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Memorandum

To: Trialists

Fr: Curt Meinert

Re: On whether coordinating centers should have names of persons studied

IRBs are legitimately concerned with patient privacy and breaches of confidentiality. Collection of names, addresses, and other personal identifiers of persons studied into datasets in coordinating centers increase the risks of breaches. As a result, coordinating centers, increasingly, have established data flows devoid of personal identifiers. The advantage is that such flows eliminate the risk of inadvertent breaches at coordinating centers and makes getting IRB approvals for coordinating centers easier. Hence, virtually all trials run from this center now are of that form.

The absence of names means that coordinating centers do not have the ability to link Id numbers to persons. That linkage is possible only through clinics at which persons are enrolled and seen.

But there are downsides to coordinating centers not having names. An obvious one is that they lack means of guarding against enrollment of persons already enrolled. The risk of duplicates depends on the trial and where clinics are located. The risk increases with multiple enrollment sites in the same general locale and when persons are paid for participation.

There are other downsides. One is that coordinating centers cannot help clinics in mailings to study participants. For example, participants in the Alzheimer's Disease Anti-inflammatory Prevention Trial (ADAPT) were unmasked to treatment by letter at the end of the trial. The logistics of mailing and unmasking would have been much easier and more efficient if the ADAPT coordinating center could have prepared the mailing.

A more serious downside is in doing mortality sweeps via queries of the National Death Index and the Social Security death index. Sweeps are required in relation to close outs in trials where mortality is a censoring variable (applicable to most trials except where the followup period is short and losses to followup nil). The coordinating center cannot do sweeps without names, addresses, and Social Security numbers. Without that information, it is necessary to rely on clinics to query death indices. The end result is likely to be spotty performance depending on clinic and complications in carrying out the searches.

A compelling argument for a central file of names and addresses is in having ability to contact study participants after close of the trial. That possibility, without a central file of names and addresses, is largely precluded once study clinics are decommissioned. General Motors has the ability to recall defective vehicles years after purchase. One can argue trialists

should have the same ability, at least in trials where late term effects are possible. Interestingly, IRBs, ours included, are largely insensitive to this need.

Also lost is the possibility of morphing to followup after clinics are closed (see morphing memo posted to trialsmeinertsway.com).

Hence, all things considered, this writer comes down on the side of coordinating centers in multicenter trials having names and addresses of persons studied. The suggestions below are relevant to that view.

Suggestion 1: The IRB submission from the coordinating center should indicate whether names and addresses will be collected.

Comment: The submission should indicate intent to collect names and addresses if:

(1) the information is needed to assist clinics in mailings during or at the end of the trial,
(2) needed in relation to enrollment to check whether a person is already enrolled at some other study site,
(3) the information is needed for mortality sweeps during or at the end of the trial,
(4) the information is likely to be needed for contact of persons after the end of the trial for additional followup (see memo on morphing posted to trialsmeinertsway.com),
(5) the information is needed to contact persons after separation form the trial to inform them of the treatment received,

or

(6) the information may be needed to contact persons after separation from the trial to inform them of late effects of treatments administered (consider this a possibility if the trial involves long-term drug treatment or use of other treatments harboring the possibility of late-term effects).

If collection proposed, expect to answer questions from the IRB concerning security of the information provided and expect to outline procedures intended to limit use of the information.

Suggestion 2: The director of the coordinating center should inform study leaders of the approach proposed and of the rationale for it.

Comment: Review, including enumeration of associated risks and benefits, is necessary for investigator buy-in. Without review, the likelihood is that most investigators will be oblivious to what is done until it is too late to change.

Suggestion 3: Assuming approval of an IRB application with provisions to receive names and addresses (Suggestion 1), determine how and when the information will be received.

Comment: Approval to receive names and addresses does not oblige the coordinating center to receive it. Unless there are real-time needs for that information (eg, as in using it to decide if persons considered for enrollment are already enrolled at other study sites), it is reasonable to delay collection until the end of the trial. Delay has the advantage of not having to receive updates to names and addresses over the course of the trial.

Suggestion 4: If names and addresses are collected, keep the file containing them isolated from other data files in the coordinating center and proscribe use, except as authorized by the director of the coordinating center.

Suggestion 5: Even if names and addresses are collected, it is prudent to design data collection forms devoid of persons names; prudent even if forms are keyed where completed.

Comment: Forms get copied and lie around. They are sent to coordinating centers for data audits. The more places there are names, the greater the risk of breaches.

Suggestion 6: Require clinics to produce consents that include mention of the possibility of transmission of names, addresses, and other identifier information (including Social Security Number) to the coordinating center and reasons for transmission.

Suggestion 7: Require clinics to update locator information at regular intervals over the course of followup; annually in long-term trials and on separation from the trial.

Suggestion 8: Even if names and addresses are not transmitted to the coordinating center as persons are enrolled, leave open the possibility of transmission later in the trial.

Comment: Instruct clinics to write applications to IRBs leaving the possibility open. It will be difficult to gain approval to collect that information at the end of the trial if IRB applications contain statements indicating that such information will not reside in the coordinating center.

Avoid consents including statements indicating that personal identifiers will not be transmitted to the coordinating center. The statement is unwise even if names are not transmitted because it is violated whenever a clinic inadvertently sends papers (like adverse events or death reports) to the coordinating center containing names.

Suggestion 9: If names and addresses are not collected as persons are enrolled, ensure collection when clinics are closed and collection for persons separated from the trial before the trial ends.

Comment: The routine, when a clinic closes, should be to update locator information and to transmit that information to the coordinating center. The routine should apply regardless of when a clinic closes including in relation to closing due to poor performance. The same applies for any set of persons separated from a trial during conduct, eg, persons assigned to a treatment stopped because of bad effects.