



Manual of Procedures (MOP)
Section 1. Organization & Administration
Appendix 1.3.5. Safety and Outcomes Subcommittee Charter

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1. OVERVIEW OF THE SAFETY AND OUTCOMES SUBCOMMITTEE

The D2d Safety and Outcomes subcommittee (SOS) implements the study's Data Safety Monitoring Plan. The SOS is accountable to the Steering Committee (SC).

2. MEMBERSHIP

2.1 Composition and Term

The SOS consists of members from the D2d Study Group (Executive Committee [EC], Coordinating Center [CC] and collaborating clinical sites) who have demonstrated a commitment to the D2d study who have knowledge in a wide range of scientific disciplines, and experience in safety monitoring of multicenter clinical trials, and adverse event reporting. In general, to maintain continuity and efficiency, members are expected to serve a minimum of 2 years. Ad-hoc members may be appointed for less than 2 years, if there is a specific short-term need.

2.2 Nomination and Election

- At inception, the Executive Committee (EC) nominates members from the D2d Study Group to form the subcommittee. Nominees must have expressed interest and commitment in serving in the subcommittee.
- During the study, the EC may remove or replace subcommittee members.
- During the study, to replace members who step down or add members (e.g. augment the scientific expertise), the EC will solicit nominations for membership from the SC. The EC approves any new subcommittee members at its next scheduled meeting.

Administrative and other support staff, members of the Executive and Steering Committee and chairpersons of the subcommittees who are managing specific areas of the protocol, members of the Central Laboratory, other representatives from the funding agency (NIDDK) may occasionally join the SOS conference call, as needed.

2.3 Leadership

- The Chairperson(s) agrees to serve for a minimum of 2 years. The Chairperson is a member of the SOS and possesses qualifications that make her appropriate for the position, including: expertise in diabetes, cardiovascular disease or vitamin D; deep knowledge of the D2d study design; experience with multicenter trials and safety monitoring; demonstrated leadership skills.
- At inception, the EC appoints the subcommittee Chairperson (or co-Chairs).
- During the study, the EC may replace the subcommittee Chair. The EC solicits nominations for Chair from the SC. The EC approves the new Chair at its next scheduled meeting.

3. DUTIES AND RESPONSIBILITIES

The committee's responsibilities include the following:

- Reviews all serious adverse events (SAE) and unanticipated problems (UAP) as they are reported. The subcommittee chair or designee will assess each SAE and UAP at the time of report to determine if immediate action is required in response to the event, as described in MOP14 and DSMB.
- Reviews periodic safety reports of all adverse events (AE).
- Evaluates whether there is any clustering of AE, SAE or UAP by clinical site.
- Considers if changes in the protocol (monitoring, consent process, etc.) are indicated based on the occurrence, frequency, or severity of AE, SAE or UAP and provides its recommendations to the Steering and Executive Committees for further discussion and subsequently to the DSMB for approval and implementation.
- Adjudicates the diagnosis of secondary outcomes.

4. MEETINGS

In general, the subcommittee meets three times a year. However, if there is a need to meet more frequently, additional meetings will be scheduled to discuss safety related issues.

Meetings are conducted via conference call. In-person meetings may occur during the annual D2d investigator meeting or at other times, if needed. A quorum for holding any official vote requires voting of at least 70% of the membership. If a unanimous consensus cannot be reached, decisions will be made by majority vote. Each member of the SOS has one vote. In the event of a tie, the Chair casts the deciding vote. Minutes will be recorded for each meeting and posted on the D2d web portal for viewing by the SOS membership.