

DRAFT CINPATHOGEN CONTRACT MILESTONES

This document spells out the expectations of the Study sponsors with regard to the contract for supplemental funding to CinPathogen for completion of the Shanghai Health Study. Consistent with the original scope of work for the Study and grant, the design, performance and conclusions of the Study are in the sole control of the principal investigators. The milestones laid out in this document are not intended to change that, or in any way to request or require divulgence of data or interim results to the sponsors prior to acceptance of manuscripts for publication in scientific journals. The purpose of requesting the milestone reporting set forth herein is for the sole purpose of allowing the Study sponsors Oversight Committee to fulfill its obligations to monitor costs and the progress of the study, with numbers of cases reported and other factors used as benchmarks of study progress.

1. Short-term milestones to be achieved in the second quarter, 2007

- a. In May 2007, provide an update of the numbers of AML and lymphoid neoplasms (WHO 2001) that can be used in the case-control study.
- b. Reestablish case accrual at participating Shanghai Hospitals.
 - i. Provide an accounting of the number of participating hospitals before and after the transition to IBS (new name?).
 - ii. Provide an estimate for case accrual in 2Q (AML and lymphoid), 3Q, and 4Q (lymphoid only) and provide an update of the numbers of cases that can be used in the case-control study on a quarterly basis (approximately July, October, and January 2008.)
 - iii. Finalize arrangements for review of original work history questionnaires by Dr. Otto Wong and his associates as necessary*
- c. Continue necessary exposure assessment activities for completion of the job-exposure matrix.
 - i. Provide expectations for exposure assessment activities until June 2008 and quarterly reports on progress toward those goals to the QA team. [RDW - Talk to Rob Schnatter]
- d. Provide documentation of data flow, data entry, and roles and responsibilities within the Shanghai Health Study for review by the QA team.
 - i. A specific objective of the QA team review will be data handling of consent forms and work history information to ensure that potential cases are included in the case-control study.

* In cooperation with the independent QA/QC team

2. Long-term milestones to complete the case accrual work by the end of 2007 and the entire study by the end of 2008.

- a. Provide to Applied Health Sciences by mid-September 2007* a test data set consisting of all diagnosed and verified AMLs and lymphoid neoplasms (WHO 2001) and their matched controls, including detailed subtype diagnostic classifications, potential confounders and job-exposure matrix, and all questionnaire information (such as medical histories, family histories, lifestyle information, etc.) for testing the case-control protocol and for developing analytical programs. [RDW – Talk to Rob Schnatter/Otto Wong]
- b. Provide to Applied Health Sciences by July 1, 2008* a final data set consisting of all diagnosed and verified AMLs and lymphoid neoplasms (WHO 2001) and their matched controls, including detailed subtype diagnostic classifications, potential confounders and job-exposure matrix, and all questionnaire information (such as

medical histories, family histories, lifestyle information, etc.) for completion of the case-control protocol.

- c. Complete a study cohort of those cases diagnosed prior to December 31, 2007 of hematopoietic and lymphoid neoplasms (WHO, 2001) and individually matched (2x) sets of controls selected randomly from the entire patient populations at the participating hospitals in Shanghai. Cases characteristics will also include:
 - i. Case selection following eligibility criteria in CinPathogen's March 18, 2007 DPME proposal, Section 8.1
 - ii. Documented informed consents and work history questionnaire administration for all cases and controls
 - iii. Cases of AML will be accrued through June 30, 2007
 - iv. Cases of lymphoid neoplasms will be accrued through December 31, 2007
- d. Complete a benzene job-exposure matrix for cases and controls used in the case-control study. The matrix will consider job, task, industry and time period in developing exposure estimates to benzene. Data sources for exposure assessment including the IPHS data set, Yang Pu database, the Chinese literature, real-time monitoring in selected factories and simulations.
- e. If possible, describe all eligible AML and lymphoid neoplasm patients at all participating hospitals, who did not agree to participate or who were not interviewed, including their basic demographic information and reasons for non-participation/non-interview.
- f. Submit for publication to appropriate scientific journals manuscript(s) presenting the findings of the Disease Progression protocol following the guidelines in CinPathogen's March 18, 2007 DPME proposal, Section 3.1-A by November 1, 2008
- g. Submit for publication to appropriate scientific journals manuscript(s) presenting the findings of the Molecular Epidemiology protocol following the guidelines in CinPathogen's March 18, 2007 DPME proposal, Section 3.1-A by November 1, 2008.
- h. Implement the recommendations of the independent QA/QC team.
- i. Provide semi-annual progress reports to the Scientific and Ethics Review Panelists, Shanghai Health Study sponsors, and API. The update should include a cumulative list of papers submitted to the SRP/ERP for their review. [Dr. Irons - Is there a way to estimate the number of "projected" publications?]

* Based on a timeline agreed upon in cooperation with the independent QA/QC team.