Guidance on Reviewing Protocol Departures and Developing Corrective Actions

The purpose of this document is to provide Overall Principal Investigators and research teams with guidance on determining causes of protocol or subject non-compliance and developing corrective actions for the Institutional Review Board (IRB).

All major protocol deviations and/or violations reported to the IRB must include a description of the Overall PI's corrective and preventative action plan to prevent recurrence.

Reviewing Protocol Deviations and Protocol Violations

- Review case report forms (CRFs) and early research activities following enrollment of the first and/or second subject to ensure that the patterns of protocol compliance are set and there are no misunderstandings of expectations from the Sponsor.
- Review specific protocol deviations and/or protocol violations and other non-compliance items as part of the research team meetings.
- For subject non-compliance: it should be determined whether compliance can be improved through more careful supervision of the subject, better understanding of protocol activities, assistance from family members, etc.
- Consistent or repeated non-compliance may require removal of the subject from the study for concerns of subject safety, data integrity or statistical validity.

Developing Corrective Actions:

- Determine whether organization aids or checklists for research activities, or instructions regarding protocol requirements may improve protocol compliance.
- Review and adjust resources to match requirements of the study.
- For PI-initiated research: it should be determined whether a protocol amendment may be required for non-compliance due to errors in study design or the assessment schedule.

Formulating the Corrective Action Plan:

- The corrective and preventative action plan for the IRB should include information regarding how the major protocol deviation and/or violation was addressed and a detailed plan to ensure this type of event or systems error will not be repeated in the future.

- Examples of Corrective Action Plans for Various Indications:

Subject was not re-consented with the new version of the consent posted on 12/10/09:

Plan: All amendments approved by the IRB are now reviewed by the Overall PI and research team members on a weekly basis to assess when reconsenting is required. When reconsenting is required for specific individuals, a list of all subjects who need reconsenting at the time of their next visit is generated and the information that reconsenting is required is provided to the investigator due to see the individual at the time of next visit Hopefully this will prevent missing any required reconsenting. However, in order to be sure the process is working appropriately, all episodes of a reconsent being missed will be reviewed by the Overall PI and discussed with the specific sub-investigator involved in the care of that individual.

Subject: On ___ the subject returned her drug supply for cycle X. Again both bottles were supposed to be empty however the Y mg bottle contained 12 capsules and the Z mg bottle contained 6 remaining capsules indicating that the subject missed 3 days of dosing (or 6 total doses). The subject also did not returd her study drug diaries.

Plan: After this incident was discovered the Overall PI, sub-investigator for this specific individual, and the research team again reviewed with the individual, the importance of following protocol procedures both for her best interests including safety and for proper overall conduct of the research. Additionally, a communication was sent to each sub-investigator and other members of the research team outlining the importance of continuing to instruct all subjects on taking the research drug as it is prescribed for them, the critical need to complete the drug diary on an ongoing basis at the time that the research drug is being taken, and for each subject on the research to know that they should contact a member of the research team for any questions they might have about any part of the research.