Progress Report
AML and NHL Case-control Study
Activities through June 2004

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July 14, 2004

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Patient Enrollment:

- Patient enrolment is the responsibility of the designated Clinical Coordinator at each participating hospital. For AML cases and controls, the Clinical Coordinators (mostly hematologists) are under the direction of Dr. LIN Guiwei of the Huashan Hospital. Dr. LIN is not only an experienced hematologist but also a trained epidemiologist (at the University of Pennsylvania). For NHL cases and controls, the Clinical Coordinators (mostly pathologists) are under the direction of Dr. Zhu Xiongzeng of the Tumor Hospital. Patients with preliminary diagnoses of AML or NHL were referred to the Joint Clinical and Molecular Laboratory (JCML) for diagnostic confirmation. Only JCML-confirmed AML or NHL cases are eligible for participation in the case-control study.

- As of mid-June, approximately 103 JCML-confirmed AML have been enrolled in the case-control study. These patients were diagnosed between mid-August 2003 and mid-June 2004, covering an interval of 9.5 months. The estimated annual accrual rate of AML patients is, therefore, 138, which is slightly higher than the assumed rate of 120 in the proposal. Based on this accrual rate, we estimate that by the end of 2006 would have approximately 460 cases of AML, which is slightly lower than the targeted sample size of 500. However, the trend of the accrual rate has been going up recently. Taking the trend into account, we estimate the number of AML cases by the end of 2006 would exceed 500.

- As of mid-June, there were approximately 60 cases of JCML-confirmed NHL (as defined by ICD 9) in the case-control study. The estimated annual accrual rate is approximately 85, which is lower than the assumed rate of 120 in the proposal.

Based on this accrual rate, we estimate that by the end of 2006, we would have approximately 285 cases of NHL, which is markedly lower than the targeted sample size of 500. Taking the recent upward trend into consideration, the best estimate at this point is that we will have between 300 and 350 NHL cases by the end of 2006.

- There are two major reasons for the deficit of NHL patients. First, patient enrollment was a year behind schedule. Second, reporting of NHL patients was incomplete at some hospitals. Meetings with responsible pathologists at participating hospitals were held in June to ensure that reporting of cases will be more complete in the future. The most important issue appeared to be related to the efforts to triage cases of non-malignant lymphoproliferative disease by recruiting patients only after an initial review of biopsy materials. This procedure had not worked well and had resulted in a relatively high rate of refusals and cases lost to follow-up. We have decided to recruit all potential candidates of NHL at the first presentation rather then to wait until we have confirmation. We estimate that this will result in an increase of 20%.

Selection of Controls

- Control selection for AML cases presented no problem. For NHL cases, however, some irregularities at a few hospitals were discovered. Most of the NHL cases came from the Tumor Hospital and many were outpatients. According to the study protocol, controls were matched to cases with respect to outpatient/inpatient status. Through a review of the patient records, I discovered that some of the NHL outpatient controls were not "real" patients at the Tumor Hospital. Once an outpatient NHL case was identified, the nurses or doctors looked for someone who would fit the matching variables (i.e., age, sex) among their friends, relatives or neighbors. I noticed that quite a few controls lived at or near the Community Center（居委会）at 1200 Xietu Road（斜土路）, which is close to the Tumor Hospital. These people were not sick. The motivation to participate in the study was purely financial. Each person got ¥240 RMB for participation. After being "selected" as a control into the study, then the control registered at the hospital as an outpatient, which costs ¥6 RMB. In the JCML database, these controls did not have any diagnosis. A similar problem was also discovered at No. 6 Hospital. (Please see the attached memorandum "Control Selection at Certain Hospitals" dated 5 May 2004.)

- Several meetings with the responsible Clinical Coordinators were held, and the importance of maintaining the scientific integrity of the protocol was explained to them. We also emphasized to them that we would closely monitor the control selection at these hospitals.

- To ensure that in the future all controls are actually patients, we further require that all controls be selected from inpatients only. We do not believe that restricting controls to inpatients will introduce any bias, whereas controls selected from the Clinical Coordinators' neighbors or friends will likely result in bias.

- We will continue to monitor the selection of controls in the future.

Exposure Assessment:

- By June 2004, we have identified 48 patients exposed to both benzene and other substances, and detailed exposure profiles have been developed for 28 patients.

- In addition, 360 patients were identified to have been exposed to other chemicals.

- Employment and exposure histories were obtained from the patients through a questionnaire interview. General employment and exposure information is obtained through the use of a "primary" questionnaire, and detailed exposure-specific information through the use of "secondary" industry/occupation-specific questionnaires.

- Primary sources for benzene exposure information include the following: the exposure database at the Shanghai Municipal Institute for Public Health Supervision (IPHS), Chinese occupational medicine literature, and *ad hoc* industrial hygiene sampling.

- For additional details of exposure assessment, please see Mr. Tom Armstrong's report on exposure assessment.

Project and Budget Management:

- To manage the project properly, it is necessary to devote more time than originally estimated, which demands greater physical presence in Shanghai. During the past 6 months, I have made more and longer trips to Shanghai than originally budgeted for. Fortunately, I was able to take advantage of my trips to Hong Kong, which were paid for by the universities there.

- I anticipate that for the second half of the year, I will have to make 3 to 4 trips to Shanghai.