The PEPPER Trial – Ancillary Science Advisory Committee

Guidelines for Proposals Involving Secondary Data Analyses, Presentations, and Publications

June 15, 2020

This document is designed to provide guidance for the development of ancillary data queries, presentations, and publications that co-investigators may wish to pursue based on the data collected for the primary purpose of the PEPPER trial. This document is not intended to address *additional data* collection on the PEPPER trial patients; such requests will be considered on a case by case basis. These policies will serve as guidance to those interested in developing ancillary study proposals and related data queries, as well as to the *Ancillary Science Advisory Committee (ASAC)* in their work of reviewing those proposals.

ASAC Purpose

The purpose of the Ancillary Science Advisory Committee is to:

- *Promote parallel studies in conjunction with the PEPPER trial and utilizing the PEPPER dataset* that augment the value of the PEPPER trial and encourage engagement of collaborating site investigators.
- *Protect the integrity* of the PEPPER trial and its dataset.
- *Preserve the high scientific standards* of the PEPPER trial as well as the anticipated reports of primary and secondary outcomes emanating from the PEPPER trial dataset.
- *Coordinate research efforts* to minimize duplication of effort.

ASAC Composition

ASAC membership will include:

- The PEPPER trial principal investigator (PI), serving as chair
- The PEPPER trial National Program Director
- PEPPER trial statistician
- Members of the Executive Oversight Committee of the PEPPER trial
- High volume contributing site PIs or their designee
- Other site PIs or contributing surgeons by invitation

ASAC Meetings

The ASAC will meet quarterly on a standing basis, and ad hoc as needed.

ASAC Jurisdiction

The ASAC alone will grant final approval for all ancillary study proposals and related publications, presentations, white papers, data summaries, and/or other related documents to be publicly released.

Overarching Review Principles

- A consistent centralized review process will provide approval of proposals at three critical time points in the life cycle of any project. Review will occur at the time of;
    - initial proposal;
    - abstract creation prior to submission; and

    - manuscript creation prior to submission
- Ancillary science proposals should not involve any primary (all cause mortality, VTE, bleeding, MI, safety issues, or related patient-reported outcomes) or secondary (hip versus knee, anesthesia type, or patient risk preference) outcome endpoints as detailed in the PEPPER study protocol.
- No ancillary science proposals will be allowed that involve research questions pertaining to outcomes segregated by treatment assignment groups for the PEPPER trial.
- PROs involving primary or secondary study outcome endpoints will be excluded from ancillary science proposals.
- All proposals must include a central PEPPER investigator as a co-author to provide data context.
- No raw datasets will be released outside of the central study oversight group. All data interrogation will be performed by the central PEPPER trial statistical staff at the request of proposal initiators and with the approval of the ASAC.
- All approved ancillary studies must acknowledge the PEPPER Trial database as well as PCORI as the funding source in printed and presented materials per ASAC requirements.

Procedural Review Guidelines

- A structured application form must be submitted to the ASAC to initiate a review, per ASAC guidelines.
- Applications will be received from all "active" status sites in good standing in the PEPPER trial.
- Review of proposals will be conducted in the order in which they are received, prioritized by scientific merit as necessary, and announced on a rolling basis.
- Scientific merit, including significance, innovation, and novelty, will be the priority
- Collaboration across multiple sites is encouraged
- Appropriate resources must be available to conduct the proposed scope of work
- The incremental study burden imposed on participating sites and the central PEPPER team (Clinical Coordinating Center and Data Coordinating Center) must be reasonable and not negatively impact the proposing site's performance.

Proposal Application

All proposals submitted for review must include:

- A structured application to include the following sections:
    - Background
    - Research question and hypotheses
    - Data elements requested
    - Planned statistical analyses
- An ordered list of authors, with designation of a lead investigator and correspondent
- All listed investigators must have appropriate certification (CITI training for human subjects research) and be listed on the appropriate IRB protocols
- No more than two pages of text, Times New Roman or Calibri 12 point font, 1" margins

Database

The ASAC will maintain a listing of ancillary studies, abstracts, presentations, and manuscripts which will be made available to the general public via the PEPPER Trial website. Lead authors are responsible for updating the ASAC on the status of their projects/proposals, abstracts, presentations, and publications. The ASAC is responsible for regular distribution of updated listings.