



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Brent E. Wallace, M.D.
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Intermountain Health Care
36 S. State Street, 17th Floor
Salt Lake City, UT 84111

Re: Human Research Subject Protections Under Federalwide Assurance FWA-7905

Dear Dr. Wallace:

Thank you for your October 27, 2009 report in response to our September 24, 2009 request. We have evaluated the documentation provided by the Intermountain Health Care (IHC) to determine compliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46). Based on review of your response, we make the following determinations:

A. Determinations regarding your institution's system for protecting human subjects

- (1) HHS regulations at 45 CFR 46.116(c) and (d) require that the institutional review board (IRB) find and document specific criteria when approving waiver or alteration of some or all of the required elements of informed consent. We determine that the IHC IRB failed to satisfy these requirements for RMS ID 1010337 and RMS ID 1011258.

Corrective Action: We acknowledge your statement that revisions have been made to the IRB reviewer forms to ensure that the criteria are met and documented, and have provided a reminder to the IRB coordinators about ensuring the criteria are documented. We determine that these corrective actions adequately address our determination.

- (2) HHS regulations described 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 each of these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research. We determine that the minutes of some IHC IRB meetings did not include the number of members

voting for, against, and abstaining for some actions taken by the IRB. In specific, we note that the procedures (tab 6, page 76) indicate an acceptable format in which the IRB is to record the votes; however this specific format is not consistently used in the minutes for all of the IHC's IRBs. The January 15, 2009 South West Region (Dixie) IRB meeting minutes failed to indicate the number of members voting for, against, and abstaining on IRB actions taken at that meeting.

Corrective Action: We acknowledge your statement that in May 2009, the South West Region began using Intermountain's Research Management System to record the meeting minutes, which reminds the IRB coordinator to record the vote and that the South West Region IRB is now meeting the requirements of HHS regulations at 45 CFR 46.115(a)(2). We determine that these corrective actions adequately address our determination.

- (3) HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted by the IRB at intervals appropriate to the degree of risk, but not less than once per year. The regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval. Additionally, where the convened IRB specifies conditions for approval of a protocol that are to be verified as being satisfied by the IRB chairperson or another IRB member designated by the chairperson, continuing review must occur no later than one year after the date the protocol was reviewed by the convened IRB, not on the anniversary of the date the IRB chairperson or his or her designee verifies that IRB-specified conditions for approval have been satisfied.

We determine that the IRB failed to conduct continuing review of research at least once per year and that research was conducted during the lapse in approval in the following studies: 1007213, 1007225, 1007923, 1008185, 1008203, 1008547, 1009077, 1009080, 1009132, 1009501, 1008898, 1009542, 1009551, 1008930, 1008894, 1008726, 1006585, 1008880, and 1008891.

Corrective Action: We acknowledge your statement that IHC initiated an automatic notification process in which investigators are notified when their study is due for continuing review and that, on the day of expiration, investigators are informed that research activities must cease. We determine that these corrective actions adequately address our determination.

- (4) We determine that the written policies and procedures are not in sufficient detail to accurately describe the following IRB activities, as required by HHS regulations at 45 CFR 46.103(b)(4) and (5):
 - (a) reporting findings and actions to the institution;
 - (b) ensuring prompt reporting to the IRB of proposed changes in a research activity;

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- (c) ensuring prompt reporting to the appropriate institutional officials, the department or agency head and OHRP of any suspension or termination of IRB approval.

Corrective Action: We acknowledge your statement that written procedures for these activities are being drafted.

Required Action: By March 5, 2010 please provide our office with a copy of the final written procedures for these activities.

B. Questions and Concerns

[Redacted]

[Redacted]

C. Recommendations

We make the following recommendations regarding IHC's human subject protection program:

- (1) HHS regulations at 45 CFR 46.117(c) require specific findings on the part of the IRB for waiver of the requirements for the investigator to obtain a signed consent form from some or all subjects. We recommend that the IRB Reviewer Guide be revised to remind the reviewer that in circumstances where the IRB has approved a waiver of the requirements for documentation of informed consent on the basis that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality, each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.
- (2) The written procedures titled "Informed Consent Research Procedure" (pages 36-38) and "Informed Consent Research Documentation Policy" (page 39-41) seem to be confusing because they imply that the use of the short form is equivalent to oral consent. We note that use of a short form written consent document, in accordance with HHS regulations at 45 CFR 46.117(b)(2), constitutes documentation of informed consent, but "oral consent" requires waiver of the requirement for the investigator to obtain a signed consent form in accordance with HHS regulations at 45 CFR 46.117(c). We note the IHC procedures (section 5, page 40) of this section refer the reader to the requirements of the "Research Verbal Consent Guideline;" however, this could not be found in the documentation provided to us. We recommend these sections of the written procedures be revised to more clearly describe these different requirements.
- (3) We recommend that, for research undergoing initial or continuing review under an expedited review procedure, the IRB document the specific permissible categories justifying the expedited review. OHRP acknowledges that this is documented in the IRB

meeting minutes in some cases, but not all. OHRP acknowledges that IHC sometimes uses an “expedited review process” for activities that are considered exempt human subjects research or non-human subjects research; it is not necessary for unregulated activities to fall within a specific category of research when an “expedited review process” takes place for such unregulated activities.

- (4) We recommend enhancing IHC’s policies and procedures with the following suggestions and considerations (page numbers for Tab 6):
 - (a) We suggest modifying the “Informed Consent Research Elements Procedure” (pages 46-47) to include all elements of informed consent required by HHS regulations at 45 CFR 46.116(a). Specifically, the elements required by 45 CFR 46.116(a)(5)-(6) appear to be absent from the procedure. We also note the informed consent template (see page 62, Tab 7) does not include all of the required information for persons to contact as described in 45 CFR 46.116(a)(7). We therefore recommend that the policies on informed consent be expanded to include these required elements.
 - (b) We suggest modification of the contingent approval procedures outlined within the “IRB Committee Determinations Policy” (page 70) and “IRB Committee Determinations Procedure” (page 73). In order to approve research at a convened meeting, an IRB must determine that all criteria for approval of research under HHS regulations at 45 CFR 46.111 are satisfied. As previously noted, when the IRB at a convened meeting requests substantive clarifications or modifications regarding the protocol or informed consent documents that the IRB needs in order to make the determinations required by the IRB under HHS regulations at 45 CFR 46.111, IRB approval of the proposed research must be deferred, pending subsequent review by the convened IRB of responsive material, unless the research is eligible for review under an expedited review procedure.
 - (c) On page 71, the “IRB Committee Determinations Procedure” indicates that lapses in continuing review will be reported to OHRP. We note that we do not consider expiration of IRB approval to represent a suspension of IRB approval and such events therefore do not need to be reported to OHRP, unless the lapse of continuing review represents serious or continuing noncompliance with the requirements of 45 CFR part 46.
 - (d) We suggest modifying the “IRB Committee Determinations Procedure” (page 74) to identify which individuals or entities are notified whenever a study is disapproved by the IRB, or whenever there is a suspension or termination of IRB approval.
 - (e) Within the “IRB Committee Determinations Procedure” there is a discussion which describes the information which should be detailed in the minutes of IRB meetings for each protocol discussed. The procedures on page 76 (section 1.1.3 –

1.1.4) and page 77 (section 1.4.4) indicate the details that should be recorded in the minutes. Based on OHRP's review of the minutes, the IHC does not appear to follow the procedures consistently. We find the procedures acceptable; however, the minutes should more accurately reflect the procedures stated. In addition, we recommend that when the IRB reviews research involving (i) pregnant women, fetuses, or neonates, (ii) prisoners, or (iii) children, the IRB document the specific findings required on the part of the IRB under subparts B, C, or D, respectively, of 45 CFR part 46. Related to this, the "Research Involving Children Procedure" includes a statement (page 141, section 2.6.1) indicating that the IRB determination will include the category of permissible research and the corresponding rationale under which the proposed research qualifies. However, this type of information did not appear to be documented in the minutes of IRB meetings reviewed by us. We suggest including language in the procedure which indicates where this type of information will be documented, if it is done elsewhere, or make sure that the minutes of IRB meetings are complete.

- (f) Within the "IRB Committee Meeting Quorum Requirements Procedure," we recommend that the definition of a quorum (page 80) be modified to be more consistent with the requirements of HHS regulations at 45 CFR 46.108(b).
- (g) Within the "IRB Committee Meeting Quorum Requirements Procedure," there is a discussion on the process for handling conflicts of interests and recusals (page 81). We suggest that the procedure be expanded to describe voting procedures for these situations. We note that recused members may not count towards the total number of members present for the review for the purposes of determining a quorum. We also noted in the January 8, 2009 minutes of the Urban Central Region IRB meeting minutes that there was a recusal on RMS #1003580. The vote is recorded in the minutes as: Total =11; Vote: For-10, Opposed-0, Abstained-0, Recused-1; however the total number of members actually voting is 10, based on 1 recusal. We recommend changing the way the vote is recorded so that recused individuals are not counted in the total.
- (h) In the "IRB Continuing Review Policy," on page 86, IHC may wish to indicate that all materials are available to all IRB members when using a Primary Review system. IHC also may want to indicate what types of information and materials must be included in the status report discussed on page 87. In the discussion for determining the continuing review date on page 87, please check for typographical errors. In the example provided for establishing a continuing review date for items received to address contingencies, the January 4, 2004 date is incorrect – it should be January 3, 2008.
- (i) In the IRB Expedited Review Policy, we note that there are typographical errors in section 2.4.6 – 2.4.8. The wrong categories for expedited review are listed and this should be corrected to prevent errors in using the expedited review procedure.

- (j) On page 105 of the “IRB Jurisdiction Policy,” there is a definition for the term “agent.” OHRP considers the term “agent” to include individuals that are students or volunteers, and we suggest modifying IHC’s definition if students and volunteers conduct research activities under IHC’s Federal Wide Assurance (FWA). Also, on page 106, in section 1.5, there is a reference to “conditions in B” which appears to be a typographical error, as we could not find these conditions stated in the procedure.
- (k) Within the discussion on “Failure to Submit a Project for IRB Review” (page 106, in section 2.2), we suggest clarifying that an investigator should submit proposals involving non-exempt human subjects research to the IRB, regardless of intent to publish. The “intent to publish” should not be used as the sole criterion for determining whether an activity involves non-exempt human subjects research.
- (l) In the “IRB Reporting Policy” (page 108), we suggest IHC specify which reports must be sent to OHRP. The HHS regulations at 45 CFR 46.103(a) and (b)(5) require prompt reporting to the IRB, appropriate institutional officials, the department or agency head, and OHRP of any unanticipated problems involving risks to subjects or others, any serious or continuing noncompliance with 45 CFR 46 or the requirements or determinations of the IRB, and any suspension or termination of IRB approval.
- (m) In the “Research Administrative Hold Suspension Termination Policy,” page 116 in section 4, we suggest stating that all suspensions and terminations of IRB approval must be reported to OHRP.
- (n) In the “Research Assent Children Cognitively Impaired Adults Procedure” (page 120), there is a discussion of when informed consent, assent, and permission is needed. The procedures state that permission must be obtained from research participants who are cognitively impaired or lack decision-making capacity. Please note that for incompetent adults, as referred to in this section, informed consent (not permission) must be obtained from the subject or the subject’s legally authorized representative, unless the requirements for obtaining informed consent have been waived in accordance with the requirements of HHS regulations at 45 CFR 46.116(c) or (d).
- (o) In IHC’s “Research Human Subject Determination Policy,” (page 125), IHC may consider providing additional information about quality improvement activities (section 2.2.4). For example, some quality improvement activities may meet the criteria for human subjects research as defined by 45 CFR 46.102(d) and 45 CFR 46.102(f).
- (p) The “Research Injury Policy” states that all participants are provided with explanations as to whether compensation or medical treatments are available if injury occurs, what they consist of, and where further information may be obtained

(Item 1, on page 130). We suggest incorporating this type of information into informed consent templates.

- (q) In the “Research Involving Prisoners Policy” (page 155), please consider revisions to the IHC’s definition of a prisoner. The regulatory definition of a prisoner is described at 45 CFR 46.303(c), and OHRP’s current thinking on the use of ankle bracelets to monitor individuals would not necessarily make them a prisoner, unless the bracelet is also used to confine or detain the individual (see <http://www.hhs.gov/ohrp/prisonerfaq.html#q2>). Within this policy on prisoner research (page 156, section 3.4-3.5) OHRP notes that IHC may occasionally add a prisoner or prisoner representative to one of the IRB rosters. The prisoner representative must be a voting member of the IRB. On page 157, in section 4.3, there is a discussion that states that all research interventions and interactions and obtaining private identifiable information must cease if a subject becomes a prisoner in research that was not approved in accordance with the provisions of Subpart C. IHC may wish to clarify that an IRB may determine that a subject may continue to participate in the research, when the subject becomes a prisoner, if it in the best interests of the subject to do so, while the IRB reviews the research under Subpart C. On page 157, in section 5.3.2, clarify what is meant by the reference to “section 1.4.1 above” – this reference appears to be a typographical error. IHC may also wish to update the information on prisoner representative membership of the IRB in IHC’s policies on “IRB Committee Meeting Quorum Requirements” on page 80. For more information on research with prisoners, please refer to OHRP’s guidance on prisoner research, available at <http://www.hhs.gov/ohrp/humansubjects/guidance/prisoner.pdf> , and OHRP’s Frequently Asked Questions on Prisoner Research, located at <http://www.hhs.gov/ohrp/prisonerfaq.html>.
- (r) In the “Research Protocol Deviation Policy” (page 165, in section 2), there is a discussion of violations that must be reported to the IRB; however, the policy does not indicate if this is to be reported to the IRB chairperson or the IRB at a convened meeting. Please note that if protocol violations lead to implementation of changes which are more than minor, they must be reviewed by the IRB at a convened meeting.
- (5) We recommend IHC revision of the policies and procedures based on the following suggestions and considerations (page numbers for Tab 7):
- (a) We note that, on the RMS application shell (page 1), some of the project types identified as other than “human subjects” may actually also involve human subjects research depending on the circumstances of the project (e.g., “Data Only,” “Research Preparation Only Project,” Registry of Project for Publication Purposes,” “Case Study Project,” and “De-Identified Data Project from Existing Research Repository”).

- (b) In the RMS shell discussion on “Exempt Review” (page 6), we recommend adding a discussion to clarify that the exemptions do not apply to research involving prisoners [see footnote 46 CFR 46.101(i)] and that the exemption described at 45 CFR 46.101(b)(2) has limited applicability to research involving children [see 45 CFR 46.401(b)].
- (c) To the list of documents required for IRB review (page 14), we recommend including the application or proposal (e.g., Grant Application) as required by 45 CFR 46.103(f). IHC may wish to refer to our guidance on Review of Applications for HHS Support at: <http://www.hhs.gov/ohrp/humansubjects/guidance/aplrev.htm>.
- (d) We note that there is a series of questions in the section for “Waiver of Authorization” in the RMS application shell (page 25). We suggest adding an additional question which asks: “Why can’t you do the study without a waiver of informed consent?”
- (e) To page 28, consider requiring that the following items be included in status reports: (i) number of subjects that withdraw from the study; (ii) complaints; and (iii) new information regarding risks (e.g. publications, new findings).
- (f) We note that the child Assent Template (pages 78-79) is very brief. While this may be appropriate for very young children, we recommend creating a separate Assent Template that can be used when a child is close to the age of majority, which most likely would include the same type of information described in HHS regulations at 45 CFR 46.116(a) and, when appropriate, at 45 CFR 46.116(b).
- (g) We recommend modifying the “IHC IRB Checklist For Consent Document” (page 107) to reflect the changes discussed in this letter and include provisions for ensuring additional elements of informed consent are included, when appropriate, as described in 45 CFR 46.116(b).

We appreciate IHC’s continued commitment to the protection of human research subjects. Feel free to contact me if you would like guidance in responding to the questions and concerns or in developing corrective action plans.

Sincerely,

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

cc: Dr. Shelby A. Moench, IRB Administrator, Intermountain Health Care

Dr. Steven A. VanNorman, Chair, Intermountain Health Care IRB #1 & Intermountain Health Care Southwest Region IRB #2

Dr. Anthony Musci, Chair, Intermountain Healthcare Family LDS Hosp - Urban Central Region IRB #1

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