



**Department of Veterans Affairs
Medical Center
Research Service Product Line (151)
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Minneapolis, MN 55417**

**Division of Dockets Management (HFA-305)
Food and Drug Administration
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Rockville, MD 20852**

To Whom It May Concern:

The Minneapolis VAMC IRB agrees with the recent letter from the Department of Health and Human Services Secretary's Advisory Committee on Human Research Protections. While the volume of adverse event reports to be reviewed by our IRB has increased, the information necessary to evaluate these reports is lacking, so it is difficult or impossible to make any responsible decisions. For example, the IRB is not told the total number of subjects on each arm, the number of adverse events in each arm, or an estimate of the expected number of adverse events likely to occur in the population selected by the study with no treatment.

Evaluation of serious adverse events occurring outside the local institution should reasonably be done by an independent data safety monitoring board for each multi-site study, and report their considerations promptly to local IRBs as well as to the sponsor. For events occurring within local institutions, the local IRB should evaluate compliance with the protocol and the clinical factors of the affected subject that might influence the occurrence of the adverse event. In order to reach any decision concerning the significance of the adverse event, the local IRB should have available all statistical information concerning the overall status of the study-wide protocol, including the frequency of adverse events in the various study arms and the likelihood of similar adverse events occurring in the study population. This data should be provided to the IRBs or the data should be analyzed by safety monitoring boards and reported to the IRBs.

Given the huge volume of adverse event reports, the requirement currently in place to review each report outside of an interpretable context represents a substantial diversion of precious personnel resources that could otherwise contribute more meaningfully to human subject protection.

Regards,

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