DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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September, 17, 2007

Albert L. Walker, Ed.D.
President
Bluefield State College
219 Rock Street
Bluefield, WV 24701

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 10457

Research Project:	Socio-Cultural Determinants of Utilization of Breast Cancer Awareness and Prevention Services Among African-American Women in Southern West Virginia (hereinafter referred to as the Breast Cancer Study)
Principal Investigator:	Anthony T. Woart, Ph.D.
Research Project:	Characterization of Molecular Diversity of HIV Sub-Types and Inter-Subtypes Recombinants Among African-Americans (hereinafter referred to as the HIV Study)
Principal Investigator:	Edward Omolo, Ph.D.
Research Project:	Identification of at Risk African-American Adolescents for Type 2 Diabetes and the Role of Screening in Early Detection (hereinafter referred to as the Type 2 Diabetes Study)
Principal Investigator:	Martha Eborall, Ph.D.
HHS Grant Number:	**RFA-MD-04-002/1R24 MD001107-01**

Dear Dr. Walker:

The Office for Human Research Protections (OHRP) has reviewed Bluefield State College's (BSC) August 3, 2007 letter that was submitted in response to a July 9, 2007 OHRP letter regarding the above-referenced research and BSC's system for protecting human subjects.

In its letter dated July 9, 2007, OHRP made the following determinations:

(1) OHRP found that prior to August 7, 2006, BSC engaged in non-exempt human subjects research under the above-referenced HHS grant award without submitting a written assurance to OHRP as required by HHS regulations at 45 CFR 46.103(a).

Corrective Action: BSC has adequately addressed this finding when it applied for and was awarded human subject assurance number FWA00010457 on August 7, 2006.

(2) OHRP found that BSC did not have a duly constituted, functioning IRB until Fall 2006 at the earliest, and that a BSC IRB did not conduct initial or continuing review of the above-referenced research prior to Fall 2006 at the earliest, in contravention of the requirements of HHS regulations at 45 CFR 46.103(b), 46.109(a), and 46.109(e).

OHRP notes that BSC has not taken any corrective action to address this finding. In specific, BSC has not provided OHRP with a revised IRB roster reflecting current IRB membership, in fact, BSC has not registered/updated its IRB roster with OHRP since November 2004. By way of background, during the June 15, 2007 videoconference OHRP learned that four (4) of the seven (7) individuals who were identified as BSC IRB members on the November 2004 IRB roster have never served on the BSC IRB. In addition, OHRP learned that one of the individuals identified as the BSC IRB chair on the November 2004 IRB roster did not serve as a BSC IRB member under Fall 2006.

Alternatively, BSC has not designated another IRB (established in accordance with the requirements of the regulations, and for which provisions are made for meeting space and sufficient staff to support the IRB review and recordkeeping duties) to review research falling under its assurance as permitted under HHS regulations at 45 CFR 46.103(b). According to the August 3, 2007 response letter, it appears that BSC is considering utilizing the services of another institutional review board to review research conducted under BSC's FWA.

Required Action: Please update with OHRP either the BSC IRB roster to reflect current IRB members, or the BSC FWA to designate another IRB to review research falling under the BSC FWA. Please note that either required action must occur prior to any further IRB review of non-exempt human subjects research to which the BSC FWA applies.

(3) OHRP found that the BSC IRB, which was constituted as of Fall 2006 and consisted of members appointed by you, did not include at least one member who is not otherwise affiliated with BSC and who is not part of the immediate family of a person who is affiliated with BSC as required by HHS regulations at 45 CFR 46.107(d).

Corrective Action: OHRP reviewed Section 3 of the Bluefield State College Institutional Review Board Policy, dated August 1, 2007 (hereinafter referred to as BSC IRB Policy) which references the requirements for IRB membership as outlined

in HHS regulations at 45 CFR 46.107. OHRP finds that this corrective action adequately addresses the finding noted above.

Required Action: If BSC intends to utilize its own IRB when reviewing research falling under its assurance, please update with OHRP the BSC IRB roster. Please ensure that the BCS IRB membership satisfies all of the criteria noted in HHS regulations at 45 CFR 46.107, including 45 CFR 46.107(d).

(4) OHRP found that the current BSC IRB Chairperson lacked a detailed understanding of the specific requirements of the HHS regulations for the protection of human subjects.

Corrective Action: OHRP reviewed Section 5 of the BSC IRB Policy. Please provide evidence that the current BSC IRB Chairperson has received the training outlined in this policy

(5) OHRP found that the revised Type 2 Diabetes informed consent documents failed to include certain basic elements required by HHS regulations at 45 CFR 46.116, including a statement that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled as required by HHS regulations at 45 CFR 46.116(a)(8). In addition, OHRP found exculpatory language in the Type 2 Diabetes Study informed consent documents in violation of 45 CFR 46.116.

Corrective Action: OHRP reviewed the two revised informed consent forms associated with the Type 2 Diabetes study, i.e., research subject information and consent form for adults (for subjects between the ages of 18 and 20) and research subject information and consent form for subjects that require parental consent (for the parents of subjects between the ages of 10 and 18) and finds that the revised forms continue to omit the following basic elements of informed consent as required by HHS regulations at 45 CFR 46.116(a):

(a) Section 46.116(a)(4): A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject. OHRP notes that subjects can consult their primary care physician to gain knowledge regarding Type 2 Diabetes risk factors, etc. in lieu of participating in the study.
(b) Section 46.116(a)(7): An explanation of whom to contact for answers to pertinent questions about research subjects' rights (should include someone other than the investigator).
(c) Section 46.116(a)(8): A statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.

Required Action: See item six (6) below.

(6) OHRP found that the informed consent documents for the Breast Cancer Study failed to include certain informed consent elements as required by HHS regulations at 45 CFR 46.116(a).

Corrective Action: OHRP reviewed the revised Breast Cancer Study informed consent form and finds that the revised form still fails to include the following elements as required by HHS regulations at 45 CFR 46.116(a):

(a) Section 46.116(a)(1): (i) A statement that the study involves research; and (iii) the expected duration of the subject's participation. OHRP notes that the informed consent form repeatedly refers to the Breast Cancer study as a program, not a research protocol.
(b) Section 46.116(a)(2): A description of any reasonably foreseeable risks and discomforts. OHRP notes that as designed, there appears that there is a risk of breach of confidentiality given that the research appears to include focus group sessions.
(c) Section 46.116(a)(4): A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject. OHRP notes that subjects can consult their primary care physician to gain knowledge regarding breast cancer risk factors, importance of early detection in lieu of participating in this study.
(d) Section 46.116(a)(7): An explanation of whom to contact for answers to pertinent questions about research subjects' rights (should include someone other than the investigator).
(e) Section 46.116(a)(8): A statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.

Required Actions:

(i) In light of these continued findings regarding IRB approval of informed consent documents failing to satisfy 45 CFR 46.116(a) requirements, please explain what steps, in addition to drafting Sections 10 and 11 of the BSC IRB Policy and creation of a BSC IRB Informed Consent Checklist, will BSC take to ensure that the BSC IRB only approves informed consent documents that contain the elements required under 45 CFR 46.116, unless informed consent or documentation of informed consent is appropriately waived by the IRB. While OHRP acknowledges that Sections 10 and 11 of the BSC IRB Policy and the BSC IRB Informed Consent Checklist were intended to provide guidance to BSC IRB members when reviewing informed consent documents, OHRP finds that these materials did not work as intended given that BSC provided OHRP with IRB approved revised informed consent documents that failed to contain all of the informed consent elements required under 45 CFR 46.116.
(ii) Provide a copy of the revised IRB-approved informed consent document(s) for the Breast Cancer Study.

(iii) Indicate what plans BSC has to contact subjects already enrolled in the Breast Cancer Study and provide them with the appropriate information required under HHS regulations at 45 CFR 46.116(a).

(iv) Provide OHRP with an explanation regarding the use of the phases "type 2 diabetes risk analysis and screening" and "blood test results" in the Breast Cancer Study informed consent form.

(7) OHRP found that that the BSC IRB lacked sufficient information, both at initial and continuing review, to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111. In addition, OHRP found that the BSC IRB failed to conduct substantive and meaningful continuing review of research, in specific, the Breast Cancer Study, at least once per year, as required by HHS regulations at 45 CFR 46.109(e).

Corrective Action: In its August 3, 2007 response letter, BSC referred OHRP to Sections 6.5 and 9 of the BSC IRB Policy. In addition, BSC provided OHRP with a revised human subject research application and an IRB reviewer checklist, both of which solicit information regarding IRB approval criteria outlined at HHS regulations 45 CFR 46.111. OHRP finds that these corrective actions adequately address the above referenced findings. OHRP acknowledges BSC's statement that these corrective actions "may be more fully addressed in the training and development of College constituencies when OHRP visits in September 2007."

(8) OHRP found no evidence that the BSC IRB made the findings required under HHS regulations at 45 CFR 46.404-407 when reviewing the Type 2 Diabetes Study, which involved children.

Corrective Action: OHRP acknowledges the corrective action detailed in its April 25, 2007 response letter. OHRP reviewed section 9.5 of the BSC IRB Policy. While this policy identifies the conditions under which child assent and parental permission(s) are required, this policy does not identify what criteria/conditions must be satisfied before an IRB can approve a specific category of research involving children. For instance, section 9.5 of the BSC IRB policy does not address the three conditions that must be satisfied before an IRB can approve research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. See 45 CFR 46.405. Moreover, OHRP notes that the BSC IRB policy does not address research involving wards of the state. See 45 CFR 46.409.

Required Action: Please provide OHRP with a corrective action outlining how BSC will ensure that human subjects research involving children will only be approved by the BSC IRB if the research satisfies all the criteria outlined in 45 CFR 46.404-409; not just child assent and parental permission criteria. For instance, in addition to revising section 9.5 of the BSC IRB policy, an appropriate corrective action might be for the BSC IRB to utilize a checklist to assist IRB members when reviewing research involving children/wards.

(9) OHRP found no documentation that the BSC IRB reviewed and approved protocol changes to the Breast Cancer Study, prior to initiation, as required by HHS regulations at 45 CFR 46.103(b)(4).

Corrective Action: OHRP acknowledges the corrective action detailed in the BSC April 25, 2007 response letter. OHRP finds that this corrective action and Section 6.7 of the BSC IRB Policy adequately address this finding.

(10) OHRP found no evidence that the BSC IRB reviewed the HHS grant application referenced above prior to the initiation of research, as required by HHS regulations at 45 CFR 46.103(f).

OHRP notes that BSC has not taken any corrective action to address this finding. OHRP reviewed the human subject research application and IRB policy and found that neither document addressed the review of HHS grant applications.

Required Action: Please provide OHRP with a corrective action outlining how BSC will ensure that the BSC IRB reviews HHS grant applications prior to the initiation of research, as required by HHS regulations at 45 CFR 46.103(f).

(11) OHRP found no evidence that BSC or the BSC IRB maintained the documentation of the BSC IRB's activities, as required by HHS regulations at 45 CFR 46.115(a).

Correction Action: OHRP reviewed sections 6.8 and 6.9 of the BSC IRB policy. OHRP finds that these sections adequately address the above-referenced finding.

(12) OHRP found that an IRB member who had a conflicting interest in the Breast Cancer Study participated in the BSC IRB 2006 continuing review of that study in violation of HHS regulations at 45 CFR 46.107(e).

Corrective Action: OHRP acknowledges the corrective action detailed in the BSC April 25, 2007 and August 3, 2007 response letters. OHRP finds that the corrective action noted in both response letters adequately addresses the above referenced finding.

(13) OHRP found that BSC did not have the following written IRB procedures, as required by HHS regulations at 45 CFR 46.103(b)(4) and (5):

(a) Procedures the IRB will follow for conducting its initial review of research.
(b) Procedures the IRB will follow for conducting its continuing review of research.
(c) Procedures 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.

Corrective Action: OHRP acknowledges the corrective action detailed in the BSC August 3, 2007 response letter, i.e., the drafting of new written IRB procedures and revision of previously drafted written IRB procedures as outlined in HHS regulations at 45 CFR 46.103(b)(4) and (5). OHRP finds that BSC still does not have written procedures adequately describing the following IRB activities:

(1) the procedures which the IRB will follow for reporting its findings and actions to the institution. While OHRP acknowledges that Section 13.1 of the BSC IRB Policy addresses the procedures the IRB will follow for reporting its determinations to the investigator, the BSC IRB Policy does not outline the procedures for reporting its findings and actions to the institution.

(2) 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 (hereinafter referred to as *unanticipated problems*);
(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 reviewed Sections 6.7, 6.10 and 7.4 of the BSC IRB Policy. OHRP finds that these sections still do not address the reporting of such events to appropriate institutional officials, any Department or Agency head, and OHRP.

Required Action: Please provide OHRP with revised written IRB procedures to address these activities.

OHRP has the following questions and concerns:

(14) [Redacted]

[Redacted]

(15) [Redacted]

(16) [Redacted]

(17) [Redacted]

OHRP has the following recommendations regarding the BSC IRB Policy Document:

(18) Section 12.1 of the BSC IRB Policy states, among other things, that full board review requires a majority of the membership of the IRB to be present. Please note that HHS regulations at 45 CFR 46.108(b) provides that an IRB shall review proposed research 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 nonscientific areas except when an expedited review procedure is used.

(19) Section 12.1 of the BSC IRB Policy states the following: "Members may participate electronically if necessary." HHS regulations at 45 CFR 46.108(b) provides that an IRB shall review proposed research 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 nonscientific areas except when an expedited review procedure is used. In order for the research to be approved, it shall receive the approval of **a majority of those members present at the meeting**. Please note that mail participation and vote, including participation and vote via email, do not satisfy the requirement that the IRB members be 'present' in the quorum/majority provisions outlined in HHS regulations at 45 CFR 46.108(b). However, telephone or videoconferencing participation and vote may satisfy the quorum/majority requirements if such participation is necessary and the members participating via telephone or videoconference have the same information and opportunity for discussion that the IRB members have who are physically present at the meeting.

At this time, OHRP acknowledges BSC's statement that "The College did misunderstand the usage of the Individual Investigator Agreement form and will no longer utilize that document in the human subject research application process."

In view of: (1) the new findings noted above; (2) OHRP determinations regarding inadequate corrective actions; and (3) the need to ensure adequate protections for human subjects, the Bluefield State College Assurance (FWA-10457) remains suspended pending satisfactory completion of the required actions described above.

As a result, all U.S. federally supported human subjects research projects to which the FWA applies remain suspended. Such suspension remains in effect until OHRP approval of the FWA is reinstated.

Please do not hesitate to contact me if you have any questions.

Sincerely,

Lisa A. Rooney, J.D.
Compliance Oversight Coordinator

cc: Dr. Tracey K. Anderson, Director of Institutional Research and Effectiveness, BSC
Dr. Anthony T. Woart, BSC
Dr. Lana Skirboll, OD, NIH
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