As for the differentiation of stem cells into gametes, there are important ethical concerns. It is possible that gametes can be used for reproduction. The gametes in question here are gametes derived in a somewhat artificial way from either embryonic stem cells or iPSCs, though they are not unnatural. The ethical implication stems from the extent to which "assistance" should be given to human reproduction. Does not the use of gametes so derived go beyond "assisted reproduction"?

26 These ethical concerns apply to both iPSCs and hESCs. Differentiation of pluripotent cells into gametes has up until now been prohibited because it was considered unethical to "create" a human being using artificially differentiated gametes from hESCs, which are derived through destruction of an embryo, the germ of human life. However, the Expert Panel on Bioethics of the CSTP and the MEXT decided to open the door to derivation of gametes from iPSCs and somatic stem cells. The reason for this is that research on the differentiation process by which gametes could be obtained would provide an opportunity to investigate deeper into the question of infertility. This objective is thereby consistent with those of reproductive medicine, which relate to the procreation of human beings through the natural reproductive process. Such an explanation is similar to the justification for allowing the destruction of a human embryo for research into regenerative medicine. However, the use of a stem cell derived gamete to create an embryo for reproduction is still prohibited. If a human embryo is to be regarded as the beginning ("germ") of human life, then the creation of gametes may be ethically contentious as they occur one stage before the biological entity (*ie*, the embryo) that acquires moral status. It may be necessary to consider what the moral status of gametes is, particularly that of human eggs. Are they simple cells like other somatic cells? The answer is probably negative in Japanese ethical reasoning. Or do they have a special status since they will generate the germ of human life? If so, which kind of status? So far the only point that is clear is that the derivation of gametes from stem cells could contribute to solving problems of infertility. In addition, the differentiation of gametes from hESCs is still not permitted because of the ethical difficulty with having to "recreate" gametes from hESCs that would have been derived from a human embryo, thus amounting to reversing the fertilisation process.

27 An additional set of guidelines on creation and utilisation of human embryos in research for assisted reproduction is still in preparation; however, a report by two committees of experts of the MEXT and the MHLW, which jointly worked on human embryos produced and utilised for the purpose of research on assisted reproduction, was already published in 2009.[18] Although the scope of this report is limited to research for assisted reproduction, creation of embryos solely for research, according to this report, is possible using oocytes obtained in the assisted reproduction treatment process or through surgery and spermatozoa donated either in assisted

18 Report on conditions of creation and utilisation of human fertilised embryos for the purpose of research for assisted reproduction by the Committee of Experts of Research for Assisted Reproduction, Ministry of Education, Culture, Sport, Science and Technology, and the Committee of Experts of Research on Human Embryo, Ministry of Health, Labour and Welfare (15 April 2009).

reproduction treatment, through surgery or in medical consultation. When either oocytes or spermatozoa are obtained in the context of assisted reproduction, the donation must be from married couples, as should also be the case with hESC research.

V. New developments in regenerative medicine: Use of pluripotent stem cells in clinical trials

28 The "road map" for regenerative medicine has already been drawn out as researchers attempt to move from basic research to clinical trials. The guidelines for clinical trials using human stem cells which permitted clinical trials using only adult stem cells were reviewed. hESCs and iPSCs, so far excluded, are now permitted for use in clinical trials. There is otherwise no substantial change to the existing guidelines. The revised guidelines were promulgated in August 2001 for both iPSCs and hESCs. Such trials using iPSCs or hESCs may only start two or three years later. During this time, there is also a need to develop appropriate standards relating to good clinical practice for iPSCs and hESCs, since the research on these stem cells has been until now done as basic research and the standard of experiments may differ between basic research done *in vitro* and clinical trials conducted *in vivo*.

VI. Concluding remarks

29 We are only now at the turning point towards realisation of the benefits of regenerative medicine using pluripotent stem cells, which started only a dozen years ago. The creation of iPSCs by Professor Yamanaka accelerated the pace of development and surpassed a hurdle to become a more practicable field. However, bioethical issues are not completely resolved, even if the question of destruction of a "germ of human life" is expected to become redundant sooner or later, when iPSCs can be derived efficiently and at minimal risk when applied to patients. Still, past experience suggests that we should be confident in resolving ethical concerns through understanding, as well as supporting the development of science and technology for the benefit of humanity, and by respecting the diversity of values and conceptions when reflecting on these concerns. The general principle of "Harmony" should be respected, upon which rests the belief of living in peace and promoting welfare through scientific and technological development based soundly on human dignity and human rights.