JOHNS HOPKINS
UNIVERSITY

Center for Clinical Trials

Department of Biostatistics
Department of Epidemiology
Department of International Health

Department of Medicine
Department of Ophthalmology
Oncology Center

10 December 2012

Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Multicenter trials: Consents and coordinating centers

Coordinating centers are not directly involved in consent processes but are bound by what is in consents. That being so, the recommended practice for coordinating centers is to produce prototype consents for distribution to clinics and then to review consents from clinics for content and accuracy before clearing them for enrollment. The prototypes should be constructed to include information as outlined in checklists (e.g., as in Meinert; *Clinical Trials: Design, Conduct, and Analysis*; Oxford University Press; 1986 and 2012).

IRBs in the U.S. and Canada and certain other parts of the world are autonomous. In those structures, there can be as many IRBs as there are centers in a trial. IRBs are not bound by what they are provided in prototype consents. The end result is clinic-to-clinic variation in language and information conveyed to study participants.

In regard to consents, coordinating centers have the option of being
(1) laissez faire,
(2) interactive,
or
(3) authoritarian.

In the laissez faire approach the coordinating center clears clinics for enrollment without review of consents.

The interactive approach is one in which the coordinating center reviews consents for content and accuracy. The review is against the prototype and content checklists. Clinic directors are asked to modify consents found to be lacking and to resubmit to their IRBs for approval.

The authoritarian approach is where clinics are barred from participation if their consents do not meet study requirements. The difference between the interactive and authoritarian approach is what happens if an IRB refuses to make requested changes. Clinics are not allowed in the trial if interaction does not produce the desired result.

The authoritarian approach requires buy-in from study sponsors and study leaders. The coordinating center does not have power to block enrollment of clinics without that support.

Good luck to coordinating centers reliant on the laissez faire option. There will be clinic-to-clinic differences in the promises and commitments made to study participants making life in the coordinating center "interesting".

IRBs require consents that inform persons that they may withdraw at anytime after enrollment without prejudice. Hence, prototype consents should contain such assurance but they should also contain statements advising persons against enrollment if they do not intend to stay in the trial because of the adverse effect of dropouts on the validity of the trial.

IRBs may also want consents that inform persons of the right to withdraw their data from the study. That option should not be allowed. Prototypes should indicate that persons can withdraw from the study but that data collected on them cannot be withdrawn.

There is tension between IRBs and investigators as to what people are told regarding the length of study. IRBs want explicit statements as to period of study. Investigators are prone to equivocate because of uncertainties regarding the length of time required for enrollment and funding. Coordinating centers have to guard against the push by IRBs for more time specificity than indicated. Differences should be resolved by interaction or authoritarianism if necessary.

Interaction/authoritarianism is also indicated in regard to what participants are told as to who will have access to their data. The prototype should indicate that study investigators and persons responsible for monitoring the trial will have access to study data and that study investigators (at all study centers) will have access to study data. Statements added to consents by IRBs implying something else should be rejected.

Even seemingly innocent additions by IRBs can be troublesome. A case in point is the statement that "de-identified data will be shared with other collaborating institutions" in the consent of one of the study clinics in a trial we coordinate. The trouble is with the word "de-identified". The word was probably inserted simply to indicate that persons would not be identified by name in study data, but there is a difference between data not identifiable to person and de-identified data. De-identification implies stripping and collapsing processes characterized in HIPAA. The coordinating center for the trial in question does not have personal identifiers and, hence, data distributed by the coordinating center are, by definition, not identifiable to persons, but it is incorrect to tell people that data will be de-identified.

Consents are seen as contracts by IRBs. Largely, if it is in the consent you can do it, if it is not you cannot without changing the consent and reconsenting. This means that investigators have to set the closeout design before they start enrollment. If the closeout design is changed after the start of enrollment, persons will have to be reconsented to update them on the design change.

Likewise, if investigators plan to collect name and addresses in the coordinating center to allow followup after the trial is finished, that fact should be in consents when persons are enrolled or persons will have to be reconsented to do the collection.

Variation in the wording of consents is the operational equivalent of a general contractor (coordinating center) forced to rely on subcontractors who write their own contacts. Coordinating centers need to be assertive in keeping IRBs from individualizing consents.