UNIVERSITY OF KENTUCKY
Center for Clinical and Translational Science (CCTS)

DATA SAFETY MONITORING BOARD (DSMB)

CHARTER

Version:	Approved by:
5 10/20/22	Lisa Tannock Digitally signed by Lisa Tannock Date: 2022.11.08 13:01:51 -05'00' **Lisa Tannock, MD** ***DSMB Chair***

TABLE OF CONTENTS

1. INTRODUCTION

The Charter defines the primary responsibilities of the Data Safety Monitoring Board (DSMB) for the Center for Clinical and Translational Science (CCTS), its membership, and the purpose and timing of its meetings. The Charter will also provide the procedures for ensuring confidentiality and proper communication, the statistical monitoring guidelines to be implemented by the DSMB, and an outline of the content of the Open and Closed Reports that will be provided to the DSMB.

2. PRIMARY RESPONSIBILITIES OF THE DSMB

The Data Safety Monitoring Board (DSMB) is established to conduct interim monitoring, oversight and analysis of study information and data. Its purpose is to assure the safety of research participants, efficacy and appropriateness of study procedures, relevance of the study questions, and integrity of the accumulating data throughout the life of a research project.

The direct responsibilities of the DSMB include:

- Initial review of the proposed research protocol, informed consent documents, data collection instruments and plans for data safety and monitoring;
- A discussion of regulatory issues, when appropriate;
- Evaluation of the progress of the study, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of the study site, and other factors that can affect study outcome;
- Review of reports from Quality Assurance audits;
- Review adverse events (AEs), protocol deviations/ violations, subject withdrawals, and protocol amendments;
- Review of study performance, making recommendations and assisting in the resolution of problems reported by the Principal Investigator;
- Protecting the safety of study participants;
- Reporting to the Principal Investigator on the safety and progress of the study;
- Making recommendations to the Principal Investigator concerning continuation, termination or other modifications of the study based on the observed beneficial or adverse effects of the treatment under study;
- Ensuring the confidentiality of the study data and the results of monitoring;
- Assisting the Principal Investigator in the resolution of problems with study conduct, enrollment, sample size, and/or data collection.
- Future use/ privacy information? From ICF template in eIRB (requested by GD)

- For multi-site studies with the University of Kentucky identified as the lead study site, the DSMB will take the role of main DSMB for the study, providing a review of data for all sites (for multi-site studies where another institution is the lead site the DSMB will only review local site data).

The DSMB will be advisory to the Principal Investigator, hereafter referred to as the PI. The PI will be responsible to promptly review the DSMB recommendations, to decide whether to continue or terminate the study, and to determine whether amendments to the protocol or changes in study conduct are required.

The DSMB's role does not necessarily end when the enrollment ends. The DSMB should continue to review summaries of safety data by treatment group at regular DSMB meetings (local IRB will be notified of the results of these reviews) until either safety follow-up ends or another entity assumes this responsibility.

The DSMB will have neither a role in, nor responsibilities for, final analyses and preparation of manuscripts for publication.

3. MEMBERSHIP OF THE DSMB

3.1 Members

The DSMB is an independent multidisciplinary group with clinical research experience representing relevant specialties. This group will include a DSMB Chairperson, Research Subject Advocate (RSA) who is a Physician, a Pharmacist, a Physician with active clinical practice, Statistician, CCTS Representatives and DSMB Coordinator. There are 4 voting members including the Chairperson, Pharmacist, Physician, and Statistician. The CCTS Representative and DSMB Coordinator are non-voting members.

Ad-hoc members may be added when experience in specific disease areas or procedures is required. This can be an internal UK employee or could be from another institution if the needed expertise is not available.

Alternate members are available as needed should a regular DSMB member be unable to attend a meeting or is conflicted on a study. It is the responsibility of the DSMB member to notify the DSMB Coordinator if they are unable to attend a scheduled meeting or are in conflict on any protocols being reviewed so that an alternate can be scheduled to take their place.

3.2 Membership Terms

Membership in the CCTS DSMB will be limited to three (3) year terms for regular and alternate members. The 3-year term is automatically renewable if the member wishes to extend their membership. Ad hoc members will remain for the length of the study for which they are providing specialized experience. Term limits will not apply to CCTS representatives or the DSMB Coordinator.

3.3 Conflicts of Interest

DSMB Members serving as voting members must disclose any potential conflicts of interest, whether real or perceived, to the Principal Investigator and all DSMB members. This applies to regular, alternate and/or ad hoc members. Conflict of interest can include financial interest, professional interest, intellectual interests, proprietary interest, service on other DSMBs, related or competing products, and miscellaneous interest. All potential conflicts that develop during a member's tenure on the DSMB must also be disclosed. Written documentation attesting to the conflict of interest is required either through a written statement or documentation in the meeting minutes that the conflict was addressed. In the event that a DSMB member's conflict of interest status changes they must notify the DSMB chair immediately and an alternate will be identified.

~~4.~~ FREQUENCY AND TYPES OF DSMB REVIEW

4. 1 Frequency of Review

The DSMB will have scheduled meetings at least three times a year. The frequency of DSMB meetings is dependent upon the nature and risk of the studies to be monitored. DSMB meetings can be scheduled on an as-needed basis to address the needs of specific protocols. Meetings can occur as convened meetings or via email. The DSMB chair has the authority to determine the type of meeting necessary for additional review.

4.2 Intake and Acceptance of DSMB Review

For a study to be accepted for CCTS DSMB review, a Principal Investigator must complete a Service Request Form on the CCTS/ CRSO website, and upload a copy of their protocol, IRB approval letter and other pertinent study documents (as available). The request will then be routed to the DSMB Coordinator. The DSMB Coordinator will forward these documents to the DSMB Chair for review. The DSMB chair will communicate with the DSMB Coordinator regarding the acceptance of the study for DSMB review. Due to volume of requests only studies using other CCTS services in addition to DSMB will be considered. Additional factors considered

when evaluating a study for acceptance includes evidence of clear necessity for a DSMB, the volume of current studies, the scope of the study, available expertise on the DSMB or through ad hoc members, and additional considerations as needed. If the study is accepted for CCTS DSMB review, the DSMB Coordinator will add the study to the next available DSMB agenda . The DSMB Coordinator will notify the PI and study team of the study's acceptance for DSMB review and the date/time of the DSMB meeting.

4.3 Types of Review
The types of DSMB review include the following:

Initial Review
The initial review is generally conducted during a regularly scheduled DSMB meeting, but may be scheduled as a separate meeting if circumstances necessitate an expedited initial review. The initial review can be done via email or at a convened DSMB meeting.

This initial review does not constitute participation in trial design, which would compromise the independence of the DSMB. Rather it gives the DSMB an opportunity to communicate to the study PI that it cannot take responsibility for oversight unless issues and concerns related to Data and Safety Monitoring are addressed. In this case, the DSMB will provide the PI with a comprehensive list of specific issues that need to be resolved before assuming oversight responsibilities.

Interim Monitoring Review
The Interim monitoring review is conducted during a regularly scheduled DSMB meeting, and reviews the study's progress from initiation through study close. During this review, the DSMB reviews the following:

- Study Abstract
- IRB Submission Log
- Study Overview
- Adverse Event Summary Log
    - When the University of Kentucky study site is listed as the lead study site, all study sites will follow UK IRB AE/SAE reporting requirements
    - *Note: Listings of adverse events and serious adverse events as well as any other information requested by the DSMB should not be presented in an unblinded manner.*
- Protocol Violation Summary Log
- Withdrawal Log
- Other pertinent updates from the study team as necessary

Email Review

When circumstances arise that prevent the DSMB from a convened meeting, meeting materials can be emailed to members to review and vote accordingly.

Study Inactivation Review

Once the study has closed to enrollment and any corresponding follow-up activities have been completed, PI's will be given the option to inactivate DSMB review.

A study can be inactivated by the PI provided that the following conditions have been met:

- Study is closed to enrollment
- Any corresponding follow-up activities are complete
- 30 days of more have passed since completion of follow-up activities

The PI must submit a written request for inactivation confirming that the conditions for inactivation, as provided above, have been met. The PI will not be required to attend a DSMB meeting to request inactivation.

Additionally, the DSMB Chair may choose to inactivate a study if the PI has not enrolled any subjects after 3 consecutive DSMB reviews (approximately one year).

If the review requires re-activation, the Principal Investigator must provide a written request to the DSMB including the circumstances for the re-activation. The PI or study team will not be required to attend a DSMB meeting to request study inactivation or reactivation.

Study Closure

Documentation of study closure with the IRB must be provided by the Principal Investigator to the DSMB upon receipt from the IRB. The PI or study team will not be required to attend a DSMB meeting to request study closure.

Adverse Event Reporting

The DSMB Chair will be the contact person for serious adverse event reporting. The PI or study team should report all serious adverse events to the DSMB Coordinator, who will forward this information to the DSMB Chair for review.

Expedited Review

An Expedited review may be held to review minor changes in previously approved research. Expedited review is performed by the DSMB chair or designee.

Emergency Meetings

An emergency meeting of the DSMB may be called at any time by the Chair.

5. DSMB Review Format

5.1 Procedures to ensure confidentiality and proper communication

Procedures will be implemented to ensure proper communication is achieved between the DSMB and the PI. To provide a forum for exchange of information among various parties to ensure the successful conduct of the studies, a format for Open Sessions and Closed Sessions will be implemented. The intent of this format is to enable the DSMB to preserve confidentiality of the studies being reviewed while at the same time providing opportunities for interaction between the DSMB and the PI who has valuable insight into study-related issues.

5.2 Meeting Format

Meetings will be held via conference call, email or face-to-face. The PI or appointed designee must be present at the meeting or available via conference call for those DSMB meetings that review his/her protocol. For interim reviews, if a PI has no data to report then neither he nor their appointed designee need to attend the meeting.

Meetings will consist of two types of sessions. Not all types will be needed at every meeting. The DSMB meetings can consist of open or closed sessions. The clinical study team, at the request of the DSMB, will be asked to attend the open sessions.

5.3 Open Session

Discussion during the **open session** will focus on the conduct and progress of the study including, but not limited to: compliance with protocol, participant accrual, drop-out rates, protocol violations, patient safety and adverse events, inclusion/exclusion requirements and problems encountered. Unblinded data will not be presented in the open session.

5.4 Closed Session

The **closed session** will be held following the open session to present comparative outcome data and to identify and discuss the DSMB's recommendations for the PI. Data presented in the closed session may include un-blinded information.

5.5 Recommendations

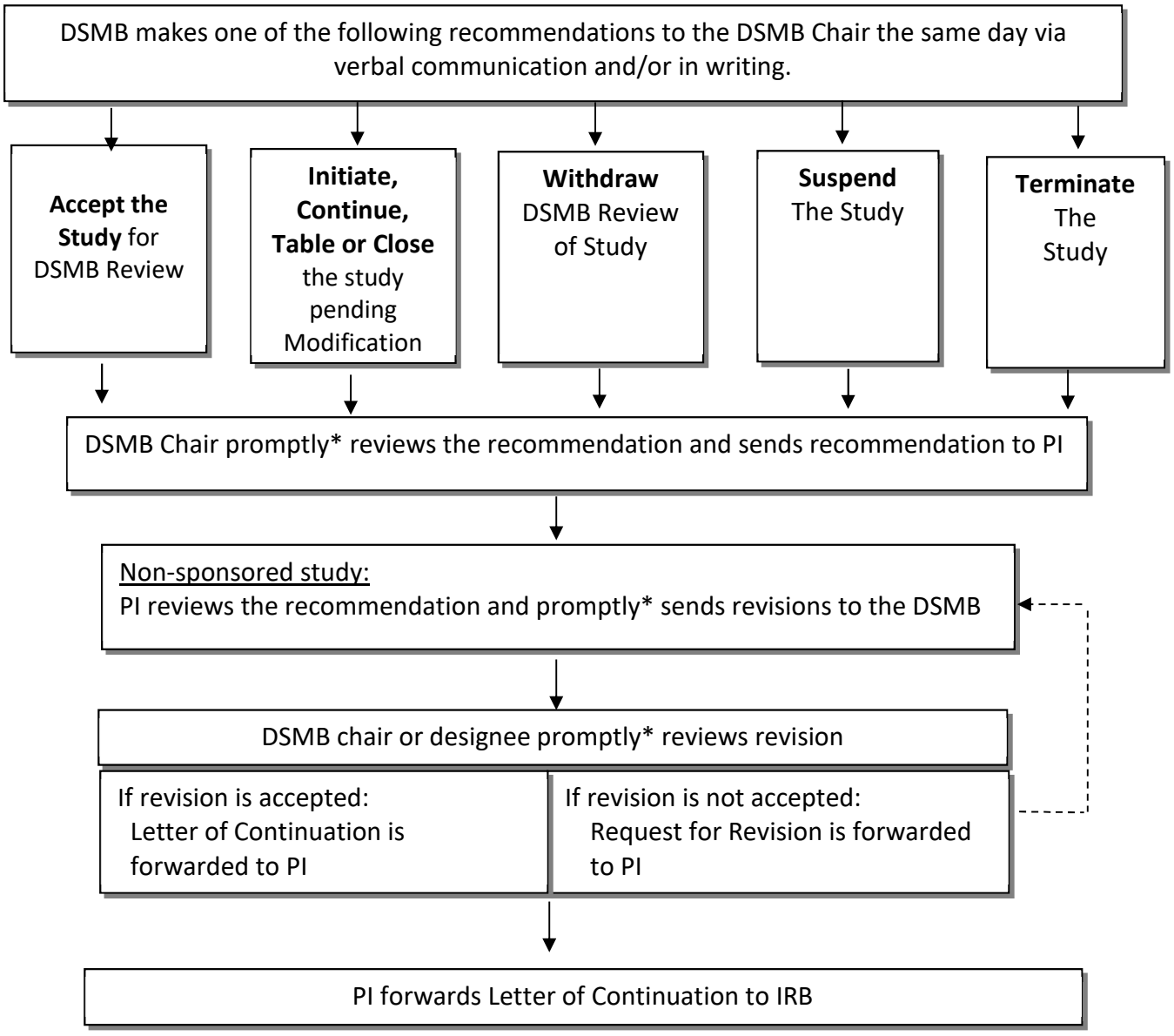
Each DSMB meeting will include a recommendation regarding study continuation. One of the following actions, appropriate to study status, will be recommended upon completion of the DSMB review.

- Accept the study for review as originally designed, in accordance with the protocol and any amendments.
- Initiate/Continue/Close the study as originally designed, in accordance with the protocol and any amendments.
- Initiate/Continue/Close the study with modification - minor changes to the study protocol (modifications may include, but are not limited to, changes in entry criteria, frequency of visits or monitoring, and alterations in study procedures), updates to the data submitted to the DSMB and/or additional information required. If the DSMB's recommendations require significant changes or follow-up, DSMB staff in collaboration with the DSMB chair will prepare an action plan outlining the steps required to implement the recommendations. *In the case of a vote for study continuation with modification or additional information required, the UK CCTS DSMB has given the individual chairing the meeting the authority to approve the minor revisions which do not involve substantive issues.*
- Table review of the study pending additional information, prior to making a recommendation.
- Withdrawal of **DSMB** review – upon review, it may be determined that DSMB review is not needed, (ex.: another body will provide a DSMB to review the study, study is low risk and does not require DSMB review).
- Terminate the study - The study should be terminated

5.6 DSMB Action and Recommendation Diagram

The following diagram shows the action to be taken upon PI receipt of a DSMB review recommendation.

Actions upon receipt of a DSMB recommendation



** Taking into consideration recommendations and circumstances. Critical information is expected to be communicated as timely as possible.*

5.7 Voting

The above recommendations are made by a formal DSMB majority vote. In order to vote on a recommendation during a meeting a quorum of 3 voting members must be present or submit their review and vote via email.

E-mail voting will be acceptable. In the event of a split vote, majority vote will rule. In the event of a 50-50 split vote, the DSMB Chair provides the tie breaker.

A recommendation for immediate suspension of a study may be made by the DSMB at any time by majority vote. The Chair should transmit such a recommendation to the DSMB Coordinator (DC) and PI immediately.

5.8 Meeting Materials

A request for data will be sent to the study staff no later than one month prior to the scheduled CCTS DSMB meeting date.

The DSMB report describing the status of the study should be prepared by study staff and submitted to the DSMB Coordinator at least two weeks prior to the meeting for immediate distribution to the DSMB. The DSMB Coordinator will distribute the reports to the DSMB members via SharePoint. If the report is not received within 2 weeks prior to the meeting the PI will receive notice that the study will not be reviewed during the DSMB meeting and will be paused until the study can be reviewed. The DSMB will notify the IRB of the pause.

5.9 Meeting Minutes

The DSMB Coordinator will prepare meeting minutes for review and approval by the Chair. Once approved by the Chair, the DSMB Coordinator will send the minutes to the full DSMB. Comments from DSMB members will be obtained and meeting minutes finalized no later than 30 days after the meeting.

6. STATISTICAL MONITORING GUIDELINES

The purpose of each review meeting is to safeguard subjects against excess harm related to treatment. The total number adverse events will be presented to the DSMB by the study group. If interim stopping rules are part of the protocol, the statistical monitoring will include a review of the primary endpoint for early stopping due to efficacy and/or futility provided the monitoring occurs at agreed upon time intervals in the study. Plans for interim analyses should

be established at the initial DSMB meeting, although changes throughout the study may be requested by the DSMB.

7. CONTENT OF THE DSMB'S OPEN AND CLOSED REPORTS

The information provided for interim DSMB review is available on the CCTS DSMB website (https://www.ccts.uky.edu/services-resources-researchers/data-safety-monitoring-board) as template tools for the study team to utilize in their report preparation. The DSMB may request modifications to the reports as the study progresses.

8. RECORDS

One set of paper copies of a documentation reviewed during each meeting (review reports, meeting minutes, and follow-up documentation, etc.) is maintained in the CCTS regulatory office. Electronic reports for each study as well as an electronic meeting minutes are maintained in a secure CCTS shared drive. Records are maintained for a minimum of 6 years after the study has been closed.

9. REFERENCES

- University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures SOP #: 3-7 Revision #: 5 Data and Safety Monitoring Plan
- FDA Guidance for Clinical Trial Sponsors

  Establishment and Operation of Clinical Trial Data Monitoring Committees- March 2006 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/establishment-and-operation-clinical-trial-data-monitoring-committees
- NIDA (National Institute for Drug Abuse):
  Guidelines for Developing a Data and Safety Monitoring Plan – October 2018
  https://nida.nih.gov/research/clinical-research/guidelines-developing-data-safety-monitoring
- NIH Policy for data and Safety Monitoring – September 2020

  https://osp.od.nih.gov/clinical-research/nih-data-and-safety-monitoring-policies/
- Further guidance on a data and safety monitoring for phase I and Phase II trials, release date June 5, 2000
  http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

Attachment A

DSMB Members

DSMB Chair

Department: Internal Medicine - Endocrinology

Lisa R. Tannock, M.D.
900 South Limestone
567 C.T. Wethington Building
Lexington, KY 40536-0200
Research Subject Advocate (RSA)

Phone: 859-323-4933 x81415

email: lisa.tannock@uky.edu

DSMB Members (Voting)

Department: Pediatrics - Endocrinology and Metabolism

Kathryn Thrailkill, MD
2195 Harrodsburg Rd., Suite 125, Room #T2092
Lexington, KY 40504
Physician with Active Clinical Practice

Phone: 859-323-6481

email: kathryn.thrailkill@uky.edu

Department: Pharmacy Practice and Science

George Davis, PharmD
800 Rose St., Rm H871 Pavilion (A)
Lexington, KY 40536
Pharmacist

Phone: 859-323-1789
Fax: 859-323-2049
email: georgedavis@uky.edu

Department: Biostatistics, Public Health

Philip Westgate, PhD
725 Rose Street, Rm 205B
Lexington, KY 40536-0082
Statistician

Phone: 859-218-2018

email: philip.westgate@uky.edu

Dick Kryscio, PhD
Rm 230 Sanders-Brown Center on Aging
800 Limestone Street
Lexington, KY 40536-0230
Statistician

Phone: 859-257-4064 x 295

email: richard.kryscio@.uky.edu

DSMB Members (Non-voting)

Center for Clinical and Translational Science
Denece Forenback, RN Phone: 859-323-6481
800 Rose St., Rm N503 Pavilion (H)
Lexington, KY 40536-0293 email: denece.forenback@uky.edu
CCTS Representative

DSMB Alternate Members (Voting)

Department: Biostatistics, College of Public Health
Heather Bush Phone: 859-218-2080
725 Rose Street
Lexington, KY 40536 email: heather.bush@uky.edu

Department: Microbiology, Immunology & Molecular Genetics
James Z Porterfield, MD, PhD Phone: 859-323-6689
MN 378
Medical Science Building email: zach.porterfield@uky.edu
Lexington, KY 40508

Department: Pharmacy Practice and Science
Kristina Naseman, PharmD, MPH Phone: 859-323-8697
1000 S. Limestone St.
MN 524 email: kristina.naseman@uky.edu
Lexington, KY 40536

Attachment B

DSMB Member Charter Agreement

I have read the CCTS Data Safety Monitoring Board (DSMB) Charter. I agree to conduct the data monitoring process for all trials that I review as stipulated in the CCTS Data Safety Monitoring Board (DSMB) Charter.

I understand that individuals invited to serve on the DSMB as either voting or non-voting members must disclose any potential conflicts of interest, whether real or perceived, to the Principal Investigator and UK CCTS. Conflict of interest can include professional interest, proprietary interest, and miscellaneous interest. Potential conflicts that develop during a member's tenure on a DSMB must also be disclosed and may require a DSMB member to recuse themselves as determined by the CCTS in consultation with the remaining uninvolved members of the DSMB.

I will notify the UK CCTS DSMB Chair promptly if a change occurs in any of the above that may affect my objectivity. In such an event, I will abstain from participation in the Board until instructed otherwise by the UK CCTS DSMB Chair. When in doubt, I will seek a determination from the UK CCTS DSMB Chair.

DSMB Member Name (Printed)

_____ _____

DSMB Member Signature Date

Attachment C

DSMB Study Status Definitions

Active:

- Open to enrollment AND/OR
- Actively following subjects for data collection AND/OR
- Actively performing research-specific procedures

Inactive:

- Closed to enrollment AND
- Any corresponding follow-up activities are complete (research procedures) AND
- 30 days or more have passed since the completion of follow-up activities

Closed:

- All data collection/ analysis is complete AND
- Study is closed with IRB (closure letter from IRB is required)

Attachment D

DSMB Charter Revision History

Version	Revised From:	By:
5	**Removed ad hoc members from listing**	
	Revised To:	**EAH** 10/20/22 *Initial* *Date*
	Include term limits for members, include DSMB suspension if report data is not submitted, include DSMB study status definitions	
	Add Philip Westgate, Porterfield and Naseman	
Version	**Revised From:**	**By:**
4	**Pharmacist: Wermeling, Carrico**	
	Revised To: Pharmacist: Davis **Alternates for all positions added:** **K. Thrailkill, G. Supinski, E. Hahn, H. Bush, G. Wells** **L. Rice position changed to CCTS representative (non-voting)**	**RB** **07/17/15** *Initial* *Date*

	General revisions	
Version	**Revised From:**	**By:**
3	**Delete R. Means**	**RB** *Initial* **01/15/14** *Date*
	Revised To:	
	Add L. Tannock and J. Carrico, Add Initial Expedited review, Update address for V. Adams	
Version	**Revised From:**	**By:**
2	**Chair: Kramen**	**RB** *Initial* **06/08/12** *Date*
	Revised To:	
	Chair: Means, added Expedited Review, PI to forward final DSMB report to IRB	
Version	**Revised From:**	**By:**
1	**N/A – initial release**	**RB** *Initial* **10/14/10** *Date*
	Revised To:	
	N/A	