PROTOCOL APPROVAL WITH MODIFICATIONS

DATE: 21 Jan 2019

TO: Erin Bengelink
University of Michigan

PROTOCOL: National Institute of Neurological Disorders and Stroke, NIH - BOOST3, Brain Oxygen Optimization in Severe Traumatic Brain Injury - Phase 3 (BOOST-3): A multicenter, randomized, blinded-endpoint, comparative effectiveness study of goal-directed critical care based upon monitoring of brain tissue oxygen and intracranial pressure versus monitoring of intracranial pressure alone in patients with severe traumatic brain injury. (Pro00030585)

APPROVAL DATE: 12 Dec 2018

EXPIRATION DATE: 12 Dec 2019

IRB APPROVED DOCUMENTATION:

Protocol Version:

- Study Protocol (Version: Draft, DSMB Reviewed: 20 July 2018)

Consent Template:

- Informed Consent and Authorization Form (Advarra IRB Approved Version 14 Jan 2019)

Other Material:

- BOOST3 Community Line Script (Not Dated)
- Ad/Flyer/Poster (Dated)
- Brochure (Not Dated)
- Slide Set (Not Dated)
- Slide Set Reduced (Not Dated)
- Video Links (Not Dated)
- Video Scripts (Not Dated)
- BOOST3 Community Consultation Focus Groups Facilitator Guide (Not Dated)
- Dear Community Member Letter (Not Dated)
- Dear LAR Letter (Not Dated)
- Dear Dr. Letter (Not Dated)
- Meeting Recruitment Flyer (Not Dated)
- BOOST3 – Opt-Out Bracelet Form (Not Dated)
- BOOST3 – Online Opt-Out Bracelet Form (Not Dated)
- Bracelet Request Letter (Not Dated)
- BOOST3 public service announcement (Not Dated)

- Suggestions for Community Consultation Opportunities and Community Consultation Methods (Not Dated)
- Suggestions for Public Disclosure Opportunities and Public Disclosure Methods (Not Dated)
- Group Evaluation Survey (Not Dated)
- Self-Administered Survey (Not Dated)
- Telephone Script and Questions (Not Dated)
- YouTube Ad (Not Dated)
- Standard Operating Procedure Electronic Informed Consent (Not Dated)
- Illustrative example site CC report from a previous trial (Not Dated)
- Revised BOOST3 EFIC Plan (Version: Draft, 26 November 2018)
- eConsent Screenshots (Not Dated)
- Standard Operating Procedure Proposed EFIC ER-CIRB Review Process (Not Dated)
- Grant Number: 1U01NS099046-01A1 (Federal Award Date: 06/22/2018)
- Administrative Letter, Re: BOOST Forthcoming Biosamples Ancillary and Protocol Update (Dated 11 December 2018)

The IRB approved the above referenced protocol with the modifications listed below on 12 Dec 2018:

- Modifications to the BOOST3 EFIC Plan
- Modifications to the Informed Consent and Authorization Form
- Modifications to the BOOST3 Ad/Flyer/Poster
- Modifications to the Telephone Script and Questions

The IRB required the following modification on 4 Jan 2019:

- A document showing the subject's age (such as medical records, driver's license or learners permit, school identification card) must be used in the absence of the presence of a family member who can verify the age of the subject (note a "source" must be a family member, not just a friend/acquaintance with the subject at entry to the emergency room).

The following updated documents were submitted in response to the above IRB modifications:

- Revised BOOST3 EFIC Plan
- Suggestions for Public Disclosure Opportunities and Public Disclosure Methods
- Ad/Flyer/Poster
- Brochure
- Slide Set
- Slide Set Reduced

The above updated documents were reviewed and approved on 21 Jan 2019.

Additional revisions to the Informed Consent and Authorization Form were reviewed and approved on 14 Jan 2019.

> 6940 Columbia Gateway Dr., Suite 110 410-884-2900 OFFICE ADVARRA.COM
Columbia, MD 21046

Please Note: Each Principal Investigator will receive a separate IRB Approval notice allowing them to conduct the study and final approval of each site Informed Consent will be issued once the PI has submitted the results of the community consultations and made any needed changes to the ICF as a result of the feedback obtained during the community consultation process.

Please Note: Each site submission must include a summary of that site/PI's community consultation and public disclosure along with a summary of comments from those consultative methods, including but not limited to the EFIC protocol, for review by the IRB. Additionally, the summary should include:

- **A narrative of how the site feels they met the goals of the EFIC plan/community consultation process. These goals are specifically described in the EFIC plan under Goals of the Community Consultation section.**
- **Any recommendations for changes to the conduct of the study pursuant to their site level consultation process.**

The IRB reviewed the project in accordance with the 21 CFR Part 50, Subpart D Federal Regulations which provide for additional protections for children as research subjects.

The IRB determined that the research study meets the criteria found in the risk category described as follows:

- 21 CFR 50.52: "*Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects*." *Permission of one parent is required.*

A waiver of consent and/or parental permission and assent was approved under 21 CFR 50.24, Exception from informed consent requirements for emergency research.

The board acknowledged the IDE exempt status agreed to by the FDA.

The eConsent Screenshots and Standard Operating Procedure Proposed EFIC ER-CIRB Review Process are approved however the board requires the final version of the eConsent be submitted to the IRB for review (this may simply be a link to the eConsent) prior to use.

The above referenced material is available on your Advarra CIRBI Platform under the "IRB Issued Documents" tab.

If there are any changes to the IRB approved material, IRB approval will be needed prior to use. This includes changes in relative size and type of font in the material to be viewed by potential subjects.

If the study is expected to last beyond the approval period, you must request and receive re-approval prior to the expiration date noted above. A report to the Board on the status of this study is due prior to the expiration date or at the time the study closes, whichever is earlier. It is recommended that you submit status reports at least 4 weeks prior to your expiration date to avoid any additional fees or lapses in approval.

Approved investigators and sites are required to submit to Advarra for review, and await a response prior to implementing, any amendments or changes in: the protocol; advertisements or recruitment materials ("study-related materials"); investigators; or sites (primary and additional).

Approved investigators and sites are required to notify Advarra of the following reportable events, including, but not limited to: unanticipated problems involving risks to subjects or others; unanticipated adverse device

> 6940 Columbia Gateway Dr., Suite 110 410-884-2900 OFFICE ADVARRA.COM
Columbia, MD 21046

effects; protocol violations that may affect the subjects' rights, safety, or well-being and/or the completeness, accuracy and reliability of the study data; subject death; suspension of enrollment; or termination of the study.

Please review the IRB Handbook located in the "Reference Materials" section of Advarra CIRBI™ Platform (www.cirbi.net). A copy of the most recent IRB roster is also available. Thank you for selecting Advarra IRB to provide oversight for your research project.

> 6940 Columbia Gateway Dr., Suite 110
Columbia, MD 21046
410-884-2900 OFFICE
ADVARRA.COM