Benzene Health Research Project Technical Committee Report to Oversight Committee

January 16, 2002

Progress Report

- Subcontract Negotiations (Dates added to payroll)
  - Fudan University (July)
  - SMCDCP (September)
  - IPHS (October)
  - EMBSI (July)
- Chinese Personnel

Progress Report

- Laboratory Renovation
- Recruitment and Organization of the Shanghai Professional Community
- Shanghai Government Liason
- University Administrative Liason
- Exposure Assessment
- Differential Diagnosis
- Ethical Issues
- Equipment and Supply Issues

Changes in Budget
Case-Control Study

- Matching the exposure assessment methodology with that used by the Disease Progression Study which shares the AML cases.
- Not doing so would be to disregard the strong recommendation of the SRP and risk the rejection of the study by the IRBs.
- Change in Budget (now includes inflation):
  ($522K AHS + $519K EMBSI) = + $1,041K

Changes in Budget
Disease Progression Study

- Increasing the number of controls for each case case from one to two
- Changes in the testing protocol, as recommended by the SRP.
- Change in Budget = + $834K

Changes in Budget Molecular Epidemiology Study

- Increases in the number of cases recommended by the SRP and the Chinese IRB
- Changes in subject compensation recommended by the Chinese IRB and the ERP
- Changes in the testing protocol.
- Change in Budget = + $240K

Balancing Priorities

- Changes in the DP and ME protocols took into account the recommendations of the SRP; but did not incorporate all recommendations verbatim.
- The SRP has accepted and ratified the proposed changes.
- The Technical Committee agrees that the proposed changes are an appropriate balance of meeting the goals of scientific merit proposed by the SRP with the financial considerations of the sponsoring consortium.

IRB Review Process - Amendments

- Amendments to the project can be submitted anytime either during or after the IRBs' review; the IRBs would decide what level of review is needed based on the nature of the amendment.
- An amendment to change the scope of the project based on scientific or feasibility grounds would be reviewed by the IRBs on those merits alone without consideration of the cost implications.

IRB Review & Amendments

- An amendment proposing to reduce the scope of the project based solely on financial considerations would receive close IRB scrutiny; and there would have to be a valid scientific rationale for the selection of those parts of the original proposal to be eliminated or truncated.
- Failure to satisfy this requirement or the appearance of any attempt to avoid adverse findings could result in withdrawal of IRB approval for continued participation by one or more investigators.

Technical Committee Recommendation

- The Technical Committee recommends accepting the proposed protocol changes as presented by the Investigators.
  - The overwhelming majority of the changes are in response to the SRP's review of the protocols.

QA/QC Activities

- QA/QC not in prior iterations of the budget
- Highly recommended to protect the sponsors and the overall project integrity
  - Based on FDA guidelines, an activity that should be performed by the sponsors and not the investigators
  - Would more closely resemble a data audit than a full GLP QA audit.
- Technical Committee is seeking outside expert opinion on the appropriate scope and costs for these activities.

Charge to the Oversight Committee

- The Oversight Committee needs to either accept the changes, reject them or request clarification/more information from the SRP regarding specific comments that have lead to the proposed modifications.
- The Oversight Committee is not being asked to increase the contribution of any company (the per share cost) but rather to increase the total budget.