DALHOUSIE UNIVERSITY
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Novel Tech Ethics
Faculty of Medicine

January 15, 2014

Interagency Panel on Research Ethics
350 Albert Street
Ottawa, ON Canada
K1A 1H5

To Whom it May Concern:

The Interagency Panel on Research Ethics (PRE) is to be commended for the decision to incorporate the CIHR *Updated Guidelines for Human Pluripotent Stem Cell Research* into the TCPS2. This is something that I, and other scholars in bioethics, have long advocated. In addition to correspondence with PRE (March 6, 2009; March 31, 2009; and February 25, 2010), there have been relevant academic publications. See for example,

> Baylis, F., & Downie, J. (2012), Unfinished Business: Ongoing Ethical Exceptionalism in the Oversight of Human Pluripotent Stem Cell Research in Canada, *Accountability in Research: Policies and Quality Assurance*, 19:1, 13-26.
>
> Baylis, F. and Downie, J. (2011). Confusion worse confounded. **Rapid Response to**: Withdrawal of clinical trials policy by Canadian research institute is a "lost opportunity for increased transparency" by Ann Silversides. *British Medical Journal*, 342: d2570.

Having said this, there are a number of very significant substantive problems with the draft that has been circulated as part of the public consultation process.

The draft text includes vestiges of the original guidelines that are no longer relevant (or appropriate) given changes in the science and the law. Indeed, in several places the proposed guidelines are not consistent with the *AHR Act* and the *AHR Act (Section 8 Consent) Regulations*. For example, Article 12.12 violates Article 4 of the *AHR Act (Section 8 Consent) Regulations*. In the attached document I draw PRE's attention to some of these problems. Sometimes I suggest corrections to better align the guidelines and the legislation. Sometimes I simply include excerpts of relevant legislation or regulations (in red).

In addition to this very serious problem, I note the following:

(i) The audience for the draft text seems to shift. Sometimes the content is relevant to researchers and REB members; sometimes the content is a general description of mandate, membership and functioning of SCOC. As the SCOC remains a CIHR

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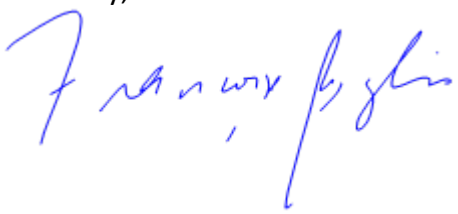
committee, issues concerning its mandate, membership, and governance do not belong in TCPS2. This information is not "research guidelines".

(ii) The draft text is unnecessarily repetitive in places, and incomplete in others.

(iii) The choice of terms is inconsistent and at times confusing.

I am pleased to have this letter and my comments posted on the Panel on Research Ethics Website

Sincerely,



Françoise Baylis, PhD, FRSC, FCAHS
*Professor and Canada Research Chair in Bioethics and Philosophy*

*Please include these comments in the public record of the consultation process on the Panel on Research Ethics Website*

**Demographic information requested:**

Province: Nova Scotia
Affiliation: Dalhousie University
Capacity in which I am submitting comments: Ethics scholar
Main discipline: Ethics

| Lines | **Reason for proposed change**<br>**Reference "Incorporation of CIHR guidelines into TCPS2"** | **Current Text (as proposed by PRE)** | **Proposed Text**<br>***(New/added text is in italics and bold)*** |
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| 9 | The title should be more precise so that it maps on to the content of this section. E.g., this section does not govern human pluripotent stem cells derived from a somatic source (i.e., induced pluripotent stem cells).<br><br>By making the title for this section more precise, there is no need to mention induced pluripotent stem cells in the sections on the national registry (at lines 136-141) or privacy and confidentiality (at lines 201-217). | Research Involving Pluripotent Stem Cells | Research Involving ***Human*** Pluripotent Stem Cells ***derived from an embryonic source*** |
| 11-15 | Instead of repeating information that applies to all of the TCPS, best to alert researcher to the fact that this section of the guidelines overlaps with legislation | Guidance regarding a proportionate approach …. | Delete text and replace with an explanation that the AHR Act (Section 8 Consent) Regulations (SOR/2007-137) and AHR Act (Section 12 Reimbursement) Regulations (not yet drafted) govern the creation and research use of human embryos. This section should direct stem cell researchers to familiarize themselves with the relevant legislation and regulations. |
| 17-20 | The TCPS2 is unnecessarily long. In some instances, this is largely because it includes superfluous text that does not serve the goal of providing researchers and REB members with guidance in the pursuit of ethical research. The information included here is dated<br><br>More generally, an economical editor of TCPS2 could easily shorten the document by about 30% without losing any of the substance. This would better serve the interests of research ethics. | Stem cell research is an area of growing interest among researchers because of its potential to lead to cures for many diseases and to improve the health of Canadians. In recognition of this, and because of the complex ethical issues that it raises, a Stem Cell | Delete text |

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| | | Oversight Committee (SCOC) was created by CIHR in 2003. | |
| 20-21 | Move up the subheading "Scope of SCOC Review" and cluster all relevant information. Some information about scope is above the current subheading.<br><br>"other ethically sensitive human stem cell research" is unclear/opaque. Best to be precise (provide an example) or delete.<br><br>It is important that the research be in compliance (not merely "accordance") with TCPS2 in general, not just Chapter 12, Section F.<br><br>The statement that SCOC review is intended to "complement" REB review is unclear and is arguably inaccurate as the SCOC and the REB may reach different conclusions. What is clear later on is that SCOC review precedes REB review: lines 48-49 state that "the researcher shall provide evidence of SCOC approval to the REB"; lines 82-84 state that "evidence of SCOC review must be provided to the local REB". The fact that SCOC review must happen prior to REB review should be stated clearly at the outset. | The committee reviews applications dealing with human pluripotent stem cells and other ethically sensitive human stem cell research to ensure that they are in accordance with Chapter 12, Section F of this Policy. | **Scope of SCOC Review**<br><br>The ***Stem Cell Oversight Committee (SCOC)*** reviews applications dealing with human pluripotent stem cells ***derived from an embryonic source*** ~~and other ethically sensitive human stem cell research to ensure that they are in accordance with Chapter 12, Section F of this Policy.~~ ***that have been submitted to CIHR (and approved by CIHR's peer review committees) to ensure compliance with TCPS2. The SCOC may also review stem cell research proposals submitted by other public or private granting agencies by mutual agreement. Applications that receive SCOC approval must then be submitted to local REBs as part of the local research ethics review process.*** |
| 23-28 | The description of SCOC membership should not be included in the TCPS2 as this is not relevant guidance for researchers or REB members. This information belongs to the SCOC and is to be managed by the SCOC. | | |
| 26-27 | The current wording is problematic as it names IVF patients as an example of patients involved with stem cell research. These are discrete categories. | … patients involved with stem cell research (such as in vitro fertilization patients) | … patients involved with stem cell research ***or*** ~~(such as~~ in vitro fertilization patients ***who provide embryos for stem cell research***~~)~~ |

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| 32-33 | Delete text so as not to repeat information introduced above | | |
| 39-40 | Logic suggests that the order of the two bullets should be inverted | • Will be transferred into humans or non-human animals; and or<br>• Have been derived from an embryonic source | • ***Have been derived from an embryonic source; and/or***<br>• ***Will be transferred into humans or non-human animals*** |
| 42-44 | On the assumption that the parameters for ethics review indicated at lines 39-40 are exhaustive, the additional sentence adds no new information.<br><br>Moreover, the proposed more precise title for the section (line 9) obviates the need for this additional content | 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 and non-human animals. | ~~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 and non-human animals.~~ |
| 45-49 | Immediately preceding Article 12.10 there is reference to the fact that the SCOC reviews "human pluripotent stem cells derived from an embryonic source". Best to use the same terminology. | Research involving human embryonic stem cells and/or grafting or any other form of transfer of human pluripotent stem cells into humans or non-human animals requires review and approval by the Stem Cell Oversight | Research involving ***the derivation of pluripotent*** ~~embryonic~~ stem cells ***from an embryonic source*** and/or ***the*** grafting**,** or any other form of transfer**,** of **these** human pluripotent stem cells into humans or non-human animals requires review and approval by ~~the~~ ~~Stem Cell Oversight Committee (~~SCOC~~)~~ and an REB. The researcher shall provide evidence of SCOC approval to the REB. |

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| | | Committee (SCOC) and an REB. The researcher shall provide evidence of SCOC approval to the REB. | |
| 71-74 | Statement in parenthesis is unclear and inaccurate (insofar as it is inconsistent with the legislation). It should be replaced with clear and direct reference to the relevant legislation | (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 health care services). | (iii) ***there were no payments for*** ~~neither~~ the ova ~~n~~or the sperm from which the embryos were created, ~~n~~or ***for*** 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 health care services).~~ ***other than reimbursement permitted under the AHR Act section 12*** **(not yet in force)** |
| 82-84 | This text should be consistent with text on lines 48-49 "the researcher shall provide evidence of SCOC approval to the REB" | evidence of SCOC review must be provided to the local REB | evidence of SCOC ***approval*** ~~review~~ must be provided to the ~~local~~ REB |
| 88-94 | The requirement should be for the stem cell lines to have been derived in a manner that is both consistent with the consent laws in the country of origin as well as Canadian consent law. Otherwise you have a race to the bottom – i.e., find the country with the most lax consent laws and import stem cell lines from that country. Moreover, the sentence at lines 89-94 is clear on this point as the consent provisions have to adhere to the TCPS2. As such, the point can be stated far more simply. | … "satisfies the laws and policies of that country …" | …"satisfies ***not only the laws and policies of the country of origin, but also*** ~~the~~ ***Canadian*** laws and policies ~~of that country." Should SCOC find that the manner of creation of these stem cell lines and the consent provisions do not adhere to the principles of~~ (i.e., this Policy, or, prior to **[insert date of incorporation of CIHR Guidelines into TCPS 2]**, ***the CIHR Updated*** *Guidelines for Human Pluripotent Stem Cell Research*~~), it shall not approve the use of these cell lines in stem cell research in Canada.~~ ***The SCOC shall not*** |

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| | See also comment re: lines 136-146 on the National registry | | ***approve the research use of human pluripotent stem cell lines not derived in conformity with the relevant legislation. Once such lines are identified, they will be listed in the national Registry [at http://] so that the information is available to other researchers to preclude further submissions to SCOC with ineligible lines.*** |
| 111 | The guidelines need to both acknowledge that there is relevant legislation and ensure that the guidelines are consistent with the legislation (this is not the case with the current draft). There should be two separate section headings in lieu of the current single heading given at line 111: namely,<br>2) Research that is not Legally Permitted under the *AHR Act*, and<br>3) Additional Research that is not Permitted under the TCPS2 | 2) Research Not Conforming to this Policy | ***2) Research that is Not Legally Permitted under the AHR Act***<br><br>***a) Consistent with 5(1)(a) of the AHR Act, 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 pluripotent stem cell lines is not permitted.***<br><br>***b) Consistent with 5(1)(b) of the AHR Act, research involving the creation of human embryos specifically to derive human pluripotent stem cell lines is not permitted.***<br><br>***c) Consistent with 5(1)(f) and 5(1)(i) of the AHR Act, research in which human or non-human pluripotent stem cells derived from an embryonic source, germ cells, induced pluripotent stem cells, or other cells that are likely to be pluripotent are combined with a human embryo or a non-human embryo is not permitted.***<br><br>***3) Additional Research that is not Permitted under the TCPS2***<br><br>***a) Research involving the directed donation of human embryos or human pluripotent stem cell lines derived from human embryos is not permitted.***<br><br>***b) Research in which human pluripotent stem cells derived*** |

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| | | | ***from an embryonic source, germ cells, induced pluripotent stem cells, or other cells that are likely to be pluripotent are grafted or transferred in any other form to a human fetus or a non-human fetus.*** |
| 136 - 146 | There is no need to reference induced pluripotent stem cells as given at lines 140-141 (see comment directed to line #9 above).<br><br>The section on the National Registry should be moved. It should come immediately before the section on Privacy and Confidentiality.<br><br>Information about the National Registry in the opening paragraph is outdated (e.g., there is no longer a need for the statement about the rationale in creating the registry) It is also incomplete (e.g., Who maintains the registry? Who is responsible to provide information to the registry – SCOC, the REB, the investigator?)<br><br>To the best of my knowledge there is no publicly available source which posts information regarding lines judged to be ineligible by the SCOC. Independent published research suggests that the following human pluripotent stem cell lines should be on the list of ineligible lines: Krahn, TM and Wallwork, T. (2011). Who Cares About Consent Requirements for Sourcing Human Embryonic Stem Cells? Are Errors *In* the Past Really Errors *Of* the Past? *Accountability in Research,* 18 at 256-257:<br><br>• hES1-hES6 [ES Cell International Pte Ltd., Biopolis Street, #01–03 Genome, Singapore 138672, Singapore. Available at <http://www.biotimeinc.com/>. Last accessed 14 January 2014]<br>• 13,16 [Joseph Itskovitz-Eldor, The Ruth and Bruce | There is an electronically accessible national registry of human embryonic stem cell lines generated in Canada. This registry is intended to minimize the need to generate large numbers of cell lines, and thereby decrease the need for donation of large numbers of embryos. Induced human pluripotent stem cell lines are not listed with the registry, as they are not derived from embryonic sources. | There is an electronically accessible national registry of human ~~embryonic~~ ***pluripotent*** stem cell lines ***derived from an embryonic source*** and eligible for use ~~generated~~ in Canada ***[at http://www.cihr-irsc.gc.ca/e/39580.html]***. This registry ***lists human pluripotent stem cell lines derived from an embryonic source that are either approved or ineligible for research use in Canada.*** ~~is intended to minimize the need to generate large numbers of cell lines, and thereby decrease the need for donation of large numbers of embryos. Induced human pluripotent stem cell lines are not listed with the registry, as they are not derived from embryonic sources.~~ |

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| | Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Efron St. # P.O.B. 9649, Haifa 31096, Israel. Available at <http://www1.technion.ac.il/en>. Last accessed 14 January 2014]<br>• H1, H7, H9 [Sander Shapiro, Department of Obstetrics and Gynecology, University of Wisconsin School of Medicine and Public Health, Box 6188 Clinical Science Center – H6, 600 Highland Ave., Madison, WI 53792, USA. Available at <http://www.med.wisc.edu/>. Last accessed 14 January 2014]<br>• CC1, CC3 [Derrick E. Rancourt and Calvin Greene, Departments of Oncology and Biochemistry and Molecular Biology, University of Calgary, 3330 Hospital Drive N.W., Calgary, Alberta T2N 4N1, Canada. Availale at <http://people.ucalgary.ca/~rancourt/>. Last accessed 14 January 2014]<br>• ES2-ES6 [Juan Carlos Izpisúa Belmonte, Regenerative Medicine Centre, Barcelona, Spain. Available at <http://www.cmrb.eu/en_index.html>. Last accessed 14 January 2014]<br>• KCL-003-CF1S. [J. Pickering, S. L. Minger, M. Patel, H. Taylor, C. Black, A. Ekonomou, and P. R. Braude, Department of Women's Health, GKT School of Medicine, 10th Floor, North Wing, St. Thomas' Hospital, London SE1 7EH, UK. Available at <http://www.kcl.ac.uk/schools/biohealth/research/rhed/stemcellgroup.html>. Last accessed 14 January 2014]<br>• CyT49 [ViaCyte Inc. (formerly Novocell Inc. and prior to that CyThera Inc.), 3550 General Atomics Court, San Diego, CA 92121-1122, USA. Available at <www.viacyte.com>. Last accessed 14 January 2014]<br>The National Registry should be expanded. It should not only include information about human pluripotent stem cell lines derived from an embryonic source created in Canada (and presumably eligible for research use) in Canada. It | | |

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| | should also include a list of stem cell lines already reviewed by the SCOC that are not approved for research use in Canada. | | |
| 147 *ff.* | Consent. All of this section needs to be consistent with the AHR Act (Section 8 Consent) Regulations. There are many "inconsistencies" some of which are noted below | | |
| 151 - 158 | Article 12.12 is inconsistent with the AHR Act (Section 8 Consent) Regulations. Decision-making about the donation of embryos to research cannot legally be made prior to the collection of gametes. See **AHR Act (Section 8 Consent) Regulations (SOR/2007-137), sec.4.** Note the options that are to be presented to individuals for consent prior to the use of gametes to create an embryo do not include the option of embryo research. To include this option would be illegal as one would be soliciting consent to the creation of an embryo for research. Section 4 of the Regulations reads as follows:<br><br>4. (1) Before a person makes use of human reproductive material for the purpose of creating an embryo, the person shall have the written consent of the donor of the material stating that the material may be used for one or more of the following purposes:<br><br>(a) the donor's own reproductive use;<br><br>(b) following the donor's death, the reproductive use of the person who is, at the time of the donor's death, the donor's spouse or common-law partner;<br><br>(c) the reproductive use of a third party;<br><br>(d) improving assisted reproduction procedures; or<br><br>(e) providing instruction in assisted reproduction | | AHR Act (Section 8 Consent) Regulations<br><br>**13.** (1) Before a person makes use of an *in vitro* embryo, the person shall have the written consent of the donor of the embryo stating that the embryo may be used for one or more of the following purposes: …<br><br>o (*e*) a specific research project, the goal of which is stated in the consent.<br><br>(2) Before a person makes use of an *in vitro* embryo for a purpose mentioned in paragraph (1)(*c*), (*d*) or (*e*), the person must also have the written consent, in accordance with section 4, of the persons whose human reproductive material was used to create the embryo, unless those persons have already consented to that use as the donor of the embryo. |

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| | procedures.<br><br>***The applicable sections for donation to research are sections 12 and 13 of the AHR Act (Section 8 Consent) Regulations.***<br><br>*http://laws-lois.justice.gc.ca/eng/regulations/SOR-2007-137/page-3.html#docCont* | | |
| 159 - 162 | Article 12.13 is inconsistent with the AHR Act (Section 8 Consent) Regulations sec.13(1)(e) that specifies consent must be for "a specific research project, the goal of which is stated in the consent". There is no requirement for a second consent to research. | | AHR Act (Section 8 Consent) Regulations<br><br>**13.** (1) Before a person makes use of an *in vitro* embryo, the person shall have the written consent of the donor of the embryo stating that the embryo may be used for one or more of the following purposes: …<br><br>o (*e*) a specific research project, the goal of which is stated in the consent.<br><br>(2) Before a person makes use of an *in vitro* embryo for a purpose mentioned in paragraph (1) *(c),* (*d*) or (*e*), the person must also have the written consent in accordance with section 4, of the persons whose human reproductive material was used to create the embryo, unless those persons have already consented to that use as the donor of the embryo. |
| 178 - 180 | The statement about the right to withdraw at Art.12.14(2) is not consistent with the AHR Act (Section 8 Consent) Regulations, sec.14(1) | | AHR Act (Section 8 Consent) Regulations<br><br>14. (1) If a donor wishes to withdraw their consent, the withdrawal must be in writing.<br><br>(2) The withdrawal is effective only if the person who intends to make use of the in vitro embryo is notified in writing of the withdrawal<br>… |

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| | | | (e) in the case of an in vitro embryo to be used for the purpose mentioned in paragraph 13(1)(e), before the latest of the following occurrences, namely,<br><br>(i) the person acknowledges in writing that the in vitro embryo has been designated for research,<br><br>(ii) the beginning of the process of thawing the in vitro embryo for the purpose of research, and<br><br>(iii) the creation of a stem cell line using the in vitro embryo.<br><br>(3) If the donor is a couple, the consent of the donor may be withdrawn by either spouse or common-law partner. |
| 195 - 200 | Article 12.15 on the creation of excess embryos is redundant. The AHR Act prohibits the creation of human embryos for research purposes. The TCPS does not need an Article that says 'know the law and don't entice physicians to break the law'. ***The fact that there is relevant law should be addressed in the opening paragraph to Chapter 12 Section F*** | | |
| 213 - 215 | There is no need to reference induced pluripotent stem cells (see comment directed to line #9 above) | … research involving the directed donation of induced pluripotent stem cells is permitted, as induced pluripotent stem cells are not derived from human embryos. | ~~… research involving the directed donation of induced pluripotent stem cells is permitted, as induced pluripotent stem cells are not derived from human embryos.~~ |
| 226 - 227 | Need to revise the Application. Statement about women feeling pressured to create more embryos than needed for reproductive purposes is outdated. The original stem cell guidelines were drafted before the AHR Act and the AHR | | Revise |

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| | Act (Section 8 Consent) Regulations. It is illegal to create embryos for research purposes. | | |
| 249 - 281 | Glossary. This should be refined. Of note, the current Glossary does not include references. | | |
| All | Consistent terminology. | i.human stem cells<br>ii.human embryonic stem cells<br>iii.human embryonic stem cell lines | ***i. human pluripotent stem cells***<br>***ii.human pluripotent stem cells derived from an embryonic source***<br>***iii.human pluripotent stem cell lines derived from an embryonic source*** |