

Guidance Regarding the Protocol Review and Monitoring System and the Clinical Trials Shared Resource*

Q: Could you provide some guidance regarding the definition of, requirement for, and support of “auditing” within the Protocol Review and Monitoring System (PRMS) and/or Clinical Trials Shared Resource, (i.e., Clinical Trials Office, Protocol Office, etc.)?

A: As per the Guidelines, auditing is not a function of the PRMS, which is focused on scientific review, prioritization and monitoring. Data auditing for quality control purposes is the function of the Clinical Trials Shared Resource. Safety auditing is a Data and Safety Monitoring (DSM) function and from our perspective, this would be best imbedded in the Clinical Trials Shared Resource or set up as a separate shared resource. However, the Committee approving the NCI institutional DSM plans has allowed some centers to establish a subcommittee or separate committee for DSM functions that is linked to the PRMS. This may mean that in the application the narrative for DSM and safety "auditing" will be within the section on the PRMS. In this case, for now, the reviewers should make sure that the functions of the two - one focusing on science, the other on safety - are distinct and separate. Greater clarity on this issue will be sought in the new version of the CCSG Guidelines.

Q: Does this mean that auditing, (i.e., the systematic checking of individual research subject files for accuracy of records and for meeting the conditions of the trial, as contrasted with monitoring for over and under accrual), is an acceptable and supportable role for the Clinical Trials Office that should be expected and/or evaluated?

A: Yes.

[Summary of the discussion above] The Clinical Trials Shared Resource (or its equivalent protocol office) should assure quality control of data. The reviewers should evaluate, within that shared resource, the merit of the applicant’s quality control system. The reviewers should not do “audits” of individual patient/subject files to check on the quality of the data, but should make a judgment on the description of the institution’s quality control *procedures*. For example, the quality control could be internal or external (e.g. Theradex), and the reviewers should evaluate the appropriateness of the method chosen.

The PRMS is for oversight of the scientific aspects of clinical research, such as the quality of the studies approved and the monitoring of over and under accrual. Poor quality control in the Clinical Trials Shared Resource need not necessarily be reflected in the evaluation of the PRMS, unless the problem is so serious as to make the results of the protocols meaningless.

DSM should really be within the Clinical Trials Shared Resource (or its equivalent protocol office), however, the NCI Committee that approves the institutional DSM plans has been permitting a sub-unit of the PRMS to function in the role of the DSM Board. As long as this sub-unit is a separate body from the group that does PRMS, and it is

appropriate to the type, complexity and possible danger of the study, the sub-unit can be within PRMS, so as not to create conflict with the other review. For the time being, there will be no further guidance on DSM review criteria beyond the NIH information**.

Further clarification of the word "body" in the paragraph above: In some instances, there is overlap in membership between the PRMS and the DSMB. This should be acceptable as long as the overlap is reasonable, (i.e. a few members may be on both committees, but not exactly the same members doing both jobs), and the *functions* of the two committees are distinct from one another.

Q: To raise another point, independent of DSM: Where should the reviewers reflect the merit for "auditing" functions when the applicant includes it as past and/or future activities? A possible solution would be the following: In cases where "auditing or other quality control activities" are described, the reviewers should place their evaluative comments on the audit/QC functions into the evaluation of the Clinical Trials Shared Resource, as well as reflect the merit and consider the budget associated with these functions there, (even if this activity is described in the application within PRMS). Thus, the reviewers would consider audit/QC merit and its budget in the Clinical Trials Shared Resource, not the PRMS.

A: This proposed solution is fine for now. (For the long term, whether/how the distinctions should be made clearer to future applicants will be considered.)

*This information does not in any way replace the information provided in the CCSG Guidelines; rather, it is meant to provide some clarification.

**see [bright pink document] [NIH Instructions to Reviewers for Evaluating Research Involving Human Subjects....](http://grants2.nih.gov/grants/peer/peer.htm#documents), or website: <http://grants2.nih.gov/grants/peer/peer.htm#documents>