

CRITERIA FOR USE OF AN INDEPENDENT DSMB^{1, 2}

All clinical trials require Safety Monitoring {21 CFR 312.32[c] and 45CFR46.111(6)}, but not all trials require monitoring by a formal committee external to the trial organizers and investigators.

Data and Safety Monitoring Boards (DSMBs) have historically been established for large, randomized, multi-site studies that test interventions intended to prolong life or reduce the risk of a major adverse health outcome (e.g., cardiovascular event or recurrence of cancer). Accordingly, a DSMB should be established for any controlled trial that has mortality or major morbidity as a primary or secondary endpoint. A DSMB is not, however, needed - or even advised - for every clinical study. Less rigorous means of monitoring study safety (e.g., use of one or two independent Safety Monitors with appropriate expertise) may be acceptable for some studies. All clinical research studies do require PI monitoring and oversight. PIs monitoring their double-blinded studies, however, must refrain from identifying study data by intervention arm.

There are several factors to consider in reaching a decision as to whether or not a DSMB is needed for a given clinical trial. These factors are outlined below.

- **Type of Trial: NIH-sponsored, multi-center, phase III clinical trials with a greater than minimal risk of harm require an independent DSMB.** Regardless of funding source, phase III single site trials with a greater than minimal risk of harm, and other phase II-IV randomized clinical trials may also require a DSMB, depending upon the following considerations:
- **Risk Level:** If the trial intervention being evaluated is novel, (i.e., there is little prior information on its clinical safety); is a significant risk device; or especially if there is a body of prior information that raises concerns about the likelihood of adverse events or serious toxicity, a DSMB may be warranted to closely monitor the study for accumulating serious adverse events.
- **Size and Duration of the Trial:** Trials that plan to enroll a large number of subjects or trials of long duration raise safety concerns because of the greater aggregate subject treatment exposure, and because cumulative adverse effect trends over time may not be readily recognized. Conversely, if the trial is of relatively short duration, a DSMB may not be feasible or practical, as there would not be adequate time to analyze study data. For short-term trials requiring a DSMB due to significant safety concerns, study sponsors need to

¹ This guidance document is intended for use by WFUHS IRB members, I-DSMB members and research investigators.

² The WFUHS Institutional DSMB (I-DSMB) is available to serve as the independent monitoring body for trials that are conducted by WFUHS-affiliated investigators. For further information, contact Susan Margitić at smargiti@wfubmc.edu.

establish mechanisms by which the DSMB can be informed and convened quickly in the event of unexpected results that raise concerns.

- Use of Blinded Interventions: Double-blinded trials that conceal the nature of the study interventions from investigators increase the risk that serious adverse events directly caused by the intervention(s) may not be recognized, or may be attributed to non-study factors. In such cases, a DSMB with access to unblinded data may expeditiously identify study-related toxicity. Double-blinded trials involving considerable risk to research participants should be monitored by *independent* DSMBs, rather than by sponsor-affiliated (especially industry-sponsor affiliated) or study-affiliated monitoring boards.
- Vulnerable Populations: If a trial proposes to test a medical intervention on vulnerable or fragile populations (e.g., children, pregnant women, or the elderly), in any group of subjects that may be at relatively high risk of death or morbid events (e.g., critically ill or trauma patients), or in subjects for whom a medical intervention might increase the risk of unanticipated adverse events, a DSMB may be warranted to further protect the rights and welfare of the subjects.
- Scientific Integrity: If the investigators conducting the trial have any conflicts of interest that raise concerns about their ability to conduct the research in an ethical and unbiased fashion, establishment of a DSMB may help assure the scientific integrity and validity of the findings.