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Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Bldg 51, Room 5356
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

October 28, 2009

Dear Dr.Prohaska:

I am writing you in regard to the certified letter (10-HFD-45-09-01), which the BRI IRB received on October 9, 2009. As Chairman of this Institutional Review Board, I express my sincere gratitude to Mr. Patrick Stone and your office for the thorough review of our procedures and for pointing out certain deficiencies that must be corrected. Accomplishing this goal will require changes in our Standard Operating Procedures (SOP's); and, the amendments to our SOP's will be discussed at our next regular Board meeting. This update will correct deficiencies pointed out in your letter and is intended to align our IRB procedures with Title 21 of the code of Federal Regulations (CFR), parts 50 and 56.

First, I accept the criticism that there is a discrepancy between the number of voting members in particular sessions (including those who did not excuse themselves because of potential conflicts of interest) and registered number of votes. In the future, the minutes will clearly note who did vote and who did not. In the particular cases that are referred to in your letter, it is more likely an error of our recording method, and not taking time to account for those who can vote and those who cannot vote. Care in the future will have to be taken to clarify "unanimous" (i.e., is it all voting members in the room, or voting members minus the chairman or someone leaving the room, or accidental inclusion of an invited

guest). In the future, anyone with a known or recognized potential conflict of interest will not serve as chairman of a session.

Re: (b) (4)

1. It is correct that the BRI IRB does not have SOP for conducting a device study to determine the safety of devices subject of review.

2. Nevertheless, when the (b) (4) study was discussed, we decided that a report on the device's safety by an independent professional engineer was needed; and, I immediately contacted the sponsor by phone. As a result, the inspection was conducted and a letter verifying its safety was received, and a copy of that letter is enclosed. (See Appendix 1)

3. The title of the original proposal was shortened to only (b) (4) because of an understanding that the conditions listed originally could not be unified in one study.

4. Although this study was never begun, the BRI IRB failed to request annual updates. We included this point in our updated SOP's; and, in the future approval letters will include a paragraph reminding the sponsor and principle investigator that annual reports will be required unless or until the IRB's relationship is terminated.

Re: Discussion of Protocol (b) (4)

1. Most, if not all, of the preliminary data presented were obtained in (b) (4) (or, by the PI) before initial contact with the BRI-IRB. At that time the IRB did not realize that considering data previously obtained overseas, or

by the PI, was in violation of the CFR 312.66. Steps are being taken to incorporate changes in our SOP's to prevent future occurrence.

2. The letter to (b) (4) of February 15, 2008 is clearly referenced to "Toxicity studies (b) (4), and the text further refers to these Animal Toxicity Studies. Thus, every use of the word "study" was intended to address the Animal Toxicity Study. (See Appendix 2)

3. The August 18, 2008 letter is addressed to (b) (4) (the sponsor) and carbon copied to (b) (4) (Principle Investigator). As you pointed out in your warning letter, the IRB clearly stated that the human study cannot be conducted without an approved IND. Furthermore, the letter begins in reference to: "(b) (4) Animal Toxicity." (See Appendix 3) Appendix 3 also includes (b) (4) response dated 9/04/08. Note that (b) (4) response is in reference to our letter to him dated 8/18/08 and which is in reference to Toxicity Studies for (b) (4) Also enclosed is the Investigator's Brochure – (b) (4)

4. I accept the criticism regarding the fact that we communicate in some instances with the principle investigator, but not with the sponsor. I plan to have this corrected, and clearly delineated in the revised SOP's.

5. On P. 2 -3rd complete paragraph of the warning letter "It is unclear why the IRB allowed the study..." We did not allow human studies to begin, rather we requested that the Animal Toxicity Studies continue. Human studies were not approved to go ahead—only Animal Toxicity Studies were allowed to continue. (See Appendices 2 and 3)

Re: Protocol: (b) (4)

1. Originally we were asked to review this protocol as a part of his quest for an IND to see if it could be "approved".

2. (b) (4) thought that such a potential approval would help them obtain an IND. We approved his protocol contingent upon his obtaining the IND. We were confident that he would not proceed without the IND; and we were aware that he was in discussions with the FDA on this very matter.

3. Since my letter dated April 2, 2009, annual updates have been requested for the protocols that are on hold. Because he has failed to receive an IND, (b) (4) does not wish pursue this project. I plan to request, at the next meeting of the BRI-IRB, that we close this protocol application. (b) (4) letter to me dated 09 October, 2009, is enclosed. (See Appendix 4) (Also included is the Investigator's Brochure).

It has become clear to the IRB during the FDA review, and subsequent correspondence, that the BRI-IRB must clearly separate its roles as (a) advisors to potential investigators/sponsors with respect to protocols and (b) the actual functioning as an IRB for a protocol(s).

Because the BRI-IRB functions independently it is, from time to time, approached by investigators outside of traditional venues like medical schools or university hospitals. In the past the IRB has provided information, advice and criticism to these investigators with respect to FDA requirements and more importantly what we, as an IRB would require of them should they choose to continue toward clinical studies.

Your criticisms and precise reading of our minutes and correspondence has made the imprecision and ambiguities in these materials abundantly clear. We will act immediately to correct this deficiency. First, our meeting agenda will clearly identify IRB studies which are ongoing as distinguished from protocols which are being developed. Those studies will be further characterized/labeled as "FDA IND – Request pending", "FDA IND – Request submitted", "FDA IND – Request denied or in discussion", and "FDA IND – Approved." Such labeling will remind and reinforce to our Board members that our role is minimal and limited to evaluating their IRB application until "FDA IND - Approved" status is achieved. Second, any correspondence with applicants will clearly identify our comments as limited strictly to elements of their application, as no human study can or should be initiated without IND status and final IRB approval.

After many years of interacting almost exclusively with the Burzynski Clinic, we were inadequate in attending to the demands of research in such early stages and sponsors lacking the Clinic's expertise in commencing IND human studies.

I again express my appreciation for the thorough examination of the BRI-IRB. Your examination has provided me with clear insight as to how we may improve our policies and alter our SOP's to align our operations in accord with the CFR.

Sincerely,

Carlton F. Hazlewood, Ph.D.
Chairman of the BRI-IRB

APPENDICES

I. (b) (4) letter dated 5/14/05

II. (b) (4) letter dated 2/15/08

III. A Letter t(b) (4) – c(b) (4) dated 8/18/08

III. B Includes(b) (4) response dated 9/4/08

III. C Investigator's Brochure (b) (4)

IV. A (b) (4) letter dated 10/9/09

IV. B Investigator's Brochure for(b) (4)