The National Institute of Arthritis and Musculoskeletal and Skin Diseases
GUIDELINES FOR REPORTING TO A SAFETY OFFICER

The Safety Officer is an independent individual, often a clinician, who performs data and safety monitoring activities in low-risk, single site clinical studies. The Safety Officer advises the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Program Director and Principal Investigator (PI) regarding participant safety, scientific integrity and ethical conduct of a study.

I. Appointment of the Safety Officer

The Principal Investigator typically proposes an independent Safety Officer, usually a physician, with relevant study and disease specific expertise, and submits the individual's name for review and approval by the NIAMS Program Officer. NIAMS invites the individual to serve as a study's Safety Officer. The Safety Officer is appointed and receives the manual of operating procedures, which typically contains the study protocol and safety monitoring plan, before study enrollment begins.

II. Independence of the Safety Officer

To remain objective, the Safety Officer must maintain independence from the study. Accordingly, the Safety Officer should not be directly involved in the conduct of the study and should not have scientific, proprietary, financial or other interests that may affect independent decision-making.

Current collaborators of the Principal Investigator are not eligible. The letter of invitation to prospective Safety Officers should state the requirement of independence. In addition, potential Safety Officers must sign a Conflict of Interest Statement prior to the appointment. Annually, the NIAMS Program Officer will seek reconfirmation that no conflict of interest exists. Such a statement may also be required prior to each review.

III. Executive Secretary

A NIAMS contractor, KAI Research, Inc., will serve as the Executive Secretary (ES) and will facilitate the distribution of reports. All communication between the study staff and the Safety Officer should be facilitated by the ES with NIAMS copied on the correspondence.

IV. Safety Monitoring Plan

Monitoring activities should be commensurate with the nature, size and complexity of the study. For further information regarding developing a safety monitoring plan, see "Guidelines for Developing a Monitoring Plan for Clinical Studies Sponsored by NIAMS" at http://niams.nih.gov/Funding/Clinical_Research/guidelines_monitoring_plan.doc.

V. Safety Reports

At predetermined intervals, the study statistician will prepare adverse event reports to be reviewed by the Safety Officer. The adverse events are reported in aggregate or by blinded treatment groups, as requested. Serious adverse events are generally reported as they occur. Sample tables for reporting to the Safety Officer are attached to this document.

The safety monitoring plan should specify how data are to be presented and triggers for presenting safety data in an unblinded manner. In addition, the safety monitoring plan should specify the process for reporting safety concerns among the Institutional Review Board (IRB), the Safety Officer, the NIAMS and, if appropriate, the Food and Drug Administration (FDA).

Report templates for reporting to a Safety Officer can be located at http://niams.nih.gov/Funding/Clinical_Research/NIAMS_sample_documents.asp.

VI. Roles and Responsibilities of the Safety Officer

The Safety Officer provides independent safety monitoring in a timely fashion to assure patient safety and study quality.

At the beginning of the trial, the Safety Officer will review the manual of operating procedures, containing the study protocol, study forms, and safety monitoring plan, for scope and comprehensiveness. The monitoring plan should delineate data preparation functions, the review process, and the role of the Safety Officer. The monitoring plan also specifies the contents and format of the reports, their frequency, and triggers for ad hoc reviews. Stopping rules, if appropriate, should outline the conditions under which a study may be stopped prematurely. The Safety Officer may suggest modifications to the protocol, the monitoring plan and the reports that will routinely be prepared by the study statistician.

The primary focus of the Safety Officer's monitoring activity is participant safety. The Safety Officer reviews adverse event reports prepared by the study statistician.

Serious adverse events are generally reviewed as they occur. The Safety Officer will notify the NIAMS if a pattern of events occurs and will suggest prevention measures (e.g., modifying the protocol to require frequent measurement of laboratory values predictive of the event).

For unexpected and/or related serious adverse events, the Safety Officer will contact the NIAMS Program representative. In addition, the Safety Officer may request individual patient records, including laboratory data, clinical records, and other study related data, to evaluate these events against the known safety profile of the study treatment and the disease. The Safety Officer may recommend actions including partial or complete unblinding, and/or modifying or terminating the study.

In addition to safety monitoring, the safety monitor may review enrollment data, demographic information, retention status, and other reports prepared by the study statistician that describe study performance and progress. The Safety Officer will provide a report to NIAMS that describes study safety, progress and performance and provides recommendations regarding safe continuation or early termination of the trial.

The monitoring plan may require the Safety Officer to evaluate the general performance of the study, including periodic assessment of participant recruitment, accrual and retention, protocol adherence, and data quality and timeliness. The Safety Officer may also review any interim analyses to ensure that once the objectives of the study are met, outcome differences are detected or stopping rule thresholds are reached, the study will conclude.

Confidentiality must be maintained throughout all phases of the trial, including monitoring, preparation of interim results, review, and response to monitoring recommendations. Thus, the safety officer should not receive patient identifiers, will maintain study confidentiality and will not share data.

After review and evaluation of the specified periodic reports prepared by the statistician, the Safety Officer prepares a summary cover letter, according to pre-specified criteria, for submission to the NIAMS. The letter provides comments on the report, discusses any concerns or suggestions for change, and recommends to NIAMS continuation or cessation of the trial.