Suggested Revisions to TCPS 2 (2018)

TCPS (2018) Definitions

- embryonic stem cell:
  A cell derived from ~~the inner cell mass of developing blastocysts~~ early stage human embryos, up to and including the blastocyst stage[1]. ~~*An embryonic stem cell is self-renewing (can replicate itself) and pluripotent.*~~

- pluripotent stem cell:
  A cell that can become all the cell types that are found in an implanted embryo, fetus, or developed organism, but not embryonic components of the trophoblast and placenta[2]. Pluripotent stem cells include embryonic stem cells, induced pluripotent stem cells and embryonic germ cells.

- Totipotent stem cell:
  A cell that can become all the cell types that are found in an implanted embryo, fetus, or developed organism, including embryonic components of the trophoblast and placenta.

F. Research Involving Human Pluripotent and Human Totipotent Stem Cells

Guidance regarding a proportionate approach to research ethics review, consent, privacy, confidentiality, and research with human biological materials and other ethical guidance described in earlier chapters of this Policy apply equally to research involving human pluripotent or human totipotent stem cells. This section provides further guidance for research involving human pluripotent or human totipotent stem cells. In addition to following the guidance provided in this Policy, researchers are responsible for compliance with all applicable legal and regulatory requirements, e.g., the *Assisted Human Reproduction Act* and its *Regulations and the Food and Drugs Act and its Regulations.*

Stem Cell Oversight Committee (SCOC)

In recognition of the complex ethical issues associated with research involving pluripotent stem cells, a Stem Cell Oversight Committee (SCOC) was created by CIHR in 2003.

SCOC reviews research involving human pluripotent ~~or~~and human totipotent stem cells that:

- have been derived from an embryonic source; and/or
- will be transferred into humans or non-human animals

to ensure compliance with Chapter 12, Section F of this Policy. Applications that receive SCOC approval shall then be submitted to local REBs as part of the local research ethics review process. SCOC does not review research involving human pluripotent stem cells that come from somatic (non-embryonic) tissue and that are not going to be transferred into humans or non-human animals.

[1] Taken from the NIH definition
[2] The cells can form trophoblast tissue

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Article 12.10 Research involving human pluripotent or human totipotent stem cells that have been derived from an embryonic source, and/or that will be grafted or transferred in any other form into humans or non-human animals requires review and approval by SCOC and an REB. The researcher shall provide evidence of SCOC approval to the REB.

Application 1) Research Conforming to this Policy and Requiring SCOC Review

Types of stem cell research that conform to this Policy and require SCOC review include:

(a) Research for the purpose of deriving or studying human embryonic stem cell lines or other cell lines of a pluripotent or totipotent nature from human embryos, provided that:

(i) the embryos used, whether fresh or frozen, were originally created for reproductive purposes and are no longer required for such purposes; and

(ii) consent was provided by the persons for whom the embryos were originally created for reproductive purposes. Where third party donor gametes were used to create the embryo, the third party gamete donor(s) shall have given, at the time of donation, consent to the unrestricted research use of any embryos created, when these embryos are no longer required for reproductive purposes. Where the third party gamete donors referred to in this paragraph are anonymous, it is not possible to seek their consent for embryo use. In such cases, the responsibility of consent for embryo use has, in effect, been transferred to the persons for whom the embryos were created for reproductive purposes; and

(iii) neither the ova nor the sperm from which the embryos were created, nor the embryos themselves, were obtained through commercial transactions (i.e., were acquired by payment of money in excess of costs actually incurred, or in exchange for services).

(b) Research on anonymized or coded human embryonic stem cell lines that have been created in Canada, or created elsewhere and imported for research purposes, provided that:

(i) those created in Canada were developed in compliance with this Policy or, prior to December 9, 2014, the *Guidelines for Human Pluripotent Stem Cell Research*. It is incumbent on the recipient of such cell lines to ensure that this is the case. The recipient shall provide satisfactory evidence to SCOC and the local REB that the cell lines fulfill the consent provisions before research can begin;

(ii) the recipient of stem cell lines created in a country other than Canada provides SCOC with satisfactory evidence that the manner in which the stem cell lines were created in the country of origin, including the embryo donors' consent, satisfies the laws and policies of that country. Should SCOC find that the manner of creation of these stem cell lines and the consent provisions vary significantly from the principles of this Policy, or, prior to December 9, 2014, the

Guidelines for Human Pluripotent Stem Cell Research, it may not approve the use of these cell lines in stem cell research in Canada.

(c) Research involving the grafting or any other form of transfer of human embryonic stem cells, embryonic germ cells, induced pluripotent stem cells, cells derived from those cells, or other human cells that are likely to be pluripotent into nonhuman animals, from birth to adulthood, provided that:

(i) the research is designed to reconstitute a specific tissue or organ to derive a pre-clinical model or to demonstrate that the cells are pluripotent (e.g., teratoma formation); and

(ii) these non-human animals grafted with human stem cells will not be used for reproductive purposes.

(d) Research involving the grafting or any other form of transfer of human embryonic stem cells, embryonic germ cells, induced pluripotent stem cells, cells derived from those cells, or other human cells that are likely to be pluripotent into humans with legal capacity shall be in compliance with the *Food and Drugs Act* and its Regulations, including the *Safety of Human Cells, Tissues and Organs for Transplantation Regulations*.

2) Research Not Conforming to this Policy

The following types of stem cell research do not conform to this Policy:

(a) Research involving the creation of human embryos specifically to derive stem cell lines or other cell lines of a pluripotent or totipotent nature;

(b) Research involving the creation of blastocysts from cells derived from pre-blastocyst stage human embryos;

~~(b)~~(c) Research involving somatic cell nuclear transfer into human oocytes (cloning) or involving stimulation of an unfertilized egg to produce a human embryo (parthenogenesis) for the purposes of developing human embryonic stem cell lines or other cell lines of a pluripotent or totipotent nature;

~~(c)~~(d) ~~(c)~~ Research involving the directed donation of human embryos or human embryonic stem cell lines to particular individuals;

~~(d)~~(e) ~~(d)~~ Research in which human or non-human embryonic stem cells, embryonic germ cells, induced pluripotent stem cells, or other cells that are likely to be pluripotent or totipotent are combined with a human embryo;

~~(e)~~(f) ~~(e)~~ Research in which human or non-human embryonic stem cells, embryonic germ cells, induced pluripotent stem cells, or other cells that are likely to be pluripotent or totipotent are grafted or transferred in any other form to a human fetus;

~~(f)~~(g) ~~(f)~~ Research in which human embryonic stem cells, embryonic germ cells, induced pluripotent stem cells, or other cells that are likely to be pluripotent or totipotent are combined with a non-human embryo; or

(h) ~~(g)~~ Research in which human embryonic stem cells, embryonic germ cells, induced pluripotent stem cells, or other cells that are likely to be pluripotent or totipotent are grafted or transferred in any other form to a non-human fetus.

Consent

Chapter 3, especially Articles 3.1 to 3.5, provides detailed guidance on the need to seek consent for participation in research. The following articles provide additional guidance for situations that are unique to stem cell research.

Article 12.11 Embryos no longer needed for reproductive purposes may be donated for use in research (including research to derive and study human embryonic stem cells). Embryo donors and gamete donors, if these are different individuals, shall be advised of all available options in respect of the use of the embryos and their consent sought prior to the use.

Article 12.12 At the time when the embryos are to be used for research to derive and study embryonic stem cells (and other human cells or cell lines of a pluripotent or totipotent nature), consent of the embryo donors shall be sought again. Research shall not proceed unless consent is obtained.

Application This requirement affirms the right of the donors to withdraw consent and is necessary because of the possible lengthy delay between the time at which the original consent is given and the time at which the embryos are utilized for research purposes. Members of the health care team treating and/or counselling prospective participants should not be the persons to seek consent from the embryo donors at the time of re-consent. A renewal of the consent provided by the gamete donors (if the gamete donors are not the same individuals as the embryo donors), is not required provided that appropriate consent for the unrestricted research use of the embryos was given at the time of gamete donation.

Article 12.13 When seeking consent for human embryonic stem cell research, in addition to the information outlined in Article 3.2 researchers shall provide to prospective research participants the following:

(a) An explanation that the cell line(s) will be anonymized or coded;

(b) An assurance that prospective research participants are free to not participate and have the right to withdraw at any time before an anonymized or coded cell line is created;

(c) An explanation that the research could result in the production of a stem cell line that could be maintained for many years, distributed to other parts of the world, and used for various research purposes;

(d) An explanation that the research participants will not benefit directly financially from any future commercialization of cell lines; nor will there be any personal benefit in terms of dispositional authority over any embryonic cell lines created (i.e., there will be no directed donation of the cells or cell lines to particular individuals).

Application Article 12.13(b) refers to the withdrawal of both consent and human biological materials. Once an anonymized or coded cell line is created, it may have a wide distribution, making withdrawal of materials almost impossible.

Creation of Excess Embryos

Article 12.14 Researchers shall not ask, encourage, induce or coerce members of the health care team to generate more embryos than necessary for the optimum chance of reproductive success. This is tantamount to creating embryos for research, which is prohibited under the *Assisted Human Reproduction Act*.

National Registry

SCOC maintains an electronically accessible national registry of human pluripotent stem cell lines and human totipotent stem cell lines derived from an embryonic source, generated in Canada. Induced human pluripotent stem cell lines are not listed with the registry, as they are not derived from embryonic sources.

Article 12.15 All human pluripotent stem cell lines or human totipotent stem cell lines derived directly from embryos under the auspices of an institution that is eligible to receive Agency funds shall be listed with the national registry of human embryonic stem cell lines and made available by the researcher to other researchers, subject to reasonable cost-recovery charges.

Privacy and Confidentiality

The secondary use of human biological materials for research purposes must meet the requirements of Articles 12.3A and 12.4 that provide detailed guidance on protecting personal information of participants. The following articles provide additional guidance for situations that are unique to stem cell research. In these cases, all human cells or cell lines should be delivered in an anonymized or coded form and, if coded, the key code should be accessible only to a custodian or trusted third party who is independent of the researcher who receives the cells (see Chapter 5, Section A, Types of Information).

Article 12.16 All human pluripotent stem cell lines or human totipotent stem cell lines shall be anonymized or coded unless the research only involves the directed donation of induced pluripotent stem cells.

Application While research involving the directed donation of human embryonic stem cell lines is not permitted under this Policy (Article 12.10.2[c]), research involving the directed donation of induced pluripotent stem cells is permitted, as induced pluripotent stem cells are not derived from human embryos.

Article 12.17 All researchers who make stem cell lines available to other academics shall ensure that the cell lines are anonymized or coded.

Conflicts of Interest

Chapter 7 (in particular Articles 7.2 and 7.4) provides guidance on conflicts of interest. The following articles provide additional guidance for situations that are unique to stem cell research.

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Article 12.18 Stem cell research teams shall not include members of the health care team treating and/or counselling prospective participants who could influence the prospective participants' decisions to donate their embryos.

Application This article seeks to minimize the risk that, for the purposes of stem cell research, women will feel pressured to create more embryos than needed for reproductive purposes or be pressured to donate embryos no longer needed for reproductive purposes. There may be a risk of undue influence where health care team members are also members of the stem cell research team (see Article 3.1).

Article 12.19 When researchers or their institutions have, or acquire, financial interests in the outcome of the stem cell research including, but not limited to, income from commercial firms supporting their research, stock holdings in corporations supporting their research, or patents in products produced through their research, they shall disclose this information to SCOC, the REB and current and prospective research participants (see Articles 7.2 and 7.4 regarding institution and researcher conflicts of interest). In some instances, disclosure may not be a sufficient response to concerns about actual, perceived or potential conflicts of interest. Researchers and/or their institutions may be asked to remedy any possible distortion of proper procedures attributable to such conflicts.

Article 12.20 Copies of contracts between researchers, institutions and industry sponsors and any relevant budgetary information shall be provided to SCOC and the REB to examine and evaluate any potential or actual conflicts of interest and to ensure the right to publish in a timely manner without undue restriction.