## DETERMINING WHEN A STUDY NEEDS AN INDEPENDENT DATA AND SAFETY MONITORING BOARD General Guidelines

## Introduction

All clinical research studies require PI monitoring and oversight as well as pre-specified Data and Safety Monitoring <u>Plans</u>. Not all studies, however, need a Data & Safety Monitoring <u>Board</u>. A less rigorous means of monitoring study safety would involve employing one (or two) independent Safety Monitors with appropriate expertise.

An *independent* Data and Safety Monitoring Board (DSMB) may be needed for high-risk human research studies, for studies in which the investigator and/or the institution may have a potential conflict of interest, for studies involving vulnerable populations or for multi-site studies. DSMB members review on a regular basis study information pertaining to human subject safety as well as study conduct, integrity and outcomes.

The Wake Forest School of Medicine (*WFSM*) Institutional Data and Safety Monitoring Board (I-DSMB) is available to serve as an independent DSMB for clinical research studies being conducted by WFSM or by WFSM-affiliated investigators (single- or multi-site). There is no charge for use of the I-DSMB for investigator-initiated, pilot trials receiving NIH, departmental or other non-industry support.<sup>1</sup> The I-DSMB, maintains a website that provides useful resource information about study monitoring <u>WFSM</u> Institutional Data & Safety Monitoring Board [I-DSMB].

## When is an Independent DSMB necessary for a Clinical Trial?

- Examples of studies that *require an independent DSMB*:
  - 1. NIH-sponsored, multi-center, Phase III clinical trials with a greater than minimal risk of harm.
  - 2. Controlled trials with mortality or major morbidity as primary or secondary endpoints (e.g., large, randomized, multi-site studies testing interventions intended to prolong life or reduce the risk of a major adverse health outcome [e.g., cardiovascular event or recurrence of cancer]).
- Double-blind trials involving considerable risk to research participants should be monitored by *independent* DSMBs. Regardless of sponsor assurances, industry-affiliated DSMBs are not truly independent (such a DSMB includes representation from the study sponsor), nor are study-affiliated DSMBs considered to be independent, as they include voting members who are affiliated with the study that is being monitored.

## When may an Independent DSMB be needed for a Clinical Trial?

- For Phase I and II trials, a DSMB may be appropriate if the studies have multiple clinical sites, are blinded, or employ particularly high-risk interventions or vulnerable populations.
- 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 require a DSMB, depending upon the following considerations:

<sup>&</sup>lt;sup>1</sup> Fees may be charged for use of the I-DSMB by WFSM-affiliated investigators who are conducting either an industry sponsored study or a full-scale (i.e., not pilot), NIH-sponsored clinical study. Fee structure information is available on the I-DSMB website.

- 1. **Type of study** (e.g., since investigators of double-blind trials must refrain from reviewing unblinded study data (i.e., by intervention group), they could miss a developing adverse event trend in one study arm).
- 2. **Risk Level of study** (e.g., little prior information about or poor safety track record for trial intervention, frail or elderly population with numerous co-morbidities that may manifest the same or similar symptoms to study intervention adverse effects, significant-risk devices).
- 3. *Size and duration of trial* (e.g., larger, longer trials raise risk of aggregate subject exposure to intervention, increasing potential for cumulative adverse effect trends ; conversely, DSMB oversight for shorter-duration trials may not be feasible or practical, since there may not be sufficient time to analyze study data).
- 4. *Vulnerable Populations* (e.g., children, pregnant women, cognitively impaired subjects or those at relatively high risk of death or morbid events [critically ill or trauma patients]).
- 5. *Scientific Integrity* (e.g., PI may have conflict of interest related to his/her ability to conduct the research in an ethical, unbiased manner, raising concerns about the scientific integrity and validity of the study findings).
- Observational studies that are large or complex may benefit from having a monitoring board (OSMB).