FORMAL INCORPORATION OF THE *UPDATED GUIDELINES FOR PLURIPOTENT STEM CELL RESEARCH* INTO THE REVISED *TCPS*

Françoise Baylis
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In an earlier submission to the Panel on Research Ethics (PRE) on March 6, 2009, (See (http://www.noveltechethics.ca/pictures/File/Health_Policy_Private/TCPS%20Proposed%20Revisions.pdf page 22, item 9) I underlined the importance of acting on the June 2003 commitment to formally incorporate the *Updated Guidelines for Pluripotent Stem Cell Research* into the revised *TCPS.* This commitment is spelled out in the Interim Tri-Agency Measures for Human Pluripotent Stem Cell Research (See, http://www.nserc-crsng.gc.ca/NSERC-CRSNG/Policies-Politiques/stemcell-cellulesouche_eng.asp) and referenced in section 3.0 of the 2005, 2006 and 2007 versions of the *Updated Guidelines.*

In discussion it became evident that there were different perspectives on how the *Updated Guidelines* should be "formally incorporated" into the *TCPS*. At least three possible interpretations were on the table: inclusion in the body of the *TCPS*; inclusion as an appendix to the *TCPS;* and reference in the *TCPS* to the *Updated Guidelines*. Some members of PRE suggested that a reference to the *Updated Guidelines* would satisfy the obligation to "formally incorporate" the guidelines. This perspective is consistent with the February 2008 recommendation to PRE from the Stem Cell Working Committee: A Working Committee of the Interagency Panel on Research Ethics (See, http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/reports-rapports/cihr-irsc/). In many ways, however, this perspective is deeply flawed. Based on my research and reflection, I have concluded that "formal incorporation" requires inclusion in the body of the *TCPS* and not inclusion as an appendix or a reference. A number of arguments in defense of this view are briefly sketched below:

1. A precedent for how to proceed with pre-existing topic-specific research ethics guidelines was set with the introduction of the original *TCPS*. The *TCPS* replaced general research ethics guidelines published by SSHRC (*Ethics Guidelines for Research with Human Subjects*) and MRC (*Guidelines on Research Involving Humans*). It also took the existing "topic specific" research ethics guidelines published by MRC (*Guidelines for Research on Somatic Cell Gene Therapy in Humans*) and incorporated them into the *TCPS* by inclusion. In other words, when the *TCPS* was introduced, a precedent was set not to allow external independent pre-existing research ethics guidelines for discrete areas of research to remain external to the *TCPS*.

2. There is no principled reason not to follow this precedent. Some have suggested that special ethics expertise is needed for pluripotent stem cell research and this justifies treating the stem cell guidelines differently. However, the need for special expertise does not justify the retention of a

Prof. Françoise Baylis
Novel Tech Ethics
Dalhousie University
1234 Le Marchant Street
Halifax, Nova Scotia
Canada B3H 3P7
Email: francoise.baylis@dal.ca

Tel: 902.494.2873
Fax: 902.494.2924
Web: www.noveltechethics.ca
Email: nte@dal.ca

separate set of topic-specific research guidelines external to the *TCPS* on anything other than an interim basis. Special ethics expertise is needed for many areas of research (as it was for gene therapy research and as it could be argued for clinical trials, qualitative research methods, and research with First Nations communities, to take but a few examples). The need for this expertise has been met for all other specialized areas by having PRE access the expertise in the course of drafting and revising the *TCPS*.

3. Failure to follow this precedent will undermine the authority of PRE as the sole authoritative source in Canada for funding agency ethics guidelines for research involving humans. If the *Updated Guidelines* are only incorporated by reference, then there will be two official bodies with the authority to write ethics guidelines for research involving humans, namely PRE and CIHR (note, the stem cell guidelines apply to research involving adults, fetuses, embryos, umbilical cord, tissues, etc). This is problematic for several reasons, not the least of which concerns the need for a final arbiter in the event of policy disagreement -- if the *Updated Guidelines* now (or in the future) conflict with the *TCPS*, who will have ultimate authority to resolve the conflict and determine which guidelines researchers and REB members should follow? (recall that PRE is an entity created by SSHRC, CIHR, and NSERC but the authorship of the *Updated Guidelines* rests solely with CIHR through the need for it to approve recommendations made by the Stem Cell Oversight Committee (SCOC), which it appoints).

4. Failure to follow this precedent may lead to a proliferation of separate research ethics guidelines for specific areas of research under the authority of one or more of the federal funding Agencies. If there can be separate research ethics guidelines for stem cell research under the authority of CIHR Governing Council, then why not separate research ethics guidelines for some other ethically challenging area of research under the authority of one of the other federal granting Agencies? Allowing the *Updated Guidelines* to be incorporated into the new edition of the *TCPS* by reference is an invitation to all three federal granting Agencies to proliferate research ethics guidelines that are, and will remain, under their sole control (as contrasted with the shared control over the *TCPS*).

5. If there can be two (or more) research ethics guidelines under the authority of two (or more) federal granting Agencies, how will the risk of confusion for the research community be managed and minimized? The *TCPS* has not had a major revision since it was introduced in 1998. Meanwhile, substantive revisions have been made to the *Updated Guidelines* three times (in 2005, 2006 and 2007) and further changes are anticipated in June 2009. Imagine that multiple discrete research ethics guidelines are revised by different governing bodies, following different processes, on different schedules as has happened with the *TCPS* and the *Updated Guidelines*. The potential for confusion and controversy would be significant.

Beyond these generic concerns about a multiplicity of research ethics guidelines under the authority of different federal granting Agencies, there are additional concerns specific to the *Updated Guidelines* and SCOC regarding matters of process and substance where there appears to be a privileging of the interests of the research community. These concerns lead me to conclude that it is important for the oversight of stem cell research to be placed squarely with PRE (as could only be done by incorporating the *Updated Guidelines* into the *TCPS* by inclusion, and not by reference or as an Appendix).

6. In 2005, substantive changes were made to the *Guidelines* "to recognize that fresh embryos (and not just frozen embryos) are also being used for stem cell research" (CIHR 2005). The 2002 *Guidelines* did not discuss the use of fresh versus frozen embryos for hESC research. Once it became clear that researchers were using fresh embryos for hESC research, the *Guidelines* were amended to legitimize this research. Leaving aside the ethics of whether fresh or frozen embryos should be used for hESC research, the fact is that the reason given for the change in policy is not a reason grounded in ethics, but a reason grounded in practice and pragmatics – that is, the reason given for the change in policy is "to recognize" that which is already being done by members of the research community.[1]

7. According to the *Updated Guidelines*, <u>all</u> *hESC lines* established through research that is funded by one or more of the federal granting Agencies or conducted in Agency funded institutions must be (i) included in an hESC registry and (ii) available to other researchers on a cost-recovery basis. For reasons that are unclear CIHR has yet to *formally e*stablish this registry. Meanwhile, in 2007 SCOC suggested excluding from the registry all hESC lines created in an Agency funded institution if these lines were created without Agency funding (such an exclusion would be in direct conflict with the clear reach-through provision in the *TCPS* and agency-institution MOUs). This proposed change in policy would not serve the public interest, but would serve the interests of some members of the research community. [2]

8. For some time, concerns have been raised regarding SCOC and conflict of interest (at both the individual and the institutional levels). The concern at the individual level stems from the fact that there are close ties between members of SCOC and researchers whose work is subject to SCOC review.

   The original guidelines for membership on SCOC include the following statement on conflict of interest: "Individuals for whom there could be actual or perceived conflict of interest will be excluded from consideration. Examples include anyone named as a Network Investigator or Network Collaborator on a research project funded by the Stem Cell Network or anyone who receives money from the Stem Cell Network, and staff members of any of the Agencies." Meanwhile, investigators with the Stem Cell Network (SCN) were initially named to the SCOC in direct violation of the conflict of interest rules set out for SCOC membership. These individuals did

not take up their positions when concerns were raised by members of the research ethics community. At the present time, SCOC does not include an SCN investigator or collaborator, but does include a member who "held a significant leadership role in the SCN", which arguably is inconsistent with the conflict of interest rules for SCOC membership.

More recently an article on stem cell research policy was co-authored by members of SCOC and investigators with the SCN. Ethics standards would certainly have it that to avoid actual or perceived conflict of interest, the investigators and those who are tasked with oversight of the research should be working at arms-length and should not be engaged in joint advocacy on the very matters that are the subject of oversight. The article in question is:

> Cohen C, Brandhorst B, Nagy A, Leader A, Dickens B, Isasi R, Evans D, and Knoppers B. 2008. The use of fresh embryos in stem cell research: Ethical and policy issues. *Cell Stem Cell*, 2:416-421.

At the time this article was published (May 2008), three of the authors (Knoppers, Isasi, and Nagy) were SCN investigators, Cohen and Dickens were former SCOC members, and Brandhorst, Leader, and Evans were current SCOC members. In the body of the article the authors acknowledge that five of the authors "are current or former members of the SCOC" (Cohen et al. 2008, 417). In the acknowledgements, three of the authors "thank the Canadian Stem Cell Network for funding support" (Cohen et al. 2008, 420).

Recommendation

Incorporate the substance of the *Updated Guidelines for Pluripotent Stem Cell Research* into the revised *TCPS* by inclusion in the *TCPS* itself (and, to be clear, not as an appendix), and not simply by reference.

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[1] For a detailed discussion, see Baylis F., and McInnes C. 2007. Women at risk: Embryonic and fetal stem cell research in Canada. *McGill Journal of Law & Health*. 1:53-67.

[2] For a detailed discussion, see Baylis F., and Herder M. (forthcoming 2009). Policy design for human embryo research in Canada: An analysis. Part 2 of 2 *Journal of Bioethical Inquiry* 6(3).