The Christ Hospital IRB
Submitted By: Erica Jones, CIP
Reviewed By: Steve Roberts, MD
Approved By: Steve Roberts, MD
(II.3.B, III.2.D)

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STANDARD OPERATING PROCEDURE

Data and Safety Monitoring for Human Subjects Research

POLICY:

It is The Christ Hospital's policy that all human subjects research involving greater than minimal risk incorporates an appropriate data monitoring plan for the safety of subjects. The Christ Hospital Institutional Review Board (TCH IRB) will determine whether the research plan makes adequate provisions for monitoring the data collected to provide for the safety of subjects during initial review, continuing review, and review of modifications to research. The monitoring should be described as part of the research protocol, and be summarized in the e-application**.** A statement should describe the timelines of reporting of the monitored data and the routing of these reports to investigators and TCH IRB. Depending on the extent and severity of expected harms in a research study, the monitoring plan should include provisions to determine whether the character, incidence, and severity of harms match expected harms and should describe the stages of research at which monitoring will occur (e.g., specific points in time, after a specific number of subjects have been recruited, upon recognition of harms). Monitoring may be conducted by investigators themselves, a medical monitor, a data and safety monitoring committee, or other appropriate mechanism for the research activity.

PROCEDURE

INVESTIGATOR:

- Outlines in the initial e-application the Data and Safety Monitoring Plan (DSMP) to indicate how safety will be monitored. If a Data and Safety Monitoring Board (DSMB) will monitor the study, detail should be provide regarding how it is comprised, how often it will meet and who will get the DSMB report. (Note: Phase III federally funded trials require a DSMB.)
- Includes the following information at the time of continuing review:
  - Copies of all data and safety monitoring reports since the last review if not previously submitted;
  - Summaries of all reportable events and/or unanticipated problems involving risks to subjects or others (UAP)
- Submits any alteration to the Data and Safety Monitoring Plan (DSMP) to the IRB by using amendment procedures. (See SOP 2.03, Proposed Amendments or Modifications in Previously Approved Research Studies.)

IRB CHAIR:

- At the time of initial review:
  - Reviews and verifies that each study application and protocol submission contains sufficient information on data and safety monitoring to permit IRB review;
  - Checks whether the submission is a Phase III federally funded—if so, ensures a DSMB is included for data and safety monitoring;
  - Requests additional information to supplement the study application or protocol if it does not adequately address the DSMP;
  - Provides additional assistance to investigators when the research plan does not adequately address the DSMP.
- At the time of continuing review:
  - Reviews continuing review report, including copies of data and safety monitoring reports received since the last IRB review;
  - Reviews continuing review report, including summary of all reportable events and unanticipated problems that have occurred since the last review.
- Receives and reviews any modifications for any changes to the DSMP (See SOP 2.03, Proposed Modifications/Amendments in Previously Approved Research Studies);
- Receives and reviews data and safety monitoring reports for completeness;
- Receives and reviews all reportable adverse events and unanticipated problems. (See SOP 2.05, Reporting Unanticipated Problems Involving Risks to Participants or Others.)
- Refers reports for convened IRB review, as necessary.
- Reviews and prepares to present at the time of initial review:
  - DSMP in relation to the size, complexity, and level of risk for the research being performed;
  - Whether the following criteria are met for imposing DSMP requirement:
    - Phase III federally funded study; or
    - Large study population;
    - Multiple study sites when investigators enroll small fractions of the participants separately;
    - Highly toxic therapies or dangerous procedures (e.g., gene therapy or gene transfer);
    - High expected rates of morbidity or mortality;
    - High chance of early termination (e.g., early stopping rules for significant evidence of benefit or harm).
  - If the above criteria are not met, whether the following additional criteria are met for monitoring either by the investigator or independent individual(s):
    - Low risk;
    - Continuous, close monitoring with prompt reporting of toxicity information to IRB, FDA, and sponsor (e.g., Pilot, Phase I or II studies).
  - Areas of expertise (e.g., experienced clinician, biostatistician, ethicist), relationship to study (i.e., internal, external, independent) and qualifications of individuals(s) performing the monitoring relative to the research being conducted;

- Summary of the oversight activities (e.g., timing or basis of interim analyses, endpoints, stopping rules, reporting mechanisms to oversight bodies, adverse event and unanticipated problem reporting);
- Whether the plan incorporates policy and procedures for reportable events and unanticipated problems.

- Reviews and presents to the IRB at the time of continuing review:
  - Data and safety monitoring information received since the last review;
  - Summary of all reportable events and unanticipated problems that have occurred during the trial;
  - Whether the DSMP remains adequate and appropriate in relation to the size, complexity, and level of risk for the research being performed.

The IRB:

At the time of initial review and after presentation by the PI or designee:

- Discusses and determines whether the DSMP is adequate based on the following criteria:
  - Description and qualifications of the monitor(s);
  - Timing or basis of interim analyses, if any;
  - Endpoints and stopping rules, if any;
  - Reporting mechanisms to federal agencies, sponsor, and IRB (*Note: Data and safety monitoring reports and communications must be forwarded to the IRB within 10 working days of receipt by the investigator*.);
  - Protocol-specific plans for reporting adverse events to the sponsor and FDA if applicable;
- Makes recommendations for additional enhancements for the safety and welfare of the participants involved in the research, including independent monitoring, if criteria are not met;
- Requests additional information, as deemed necessary, if criteria are not met.
- When participants withdraw from a clinical trial, the IRB determines:
  - When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.
  - A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.
  - The researcher must obtain the participant’s consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.
  - If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the

researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

At the time of continuing review:

- Discusses data and safety monitoring information received since the last review;
- Discusses summary of all reportable events and unanticipated problems that have occurred during the trial;
- Determines whether the DSMP remains adequate;
- Receives and reviews data and safety monitoring reports when referred by the Chair.