DEPARTMENT OF HEALTH & HUMAN SERVICE

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 240-453-8132
FAX: 240-453-6909
Email: Kristina.borror@hhs.gov

December 18, 2007

Murray G. Ramsden, HBA, DHA, CHE
Chief Executive Officer
Interior Health Authority
Kelowna, British Columbia V1Y 4N7
CANADA

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 10352

Dear Dr. Ramsden:

The Office for Human Research Protections (OHRP) has reviewed the Interior Health Authority's (IHA) July 31, 2007 report responding to OHRP's May 24, 2007 letter regarding compliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

Based upon its review, OHRP makes the following determinations:

(1) OHRP finds that IHA does not have written IRB procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5):

(a) The procedures which the IRB will follow for conducting its continuing review of research.

(b) The procedures which the IRB will follow for reporting its findings and actions to the institution.

(c) The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

(d) The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given,

> may not be initiated without IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subject.
>
> (e) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP of: (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

OHRP notes that while the IHA IRB does have written procedures to ensure prompt reporting to the IRB and sponsors of unanticipated problems, they do not have procedures for reporting these events to OHRP, nor do they have written procedures to ensure prompt reporting of any serious or continuing noncompliance or suspension or termination to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP.

Corrective Action: OHRP acknowledges that the Terms of Reference for the IHA IRB are being revised to accommodate these requirements, and that the Terms of Reference were going to be forwarded to OHRP in September 2007. OHRP has not yet received them.

Required Action: By February 5, 2007 please provide OHRP a copy of the written procedures that address these regulatory requirements.

(2) HHS regulations at 45 CFR 46.108(b) require that, except when an expedited review procedure is used, research be reviewed at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in a nonscientific area. In its May 24, 2007 letter OHRP expressed a concern that the IRB written procedures for the IHA IRB state "A quorum will be the Chair...and not less than four of the standing members or substitute members…." As the IHA IRB has 11 members, this would not be a majority of members and therefore would not constitute a quorum under HHS regulations; in addition, this procedure does not include a statement regarding the regulatory requirement for including at least one member whose primary concerns are in a nonscientific area.

Corrective Action: OHRP acknowledges IHA's statement that the Terms of Reference for the IH IRB are being revised. As noted above, please provide OHRP with a copy of the revised Terms of Reference which address quorum requirements.

(3) HHS regulations at 45 CFR 46.115(a)(2) require that minutes of IRB meetings be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. OHRP finds that IHA and Penticton IRB minutes failed to meet some of these requirements. In specific, the minutes do not include the vote on actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

Corrective Action: OHRP acknowledges that in the revised Terms of Reference, the requirement for recording of voting will be made explicit. OHRP also acknowledges that following the meeting, the Chair develops a Report of Review which sets out details of the discussion regarding the study and recommendations for change. The Report of Review is filed in the research file. OHRP notes that such documentation should become part of the documentation of the meeting minutes to meet the requirements under HHS regulations at 45 CFR 46.115(a)(2) for HHS-supported research.

Required Action: By February 5, 2007 please provide OHRP with the revised Terms of Reference.

OHRP has the following concern:

(4) [Redacted]

[Redacted]

OHRP offers the following guidance:

(5) OHRP notes that the IHA Administrative Guidelines Governing Ethics Review of Research Involving Human Subjects in section 4.6 indicates "Certain classes of research involving human subjects are excluded from the requirement for ethics review, including:…research on public policy issues, public institutions and other matters that in a free and democratic society can properly be considered to be part of the public domain is not required to undergo ethics review, even when individuals occupying positions connected to such matters are involved." OHRP notes that this could include activities that meet the definition of human subjects research under HHS regulations at 45 CFR 46.102(d) and (f) and would not be exempt; therefore such activities could require IRB review if funded by HHS.

Your July 31, 2007 report states: "The wording in this section comes directly from the Canadian Tri-Council Policy Statement (TCPS), which to our understanding is accepted as being equivalent to the Common Rule." We wish to clarify that as of the date of this letter, **no** foreign procedures have been deemed by HHS to be at least equivalent to the protections in the Common Rule. Therefore, 45 CFR part 46 is the procedural standard which must be complied with for all HHS-conducted or –supported human subjects research, conducted either domestically or internationally. For further information, see the related June 7, 2006 *Federal Register* Notice (http://www.hhs.gov/ohrp/documents/20060707.pdf).

Please provide OHRP with a response to the above required actions and concerns by February 5, 2007.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please feel free to contact me should you have any questions.

Sincerely,

Kristina C. Borror, Ph.D.
Director
Division of Compliance Oversight

cc: Dr. Anne-Marie Broemeling, Director, Research & Evaluation, Strategic Information & Planning, Interior Health Authority
Ms. Susan Valley, Chair, Penticton Regional Hosp IRB
Ms. Beryl A, Ferguson, Chair, Interior Health Authority IRB
Commissioner, FDA
Dr. Joanne Less, FDA
Ms. Lou Valdez, OGHA
Dr. Sherry Mills, NIH
Dr. Joe Ellis, NIH
Dr. Ivor Pritchard, OHRP
Dr. Melody H. Lin, OHRP

Dr. Michael Carome, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP