



DEPARTMENT OF HEALTH & HUMAN SERVICES

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: 240-453-8298

FAX: 240-453-6909

E-mail: [Lisa.Buchanan@HHS.gov](mailto:Lisa.Buchanan@HHS.gov)

April 12, 2012

Clyde L. Briant, Ph.D.  
Vice President for Research  
Office of the Vice President for Research  
Box 1937  
Brown University  
Providence, RI 02912

RE: Human Research Subject Protections under Federalwide Assurance FWA-4460

Dear Dr. Briant:

Thank you for your January 5, 2012 report in response to our November 29, 2011 request that Brown University respond to determinations, questions and concerns from our August 15-17, 2011 on-site evaluation of compliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

In our November 29, 2011 letter, we made the following determinations:

- 1) We determined that the institutional review board (IRB) lacked sufficient written policies and procedures as required by HHS regulations at 45 CFR 46.103(b)(4) and (5). We note that while the IRB utilized various submission forms, it did not have written procedures that outlined or described key operational details for each of the items listed in HHS regulations at 45 CFR 46.103(b)(4) and (5).

**Corrective Action:** We have reviewed the Brown University Human Research Protection Program (HRPP) Policy and Procedure Manual submitted with your response and note that it appropriately incorporates the key operational details required by HHS regulations at 45 CFR 46.103(b)(4) and (5). This corrective action adequately addresses our determination.

- 2) We also determined that for some studies, informed consent was waived without documenting the appropriate criteria required in HHS regulations at 45 CFR 46.116(c) or (d).

**Corrective Action:** According to your response, we note that the IRB has adopted use of the OHRP informed consent guidance document "Informed Consent Checklist (1998)", in order to ensure that the IRB find and documents specific, HHS required, criteria when approving a waiver or alteration of some or all of the required elements of informed consent. Further, IRB members and IRB staff received training on the use of the checklist including a review of (a) the elements of informed consent, (b) documentation of informed consent, (c) latitude to approve a consent procedure that alters or waives some or all of the elements of consent, and (d) special consent/assent requirements for children involved as research participants. This corrective action adequately addresses our determination.

- 3) Lastly, we determined that for at least two studies, the institution applied an exemption to research activities that exceeded the six categories listed under HHS regulations at 45 CFR 46.101(b).

**Corrective Action:** Per your response, we note that the IRB adopted the use of an exempt categories checklist that complies with the six categories listed under HHS regulations at 45 CFR 46.101(b) to ensure that the institution appropriately applies exempt determinations. IRB members and IRB staff received training on the use of the exempt checklist. This corrective action adequately addresses our determination.

#### A. Additional Determination

- 1) Based on our review of IRB records, the convened IRB approves research when additional information is needed to make determinations required under HHS regulations at 45 CFR 46.111. One example of this occurred in protocol #0512991954, titled "Group IPT for Women Prisoners with Co-morbid Substance Use and Depression." This research involved vulnerable subjects and was determined by the IRB to be greater than minimal risk. The convened IRB conditionally approved a modification (dated November 14, 2006) to enroll new group of subjects. However, according to the IRB meeting minutes, the IRB requested, among other things, information about how the new group of subjects would be identified and recruited, as well as how the study instrument would affect subjects. Sometime after the meeting, the investigator provided the requested information and the IRB manager reviewed the response and granted final approval.

Your January 5, 2012 response to OHRP's questions about this and other examples stated that "[t]he IRB outlines for [IRB] staff which issues need clarification, and for non-

substantive issues, the IRB identifies the responses they would find acceptable and they expect back from the PI.” In the example given above, the convened IRB did not see the additional information, and there was no indication in the IRB file or meeting minutes that the IRB identified what responses they would find acceptable or expected back from the PI.

Additional clarification provided in your email dated February 3, 2012, indicates that “email discussions between the PI and the IRB Manager document that the PI’s responses were discussed with the IRB prisoner advocate member for acceptability.” However, the IRB did not indicate that the PI’s response should go only to the prisoner advocate for review, nor did the IRB delineate clearly what parameters that the information must satisfy. We determine that the IRB approved research contingent upon substantive modifications or clarifications that were directly relevant to the determinations required by the IRB under HHS regulations at 45 CFR 46.111 without requiring additional review by the convened IRB.

**Required Action:** Please provide a plan that the IRB will use to ensure the it does not approve research contingent upon substantive modifications or clarifications that are directly relevant to the determinations required by the IRB under HHS regulations at 45 CFR 46.111 without requiring additional review by the convened IRB. For more information, please refer to OHRP’s Guidance on IRB Approval of Research with Conditions at (<http://www.hhs.gov/ohrp/policy/conditionalapproval2010.html>)

## B. Recommendation

- 1) We have reviewed the HRPP Policy and Procedure Manual provided with your response and we recommend that you add more step-by-step details regarding the operations of the IRB’s pre and post IRB meeting processes and how IRB meetings are managed. For example, your response points out that the “IRB outlines for RPO staff which issues need clarification, and for non-substantive issues, the IRB identifies the responses they would find acceptable and they expect back from the PI.” However, this kind of detail is not included in the IRB written procedures and was not apparent in the meeting minutes that we reviewed. Please refer to OHRP’s “Guidance on Written IRB Procedures” at <http://www.hhs.gov/ohrp/policy/irbgd107.html> for examples of the level of operational detail to include for each of the items listed in HHS regulations at 45 CFR 46.103(b)(4) and (5).

Please provide responses to the above determination by May 25, 2012, including a corrective action plan to address the determination. If you identify any additional areas of noncompliance, please describe corrective actions that you have taken or plan to take to address the noncompliance.

Dr. Briant — Brown University  
Page 4 of 4  
April 12, 2012

If you have any questions or need assistance in developing a corrective action plan, please feel free to contact us. We appreciate your institution's continued commitment to the protection of human research subjects.

Sincerely,

Lisa R. Buchanan, MAOM  
Compliance Oversight Coordinator  
Division of Compliance Oversight

cc:

Ms. Dorinda Williams, Human Protections Administrator  
Dr. Regina White, Associate Vice President for Research Administration  
Dr. Ronald Seifer, IRB Chairperson  
Dr. Brandon Krupp, IRB Vice Chairperson  
Dr. Margaret Hamburg, Commissioner, Food and Drug Administration  
Dr. Joanne Less, Food and Drug Administration  
Mr. Joseph Ellis, National Institutes of Health, Office of Extramural Research  
Dr. Sherry Mills, National Institutes of Health