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Subject: possible issues for discussion at Monday's conference call (II)

This second memo relates to the material sent to all of us by Rich.

It considers first the material related to the proposed disease progression study. As I now understand the study, it is a case control study for patients with AML, which involves no routine followup, and a case control study for BP, AA, and MDS which involves followup every 6 months (section 2G). It differs from Otto's study primarily in this followup to assess disease progression (which is why it covers BP, AA, and MDS) and in the resolution of certain basic science issues related to these diseases and to AML.

Questions which seem to me to need discussion:

(a) burden on subjects-- Is any biological material obtained other than the material needed to confirm their diagnosis in a scientifically sound fashion (the same confirmation which will be done for Otto's protocol)? What questions about confounders and cofactors will be asked (this is the same as the question from Otto's protocol about the questionnaire)? Are there any burdens and/or risks associated with the storage of material for further study, especially for further genetic study, and from the extra analyses?

(b) benefits to subjects and to Shanghai-- These seem to be the same as in Otto's study, with the extra point (really relevant to both protocols) that a diagnostic laboratory of the highest quality will be developed and left for them. Whether there needs to be any further justification in terms of the benefits to the subjects depends on the answer to (a). The suggestion, that there is additional benefit in light of better management made possible by better diagnosis, should be clarified.

(c) control over publication-- the basic principle is clearly enunciated ✓

(d) issues needing clarification and/or development- we need a communication of results plan, a clarification of the payments issue, the detailed consent form, a clarification of the questionnaire about the confounders, and a discussion of interim monitoring. We also need a data management plan about the preservation of confidentiality and about the separation of data bases between the two studies (Otto's and this study). Finally, we need to discuss how disease progression information will be shared with the subjects and with their clinicians.

I turn now to the material related to the shoeworker's study. This has always been the most sensitive study, and I must confess that I am not confident about forming any judgement about it until we can get a better picture of what is involved in the study in terms of initial testing and followup, how it adds to the information from the disease progression study, the management of discovered dangerous workplace exposure and discovered disease, etc. One good thing is that Rich has concluded that "the study outcomes do not depend on continued exposure," so our initial fear that we will be exploiting workers by the study's following them as they remain in clearly unsafe conditions is no longer present.

I would like to suggest that we have a preliminary discussion of these issues on Monday and we then

→ biological monitoring --

see what can be reported to Friday's meeting.

BARUCH