

Françoise Baylis, Professor and Canada Research Chair www.noveltechethics.ca
Presentation to the Standing Senate Committee on Social Affairs, Science and Technology on
Clinical Trial Registration, Ottawa, May 10, 2012

Recent history

December 2010, the three federal research granting Agencies released the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2)*.

December 20, 2010 (weeks later), CIHR released its *Policy on registration and results disclosure of controlled and uncontrolled trials funded by CIHR*. This policy was developed “to increase the transparency and accessibility of trials by improving their registration and disclosure of their results”.

Mid-March 2011, CIHR rescinded its *Policy on registration and results disclosure of controlled and uncontrolled trials funded by CIHR* in favour of *TCPS 2*. At the time, the reason given for the decision by CIHR’s vice president Knowledge Translation and Public Outreach, Ian Graham, was that overlap with *TCPS 2* would “cause confusion and inconsistent application of the requirements” (Silversides 2011). Thereafter, the President of CIHR, Alain Beaudet, has explained the decision as:

an effort [by CIHR] to harmonize all of its ethics policies on research involving humans and to integrate operational requirements in relevant programs where appropriate and feasible. In so doing, CIHR recognized that the second edition of the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS-2)* was now the single reference document dealing with these issues (CIHR 2011).

March 29, 2012, in testimony before the Standing Senate Committee on Social Affairs, Science and Technology, Dr. Beaudet explained:

We decided that our side policies — we had one on trials, one on stem cells, one on Aboriginal people — should all be integrated within the single tri-council policy. It obviously gives these council policies greater gravitas if they are integrated in the real policy rather than being local policy.

There is not, however, a single reference document in Canada for research involving humans (Baylis & Downie 2011; Baylis & Downie 2012). In 2010, when *TCPS 2* was endorsed by the three federal research granting Agencies, CIHR announced that the *CIHR Guidelines for Health Research Involving Aboriginal People* were superseded by *TCPS 2*. Later, in 2011, CIHR rescinded its “Policy on registration and results disclosure of controlled and uncontrolled trials funded by CIHR” in favour of *TCPS 2*. To this date, CIHR retains exclusive authority over

human pluripotent stem cell research as regards development, interpretation and implementation of stem cell research guidelines, as well as oversight for this area of research (Baylis & Downie 2011; Baylis & Downie 2012).

Does Canada have a robust policy on clinical trial registration?

Dr Beaudet has assured this committee that,

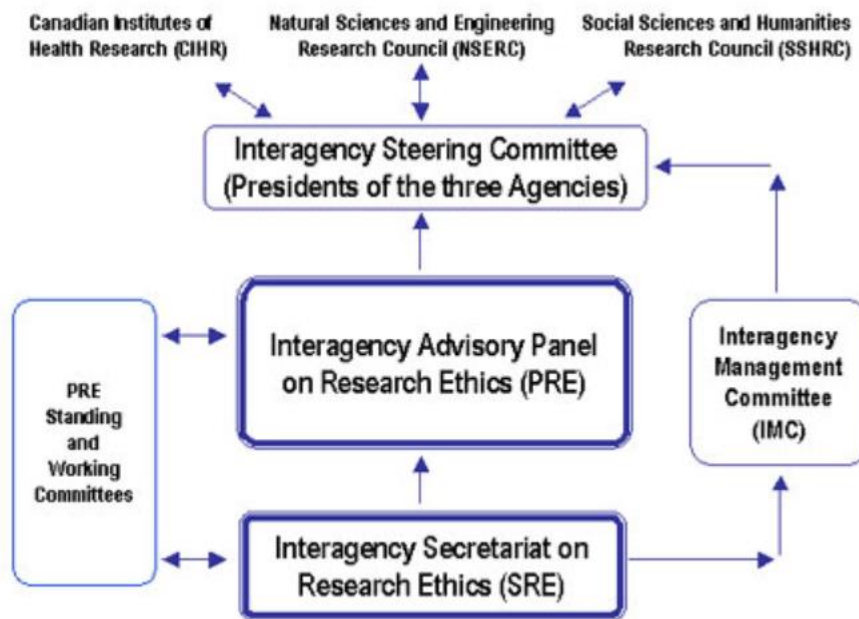
“concerning clinical trials — and we have integrated that in the policy — all clinical trials must be registered in a public registry before the first participants are recruited.

There are only *minor elements from the original policy that are not yet in the tri-council policy* [sic] because we have to consult with the other councils and the committees of ethicists across the country who update the policy. I know this will eventually be integrated. I want to dispel the misunderstanding that we are withdrawing or decreasing our standards. We just want to give them more formality and gravitas, and we want them to apply to all research that is under the umbrella of the tri-council not only under CIHR.”

Attached, for your information, is the section of TCPS 2 on Clinical Trials and the original CIHR Policy on clinical trial registration. The Chart below compares the two documents.

TCPS 2	Policy on registration and results disclosure of controlled and uncontrolled trials funded by CIHR
PRE responsible for development, interpretation and implementation	CIHR responsible for development, interpretation and implementation. CIHR policy document could have co-existed with TCPS-2 (would have set a higher standard set for CIHR-funded trials)
<p>Article 11.3 All clinical trials shall be registered before recruitment of the first trial participant in a recognized and easily web-accessible public registry.</p> <p>Researchers shall provide the REB with the number assigned to the trial upon registration.</p>	<p>5.1 Prospective Registration of Trials Grantees are required to:</p> <ol style="list-style-type: none"> 1. register all CIHR funded trials following the 2006 WHO international standards prior to the recruitment of the first study participant by providing at least the WHO Trial Registration Data Set, ethics approval (one per country, generally for the main site), a reference to the systematic review that justifies the need for proposed trial, and other trial details, to any WHO/ICMJE endorsed registry. 2. register the trial in only one WHO primary registry or registry acceptable to ICMJE (such as ClinicalTrials.gov) following the WHO international standards for prospective trial registration. In instances when trial is registered in more than one registry, the grantee must provide cross-references to each registry including the identification number. 3. provide CIHR with the name of registry and the identification number issued by the registry. This ID should be used in all further communication with CIHR, publications, presentations, and on the trial website if it exists.

	<p>5.2 Public disclosure of trial information during trial Grantees are required to:</p> <ol style="list-style-type: none"> 1. update trial information in the registry at least once a year, usually following annual ethics review and re-approval. 2. report to CIHR and the registry major changes to the protocol such as the change of a primary or secondary outcome, or any other protocol amendment that requires ethics approval, upon approval by the ethics board, within 30 days. 3. report to CIHR and the trial registry early stopping or termination of a trial, within 30 days. <p>5.3 Public reporting (disclosure) of trial results Grantees are required to:</p> <ol style="list-style-type: none"> 1. submit, for RCTs, the CONSORT -based final report to CIHR within 12 months after the end of the trial, its early stopping, or termination regardless of the reason. CIHR considers this report public and has the right to publicly disclose it within 18 months of its submission. The grantee must follow the most recent CONSORT that corresponds to a design of his/her trial. For all other trials, the grantee must follow CIHR reporting guidelines. 2. comply with the CIHR Policy on Access to Research Outputs by publishing trial results in an open access journal or archive peer reviewed manuscripts in an open access repository (such as PubMed Central Canada). 3. submit trial results to a publicly accessible results databank such as ClinicalTrials.gov by completing all required fields (tables) within 18 months after the end of the trial. 4. post the aggregate (summary) data and micro (participant) level data on an unbiased freely accessible website. 5. report any severe adverse event or harm in the publication of the trial results following the CONSORT for harms. 6. submit any severe adverse event or harm to the trial registry along with the results if appropriate fields exist in the registry. <p>5.4 Data retention Grantees are required to:</p> <ol style="list-style-type: none"> 1. retain all trial information including original micro-level data and metadata data for twenty five years unless they are deposited in a freely accessible data repository (to align with the Health Canada requirements).
--	---



REFERENCES

Baylis, F. & Downie, J. 2011. 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. DOI: 10.1080/08989621.2012.638595.

Baylis, F. & 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* 2011;342:d2570.

Canadian Institutes of Health Research. 2011. *Policy on the registration and results disclosure of controlled and uncontrolled trials funded by CIHR*. Originally available at: <http://www.cihr-irsc.gc.ca/e/42831.html> (no longer available at this URL). Available at: <http://sjlibrarian.wordpress.com/2011/04/06/cached-copy-policy-on-registration-and-results-disclosure-of-controlled-and-uncontrolled-trials-funded-by-cihr/>

Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada. 2010. *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*. Available at: www.pre.ethics.gc.ca.

Silversides, A. Withdrawal of clinical trials policy by Canadian research institute is a "lost opportunity for increased transparency" *British Medical Journal* 2011;342:d2570