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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: My don'ts as a trialist

If you spend your life doing trials you develop don'ts. Here are mine.

1 Don't get involved if you believe the trial is unethical or unnecessary
2 Don't get involved if you do not trust the sponsor or investigators
3 Don't get involved if the sponsor has final say over the protocol
4 Don't get involved if the coordinating center is located in the sponsoring agency or under its direct control
5 Don't get involved if the sponsor and investigators are not committed to publishing, regardless of the nature or direction of the results, when the trial is finished or stopped early for safety or efficacy
6 Don't get involved if the sponsor has final say on what gets published
7 Don't get involved if funding is not adequate to do the trial
8 Don't get involved if the sponsor is not willing to support analysis and paper writing after the trial is finished
9 Don't get involved if there is no Data and Safety Monitor Committee (DSMC)
10 Don't get involved if the DSMC deliberates in isolation from study leaders
11 Don't get involved if the organizational structure for managing the trial is weak or nonexistent

Comments

Don't # 1 is a no brainier. You should not be researching on human beings if you believe the trial is unethical or unnecessary. Walk if that is what you believe. (See Ch 8 and "Mother Test" (Appendix E) in 2nd edition of Meinert's *Clinical Trials: Design, Conduct, and Analysis*; Oxford University Press 2012)

Trust is what the world runs on. Life gets difficult when it is in short supply. The trouble with **Don't # 2** is that you may be involved before your doubts regarding trust arise. If your concerns reach the tipping point, walk.

Don't # 3 is a don't for not getting involved where there is not sufficient separation between the sponsor and investigators. (Note: The term sponsor is subject to confusion. Typically, the term refers to the agency that funds the trial. In regard to FDA regulated products, the term refers to the holder of the IND or IDE, usually the drug company or device manufacturer. Here use is in reference to the funding agency, regardless of who holds the IND or IDE). If the sponsor wants control over the study protocol that is an indication of lack of sponsor-investigator separation and reason to walk.

Don't # 4 follows from the separation principle referenced in **Don't # 3**. "Ownership" of the center responsible for receiving and analyzing data vests too much power in the sponsor.

If one undertakes a trial there is an ethical obligation to publish when it is finished or stopped early for safety or efficacy reasons. **Don't # 5** is a reminder of the importance of that obligation. One should not enter a study absent a commitment to publish no matter what, and assurance that the sponsor will provide support for analysis and paper writing after the close of the trial. (See Ch 40 in *Clinical Trials: Design, Conduct, and Analysis*; Oxford University Press 2012)

Don't # 6 is a reminder to stay away from arrangements in which the sponsor, whether public or private, exercises control over what is published. The trouble with this don't is that you may not know the sponsor's intent at the outset. This is why it is a good idea to insist on explicit policy regarding the role of the sponsor in publications before starting the trial.

Don't # 7 is a reminder to stay away from trials not adequately funded to accomplish their aims. Generally, the euphoria of being funded blinds people to the reality that the funding is not adequate or to the realities of what is really needed by way of funding to do an adequate job. In the end, the only thing that matters to the world is whether you did a decent job. The world does not care about excuses as to why performance was subpar.

Stay away if the sponsor is not willing to fund analyses and paper writing after the trial is finished (**Don't # 8**). Stay out if data processing and analyses are done by a CRO under the control of the sponsor (see **Don't # 4**).

Don't # 9 exists as a reminder that virtually every trial needs a DSMC. Be distrusting of arguments to the contrary. (See Ch 32 and 33 in *Clinical Trials: Design, Conduct, and Analysis*; Oxford University Press 2012)

Don't # 10: DSMCs without investigator input as nonvoting members increases the risks of mistakes and misunderstanding nuances of the protocol and data collection procedures. Recommendations for change out of the blue, without prior knowledge of study leaders leaves, them behind the eight ball in dealing with the recommendations.

The unknown in any trial at the outset is what its leadership structure is for managing the trial (**Don't # 11**). If you are courted to be a coordinating center for a multicenter trial, stay away if study leaders do not know what a coordinating center does or believe one is not necessary!