



Norton Audits, Inc.

Defining and Driving Clinical Research Excellence

Proactive Visit Report Review

Protocol:	Investigator:	
	Address:	
NAI Reviewer:	Review date: 09Jan2009	

1. NAI's recommendation

- Halt investigator enrollment
- Add to the "to-be-audited" list
- Increase monitoring frequency by CRO
- Flag for further follow-up
- No concern identified at the time of review

2. Visit reports reviewed:

Visit type	Visit date(s)	# of subjects screened	Site Monitor(s)
PSV	20Sep07	0	
SIV	31Jan07	0	
MV1	15Jul08	2	
MV2	6-7Nov08	4	

3. Alerts

Investigational product	<input type="checkbox"/> Wrong dose/drug/kit dispensed to subject <input type="checkbox"/> Expired drug dispensed/taken by subject <input checked="" type="checkbox"/> Error or problems with investigational product (IP) dispensing <input type="checkbox"/> Blind broken (without prior approval/knowledge of clinical team) <input type="checkbox"/> Improper storage/handling of IP at site (e.g., IP not stored accordingly) <input type="checkbox"/> Non-authorized staff dispensed IP
Human subject safety, rights, and welfare	<input type="checkbox"/> Lack of Principal Investigator's (PI) involvement/supervision that could lead to subject risk (e.g., inc/exc criteria not met and subject enrolled; critical test not done) <input type="checkbox"/> Suspected scientific misconduct <input type="checkbox"/> Ineligible subjects enrolled (actual or potential) <input type="checkbox"/> IRB approval or re-approval not obtained <input type="checkbox"/> Regulatory action (Form FDA 483, Warning letter) or IRB termination/suspension <input type="checkbox"/> Informed consent not obtained prior to trial related procedure, HIPAA not obtained, CA Bill of Rights not obtained (includes use of non-IRB approved ICF) <input type="checkbox"/> Staff not qualified to perform assigned tasks <input type="checkbox"/> Unreported or late reporting of SAE
Data integrity	<input checked="" type="checkbox"/> No access or limited access by site monitor to medical records/source <input type="checkbox"/> Suspected data misconduct*
Investigator research operation	<input checked="" type="checkbox"/> Lack of PI's availability to meet with site monitor <input checked="" type="checkbox"/> Delegation of Responsibility Log incomplete or missing <input checked="" type="checkbox"/> IND Safety Reports missing or unknown if submitted to IRB <input checked="" type="checkbox"/> Failure to list additional investigators on the Form FDA 1572 <input type="checkbox"/> Lack of study supplies or information at critical points of the trial which could impact subject safety or data integrity
Sponsor/CRO/Monitor	<input checked="" type="checkbox"/> Failure to secure compliance <input type="checkbox"/> Conflicting or inaccurate reports/documents (i.e., visit reports, CRO project management reports, other documents available on Trial-Web or provided by CRO)

The information in this Visit Report Review is based on the information provided by the CRO Monitor in the visit reports and supplemented with other documents to which NAI has access. NAI provides this evidence-based review to the sponsor to assist in the mitigation of regulatory risk on Protocol 434 study.

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* Sponsor will be notified within 24 hours of NAI Reviewer learning of event.

4. FDA Inspection History

Inspection date	Type	Classification	Deficiency
No inspection history.			

5. Summary

Evaluation of Dr. Johnson's visit reports (up to MV2 report) was completed by XXXXXXX. The summary of evaluation as well as a recommendation to audit this site was submitted to the sponsor on (put exact name) 12 Dec 08. On Dec 15, the sponsor authorized NAI to contact Dr. Johnson to schedule an audit.

There are indicators of problem at this site. Specifically,

- Dr. Johnson's absence from initiation visit (Jan08), monitoring visit #1 (Jul08), and monitoring visit #2 (Nov08)
- Source records not available for monitoring; therefore, the CRA is not able to confirm eligibility of 4 subjects
- Study drug not dispensed for 3 subjects during Week 2 visit
- Delegation Log not completed
- Missing safety letters from site files plus other regulatory document nonconformities

A breakdown of the observations per visit report is as follow:

- Pre-study visit (20Sep07):
 - Dr. Johnson was present during the PSV
- Site initiation visit (31Jan08):
 - Dr. Johnson was not present during the SIV. There was documentation of phone review of protocol on 22Feb08, about 1 month after the on-site visit.
- Monitoring visit #1 (15Jul08): 2 subjects randomized and 1 withdrew consent before receiving study drug. First subject was screened on 23Jun08.
 - Dr. Johnson was not present during the MV #1.
 - Safety Letter was missing from regdoc files and there was no evidence of the safety letter submitted to local IRB. IB v6 was missing. There were other regdoc issues noted in the MV report.
 - Delegation Log was not completed. (This is a key document during sponsor audits and FDA inspection)

Other area of concern that the monitor did not identify in the reports:

- Pharmacist and coordinator were not listed as subinvestigators at Dr. Johnson's site. They should be listed based FDA's recent warning letter dated 01Oct2008 which clearly stated that coordinator and anyone delegated significant tasks should be listed as subinvestigator.
- Not all clinical laboratories are listed on the 1572.