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Subject: FW: Review of benzene health effects study
Attach: API_Sponsored_Benzene_Health_Effects_Study.doc

I have already forwarded to the researchers separately.

George Woodall

-----Original Message-----

From: Carol G. McFadden [mailto:mcfadden+@pitt.edu]

Sent: Wednesday, October 03, 2001 3:55 PM

To: woodallg@api.org

Subject: Review of benzene health effects study

Dr. Woodall,

Attached is Howard's review of the study. Let me know if there's anything
else you need.

Carol McFadden

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Review of API-Sponsored Benzene Health Effects Study

Reviewer: Howard Rockette, Ph.D.
University of Pittsburgh

General Comments: The proposed studies have the potential to add considerably to our knowledge of various aspects of hematologic toxicity due to benzene exposure. For the most part the individual projects are well described and the scientific approach is sound. However, the interrelationship of the Case Control Study to the Disease Progression Study is at times unclear, particularly in regard to the AML patients and their controls. Although attempts were made to clarify the relationship of the two studies (pg. 43 of the Case Control Study and pg. 62 of the Disease Progression Study), some aspects of the logistical and scientific interrelationship between the studies remains unclear. This problem could be addressed by providing an Introductory Section at the beginning of the Project Protocol addressing general protocol objectives and the relationship of the various component studies to one another.

Case-Control Studies of ANLL and NHL in Shanghai:

The investigators propose a hospital-based case control study of ANLL and NHL in Shanghai. Cases would be identified from 15 participating hospitals, the Shanghai Tumor Registry and members of the Shanghai Hematology Association. Controls will be selected from other patients at the same hospitals and will exclude patients with lymphohematopoietic cancers or nonmalignant diseases of the blood or blood-forming organs. Strengths of the proposed project include the ability to obtain a relatively large number of cases and the plan to obtain individual exposure histories. Some aspects of the study protocol that could be addressed are as follows:

- 1) The difference in terminology (AML and ANLL) for the two studies is confusing and should be made consistent.
- 2) Given that one of the criticisms of the CAPN-NCI study is the inadequacy of the exposure assessment, is there any information on the completeness and adequacy of such information in the proposed study, i.e. given 50 randomly selected individuals from hospital records, for how many can adequate exposure histories be obtained?
- 3) The sample size estimates given for the case control study should include the percentage assumed to be exposed. Not only does the statistical power depend on this number but the estimated percentage exposed is of some interest since in doing a hospital-based case-control study of an occupational exposure, there is always a concern as to whether there are adequate numbers of individuals in the occupational groups that are included in the study.

Disease Progression and Molecular Epidemiology Study: This study will perform morphological, cytogenetic and molecular analysis in order to identify the continuum of various blood disorders and to identify features that characterize them. The Molecular Epidemiology Study proposes to identify early markers of benzene toxicity and to investigate genetic markers that may indicate increased sensitivity.

- 1) As mentioned previously there is some confusion in regard to the overlap of some aspects of the Disease Progression Study and the Case-Control Study.
- 2) If feasible, it may be desirable (and more consistent with the case control study) to use two controls/cases instead of one.
- 3) More detail could be provided in regard to the statistical aspects of the molecular epidemiology project.