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Sent: Thursday, July 26, 2007 11:51 AM (GMT)
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Cc: Russell White <whiter@api.org>; Howard Feldman <Feldman@api.org>; Bruce Jarnot <jarnotb@api.org>
Subject: Shanghai BHRC-TC, -OC... Case Control mid-year progress report (7-25-2007)
Attach: CC Progress Report Jul-2007.pdf

BHRC Technical & Oversight Committees –

Attached is a pdf copy of Dr. Otto Wong's mid-year Case Control Progress Report, received 7-25-2007.

Best Regards - Bruce.



**Case-control Study of
Acute Myeloid Leukemia and Lymphoid Neoplasm
Shanghai Health Study**

Progress Report
Activities through June 2007

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Status of Patient Enrollment

The number of participating hospitals remained unchanged. That is, there are 33 participating hospitals; including 17 municipal hospitals, 13 district hospitals, 2 occupational disease hospitals and one private hospital. However, as stated in the previous progress report, some of these hospitals did not contribute any patients during the time period June-December 2006. The lack of patients from some of the same hospitals persisted through January-June 2007.

Some of these hospitals are relatively small (especially the community or district hospitals) and it was likely that no eligible patients were available from these small hospitals, but many of them (e.g., No. 2 Medical University Hospital and the Fudan-affiliated Hua Shan Hospital) are large teaching hospitals and serve large patient populations. For example, the latest records show that the No. 2 Medical University Hospital did not contribute any patient in the entire second quarter of 2007. The Fudan-affiliated Hua Shan Hospital contributed one patient each in May and June, 2007. Therefore, case ascertainment at some hospitals might not be complete. The magnitude and the reasons for incomplete case ascertainment should be investigated. The pattern of patient accrual at each hospital should be closely monitored. The impact of such an incomplete and sporadic patient accrual needs to be assessed.

During my trip to Shanghai in May, I was told that patient enrollment was stopped because of budgetary issues. Subsequently, the diagnosis of patients resumed, but patients were not interviewed. Further, no controls were selected during this time period.

According to Ms. Lu Yunhua (the retired nurse working at the Tumor Hospital), from January to June 2007, 124 new patients with a preliminary diagnosis of lymphoid neoplasm were admitted at the Tumor Hospital, and 48 gave consent and were actually interviewed. The participation rate during this time period at the Tumor Hospital was 48/124 or 39%. It should be noted that only patients with a final diagnosis of lymphoid neoplasm will be included in the case-control study.

Ms. Lu continued to try to locate and interview former lymphoid neoplasm patients at the Tumor Hospital (admitted prior to October 2006), who were not interviewed. According to Ms. Lu, she was able to locate and interview 42 former lymphoid neoplasm patients between January and June 2007. In November and December 2006, Ms. Lu located and interviewed 16 former patients at the Tumor Hospital. Therefore, as of 30 June 2007 Ms. Lu was able to "recapture" 58 former lymphoid neoplasm patients at the Tumor Hospital, who were not interviewed previously. Ms. Lu will continue to locate and interview former lymphoid patients at the Tumor Hospital.

Exposure Assessment

Under the direction of Dr. Thomas Armstrong, the exposure assessment (EA) team continues to develop exposure data/estimates using the "sector analysis" approach. Two Scientific Review Panel members, Dr. John Cherrie and Dr. Robert Herrick, have agreed to work with and provide expert advice to the EA team. The analysis for several commonly encountered industries (shoe, rubber, paint) has been completed. A more thorough discussion of exposure assessment based on the sector analysis is provided by Dr. Armstrong in a separate report.

Exposure data from other sources are also being collected, including published literature. According to Professor Liang, who heads the literature review task, preliminary exposure data for the following occupations/industries have been completed: shoemakers, painters, paint manufacturers, printers, dyers, and rubber workers. These literature data will supplement the Shanghai Municipal IPHS database and district IPHS data in the development of job-exposure matrix (JEM).

A report of benzene exposure in the shoe industry based on the Chinese medical literature entitled "Benzene exposure in the shoemaking industry in China, a literature survey, 1978-2004" was published in *Regulatory Toxicology and Pharmacology* in November 2006. A similar report of benzene exposure in another two industries, paint manufacturing and painting, has been completed. The report is now in the review process.

QA/QC

Pei Xiaodan, who was responsible for QA/QC, left the project in February 2007. Her replacement is Pan Miaoting. I continue to receive monthly QA/QC reports from Pan Miaoting. These monthly reports include accuracy checks of the following items: primary and secondary questionnaires, data entry and initial exposure assessment.

QA/QC of questionnaires taken between January and June 2007 indicated that approximately 97% of primary questionnaires sampled for review were "qualified" (i.e., no problems were found), which was similar to the 96% for the previous 6-month period, July-December 2006.

Once the questionnaires are completed, the information is entered into the SHS database at Fudan. The overall data entry error from January to June 2007 was approximately 2%, which is acceptable.

During my trips to Shanghai in March-April and May-June 2007, I conducted *ad hoc* QA checks of samples of questionnaires taken in the recent months. Only a few minor mistakes were found in these questionnaires (with literally thousands of items/entries) per QA check. These results reinforce/validate the routine QA/QC checks by Pei Xiaodan and Pan Miaoting.

Epidemiology Review of Risk Factors of AML and NHL

We continue identifying and reviewing epidemiologic studies of AML and NHL in relation to occupational and environmental risk factors. We are particularly interested in studies that provide information on subtypes of AML and NHL. We have collected the abstracts of more than 300 potentially relevant papers. We have reviewed a portion of these abstracts and retrieved selected papers.

Project Management and Timeline

Communication with the Fudan team in Shanghai remains a high priority item. In addition to email and telephone calls, I made 2 trips to Shanghai in the first half of 2007. Professor Fu and his staff remain as my primary contact in Shanghai for the case-control study. Professor Fu's group continues to monitor and update me the progress of the study when I am not in Shanghai. His group also provides the necessary support when I work on the study in Shanghai. During my May-June trip to Shanghai I assisted Professor Fu in preparing a proposal to amend the case-control study contract between API and the Fudan University School of Public Health.

The timeline of the case-control study depends heavily on the timing when diagnostic and exposure data (both test data samples and final complete data sets) are provided to us. The delay of any one event in the timeline will likely affect the others. We understand that in the future both diagnostic and exposure data will be provided by Cinpathogen, Inc. according to a new schedule. As a result of the new schedule of deliverables from Cinpathogen, the timeline for the case-control study will be significantly affected and needs to be revised. In preparing a new timeline for the case-control study, I have assumed that AML case accrual will end by June 2007 and that for lymphoid neoplasm patients by December 2007. Further, API has indicated that we will receive from Cinpathogen a comprehensive test dataset by the end of September 2007 and the final dataset with complete diagnostic, exposure and questionnaire information ready for analysis by the end of August 2008.

Based on these newly projected dates of deliverables, I have revised the timeline for the completion of the case-control study (see below).

Revised timeline for the case-control study

Tasks	Date
Test dataset to AHS*	September 2007
Exploration of test dataset	October-November 2007
QA/QC of test dataset	November-December 2007
End of patient accrual*	December 2007
Development of analytical programs/plans	December 2007-May 2008
Final diagnoses of all patients completed*	March 2008
Interviews of all patients completed*	March/April 2008
Questionnaire data entry completed*	May 2008
Exposure assessment completed*	July 2008
Final dataset ready for analysis to AHS*	August 2008
Final QA/QC and data editing	September-October 2008
Statistical/epidemiological analysis	September-November 2008
Preparation of draft report	September-November 2008
Consultations with SRP members	September-December 2008
Preparation of final report	December 2008

* activities not under AHS control.

As indicated in the timeline above, some of our most important tasks can be carried out in 2008 only after patient accrual has been completed, diagnoses have been finalized and exposure classifications have been assigned. In projecting the above timeline, we assume that we will receive a final dataset with complete information ready for analysis by August 2008. Any delay in receiving the final dataset or any unanticipated additional preparation or processing of the final dataset will have an impact on the projected timeline.