sponsor is free to evaluate the technical expertise and conflict of interest of the outside experts, before the outside experts are admitted to participate.

ACCESS TO INTERIM RESULTS

To maintain the integrity of the study, all study information and interim results must be strictly controlled. DMC review materials may not be given to anyone other than members of the Closed Sessions. Copies of these review materials must not be made.

STOPPING RULES

The DMC will not use a formal statistical stopping rule for decision-making based on the safety reviews.

The study may be stopped early or design modifications may be recommended in case of safety needs or possible optimization based on the DSMC review of the safety data. Possible recommendations include no action needed and trial continues as planned; early stopping due, for example, to clear benefit or harm of a treatment, futility, or external evidence, or stopping recruitment within a subgroup. Other possible recommendations include stopping the trial on the basis of futility of recruitment, extending recruitment, or extending follow-up time, and sanctioning or proposing changes to the Clinical Study Protocol.

Three futility analyses will be performed, the first when 300 adverse events of death have been noted, the second when 450 adverse events of death have been recorded, and the third when 600 adverse events of death have been recorded. The last futility analysis will coincide with the formal interim analysis of overall survival for superiority. Following such an analysis, the DMC may recommend terminating the study for futility. At this time, the sponsor, after reviewing the summarized data, may decide to terminate the study.

If the interim overall survival results show that the study drug confers a significant benefit, then this could form the basis of a submission for an approval, and the study would be terminated at that time. If the interim overall survival results are not statistically significant, and the study is not terminated following a futility assessment, then the study would continue to enroll subjects and accumulate data until 900 adverse events of deaths have been recorded. At this time, the study will be terminated and a final analysis of the overall survival data will be conducted.

COMMUNICATIONS

MEETING MINUTES

Minutes of the Open Session and Wrap-Up Session will be prepared by *PharmaDrug* and will be distributed to appropriate members of DMC and *PharmaDrug*. Minutes of the Closed Session will be prepared by the DMC. Under 21 CFR §312.58, the FDA may request copies of the meeting minutes.

OTHER COMMUNICATIONS

PharmaDrug, *Inc.,* urges that any communication between the DMC and *PharmaDrug* outside the meeting format, be directed through the DMC Chair and *PharmaDrug*'s Drug Safety group, respectively. These pathways of communication will ensure the DMC's role as an objective and independent entity.