

# Scripps Cancer Center Institutional Review Board

10150 Sorrento Valley Road, Suite 330  
San Diego, CA 92121

Telephone: 858 587-4444

Fax: 858 587-4451

Chair: Robert Bjork, Jr, MD  
Tel: 858 459-4351

Administrator: Barbara G. Bigby, MA, CIP

Tel: 858 587-4442

SCCIRB@scrippshealth.org

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For MCTs in which an independent Data and Safety Monitoring Committee (DSMC, or its equivalent) is involved, FDA should nevertheless have a role to ratify the completeness and adequacy of SAE reports that arise from the study, whether or not these reports pass through the DSMC first, before these reports should be sent to local IRBs at participating sites in the MCT.

In conclusion, local IRBs should not be given unprocessed SAE reports arising from MCTs because local IRBs should never be primarily responsible for stopping a study, changing a procedure or protocol, or deciding what additional information should be given to current, past, and prospective study subjects based on new data that emerges during the conduct of MCTs.

## **Question 2. The Types of Adverse Events about which IRBs should receive Information.**

Once again, the answer should depend primarily on whether the adverse events occurred in a small or single-center study, or in a large MCT. Local IRBs should receive reports of all adverse events that occur in small or single-center studies, as is now being done according to current Federal regulations.

However, in large MCTs, local IRBs should only receive reports of adverse events (whether or not the events are serious in nature) that have been fully processed, analyzed, and ratified (as outlined above) in the context of the severity, number of subjects exposed to the drug or device, and the duration of the study, and *only if* the results of the analysis of these events dictates changes in the consent form, the conduct of the study, or otherwise gives rise to new information that must be provided to all research participants. Then, it would be the local IRBs' role to implement the recommended changes at their own research sites.

There should not ever be the perception that local IRBs have a crucial role in the interpretation of the significance of any adverse event that occurs in a large MCT, particularly any serious adverse events, because common sense dictates that a large clinical trial involving thousands of human research subjects and funded by a large pharmaceutical company should not be monitored for safety by small, overworked local IRBs composed mostly of unpaid volunteer Board members. Therefore, no "raw" SAE reports, nor any unprocessed adverse event reports arising from MCTs should be sent to local IRBs under any circumstances.

## **Question 3. Approaches to Providing Adverse Events Information to IRBs.**

As implied above, adverse events information arising from large MCTs should arrive at local IRBs in the form of recommendations of how the informed consent, protocol, or information given to research subjects should be changed, along with an evidence-based explanation of the reasons for the recommended changes. This information could come from the MCT sponsor, DSMC, or FDA. The explanation should include a description of the adverse events that led to the communication with the local IRB, along with an adequate summary of the scientific analysis that led to the conclusion that changes in the research were necessary.

Due to the predominance of large multicenter clinical trials in today's medical research, it stands to reason that new regulations are necessary to assure the safe conduct of these large-scale experiments on human beings. I am confident that FDA will see to the successful implementation of new policies designed to govern the conduct of these much-needed vast clinical trials which are the "superhighway" leading to a better understanding of how to fight human diseases.

Sincerely,  
Robert L. Bjork, Jr., MD

*The Scripps Cancer Center is a collaboration of ScrippsHealth, The Scripps Research Institute  
and Scripps Clinic for cancer care, research and education*