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Memorandum

To: Center faculty, staff, and friends

Fr: Curt Meinert

Re: Presentation of primary results

This is the sixth in a series of memos concerning issues in the presentation and publication of results from trials. Previous memos have dealt with the obligation to publish, investigator right of primacy, limits to that right, type and place of publication, and deposit of finished datasets.

Presentation, in this context is a paper or poster presented by study investigators at an open scientific meeting. Internal presentations are discussed in a subsequent memo in this series.

Investigators have to establish policy on presentation of results. The options they have are:
(1) to proscribe presentation until results are published; *publish first, present later* policy
(2) to present and then publish; *present first, publish later* policy
(3) to orchestrate presentation to coincide with publication; *present and publish simultaneously* policy.

The first problem the trialist has to overcome, when addressing policy on presentation, is the tendency of investigators to procrastinate. "Why do we have to waste time addressing this issue now? Why not wait until we have results?"

Why? Because the worst time to establish policy is when the "fat is in the fire". Heads are cooler and deliberations more measured when issues of presentation and publication are on the distant horizon.

There are good reasons to prefer option 1, but convincing investigators of the wisdom underlying the option is another story. They are innately predisposed to option 2. The usual arguments for the option and counters to them are as listed below:

- Results of trials should be communicated as rapidly as possible; especially if the results are "medically important" (**Counter**: True, but presentation does not provide an efficient or reliable means of dissemination of results; the audience attending a meeting, even if large, is but a minuscule fraction of the audience having a need to know the results; publication is a more efficient means of disseminating results)

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- The general norm in science is to present as a prelude to publication (**Counter**: That norm has emerged largely from the laboratory sciences where presentation is considered to be important in developing and refining ideas and procedures. The purpose in presenting finished results from a trial is not for development or refinement.)
- The only way the group will have the opportunity to present is if they present prior to publication (**Counter**: If the results are important there will be ample opportunity to present after publication.)
- Prior presentation will speed production of a publishable paper (**Counter**: An intuitively appealing argument, but likely false; indications from a study of presentation and publication behavior of groups doing trials suggest that presentation prior to publication increases the time to publication; see below.)
- Presentation will make for a better paper (**Counter**: Maybe, but the mediums of presentation and publication are different. Hence, there is question as to the amount of improvement presentations confer on publications. Operationally, the likelihood is that the greater improvement would be achieved if the time spent on preparing for the presentation was spent on the publication.)
- The study could benefit from the media attention a presentation is likely to receive (**Counter**: The likelihood is for the reverse if the results are seen as having immediate clinical relevance or as running counter to prevailing wisdom. Clinicians are likely to be frustrated in dealing with questions from patients raised by the trial if all they have is what they read in newspapers and words uttered in an auditorium.)

Investigators are likely to want their cake and eat it too when it comes to presentation versus publication. Hence, if dissuaded from option 2 they will try for option 3. "Why don't we present and publish at the same time? We can get on the program for the XYZ Society meeting this coming fall. If we submit our manuscript a couple of months prior to the meeting it should be in print by the meeting."

The argument has intuitive appeal but is unrealistic because the likelihood of "orchestrating" publication to correspond to presentation is remote. The time table for publication is driven by reviews, revisions, editors, and publication schedules, not by external time schedules related to presentations.

The "have our cake and eat it too" approach drove investigators in the UGDP to present the first set of results (interim results indicating that tolbutamide, a widely used oral agent for treatment of type II diabetes, was no better than placebo, if not even harmful) at the annual meeting of the American Diabetes Association in St Louis on 14 June 1970. The plan, when the abstract for the presentation was submitted to the Association, was to have a finished manuscript published in the June issue of Diabetes. But alas, it was November before the manuscript appeared. There is no doubt that the presentation worked to the disadvantage of the

UGDP. The criticisms that followed the presentation were wilting. By the time the paper appeared most diabetologists had "decided" that the study was "flawed" and, therefore, that results from it should be ignored. The lesson is that once a presentation is out, investigators are sitting ducks until they have a manuscript to reference (for more on the UGDP, read Chapter 7 in Meinert and Tonascia; *Clinical Trials: Design, Conduct, and Analysis*; Oxford University Press; 1986).

Other reasons to reject presentation prior to publication or "simultaneous" presentation and publication are that:

- Presentation may make publication difficult (most journals want new results; results that have been presented are "old")
- Presentation may reduce the drive for publication; once the rush and sweat of presentation has dissipated there is likely to be a "let down"; there is evidence that the letdown increases the chance of results going unpublished; in work by Aynur Ünalp-Arida (PhD dissertation: *Presentation versus publication of primary results in clinical trials*, 2000)
- Presentation may increase the time to publication; evidence of this is seen as well in the work of Ünalp-Arida
- Analyses are likely to be "preliminary" and different from those ultimately published; changes will be seen as suspicious if the results are controversial
- No good way of answering criticism until the paper is published
- Negative imprinting; as likely in the case of the UGDP

The so-called Ingelfinger Rule of the *New England Journal of Medicine* (named for Franz Ingelfinger; NEJM editor 1967 - 1977), as originally written, specified that *Papers are submitted to the Journal with the understanding that they are, or their essential substance, have been neither published nor submitted elsewhere (including news media and controlled-circulation publications).*[NEJM 281:676-677, 1969] The policy, because of criticisms, has been softened, to a degree, but remains a policy hostile to prior presentation.

The safest and best policy is for study groups to impose an outright ban on prior presentation, no matter what and no matter how appealing the arguments may be for simultaneous presentation and publication.

But, do not be surprised, even if investigators agree to *publish first, present later*, with moves to revise the policy as results loom. For that reason, it is important to make sure that the policy finally adopted is documented and that amendment of that policy requires a 2/3rd or 3/4th majority vote of the steering committee.

A caveat: Even if the group adopts a *publish first, present later* policy, it may be forced to deviate from that approach in the case of trials involving proprietary products of publicly traded

stock companies. Knowledge of results exposes investigators to risk of charges of "insider trading". That concern, eg, in the case of the MACRT in SOCA led investigators to present a summary of the results leading to the decision to stop the trial on financial wire services. The announcement was on the Monday following the week in which investigators were instructed to start notifying patients of the decision to stop the trial. The product being tested was under an IND held by the Protein Design Labs (PDL). As it turned out, the stock dropped about 40% with the announcement and triggered an investigation by the Chicago Board of Options Exchange (routine practice following any precipitous change in the price of a publicly traded stock).