

SHANGHAI HEALTH STUDY

Descriptive Overview

In December 2003, a gathering in Shanghai, China marked the opening of the Joint Sino-U.S. Clinical and Molecular Laboratory. The new Laboratory is central to the Shanghai Health Study, a cooperative research project involving leading researchers from the U.S. and China, facilities at Fudan University, and a network of Shanghai hospitals. This project, designed to further the understanding of the human health effects of benzene exposure, is funded by a number of oil and chemical companies. Data collection is scheduled for completion late 2006.

Purpose: The Shanghai Health Studies were designed to advance the medical and scientific understanding of the relationship between benzene exposure and the risk of certain hematopoietic diseases (certain blood- and lymph-related disorders). The sponsor companies view the project as important to their product stewardship programs.

A unique set of circumstances in Shanghai enabled investigators to launch this meaningful benzene research. These include a long history of working with occupational exposures and qualified, experienced investigators familiar with the local scientific, medical and regulatory establishments. The studies should contribute to the scientific literature regarding a number of issues that have long complicated benzene health risk assessment.

The Studies: The program involves three interrelated studies:

1. **Case-Control Study** – A hospital-based case-control study investigating the potential relationship between exposures to benzene, other diverse variables and both Non-Hodgkin Lymphoma (NHL) and Acute Myelogenous Leukemia (AML).
2. **Disease Progression Study** – A hospital and clinic-based investigation of the potential relationship between non-cancer diseases of the bone marrow and AML to determine if effects on bone marrow may progress through non-cancer stages to leukemia. This study is also attempting to define the shape of the dose response for possible "precursor" diseases.
3. **Molecular Epidemiology Study** – An investigation of whether there is a quantitative relationship between benzene exposure and potential early biological indicators of both exposure and effect in a focused population of workers.

The combined studies apply advanced technologies to advance the medical and scientific knowledge of benzene-induced disease. The investigators are leading experts in their fields. The three Principal Investigators are Dr. Fu Hua of Fudan University, Dr. Richard Irons of the University of Colorado Health Sciences Center, and Dr. Otto Wong of Applied Health Sciences (an independent U.S. research firm).

Benefits: Beyond advancing knowledge of benzene toxicology, these studies will further assist the contributing companies in their continuing efforts to provide high quality product stewardship and continuous improvement of their risk management programs. In addition, the studies may contribute to analyses conducted when governments debate future regulatory standards.

Challenges: Study protocols, facilities and data management have undergone several rigorous, independent technical and ethical reviews, which were addressed with the assistance of a Scientific Review Panel and an Ethics Review Panel. They will remain available to the investigators throughout the research program.

- A. **Scientific Review Panel** – An independent Scientific Review Panel, composed of international experts in relevant scientific disciplines, was assembled to assure that the studies are well-managed, incorporate best available technology and are able to withstand rigorous scientific peer-review. They reviewed, commented on, and, after revisions, endorsed the research protocols. Study protocols also met the rigorous requirements of three separate *Use of Human Subjects* Committees (Institutional Review Boards, or IRBs) – two in the U.S. and one in China. The Scientific Review Panel is also available to Principal Investigators during the course of this study, to discuss progress and provide perspectives on any issues that may arise.
- B. **Ethics Review Panel** – Study protocols (including informed consent and data management), were thoroughly reviewed to ensure that they meet international standards for human research (guidelines established by the Council for International Organizations of Medical Sciences, CIOMS) by a dedicated Ethics Review Panel, which provides oversight for this project. The Panel, consisting of independent bioethicists from the U.S., China and Europe, continues to support and consult with Principal Investigators during the course of their research.

Collaboration: A key to the program's success is local partnerships. Collaborators on these studies include researchers from the Medical School at Fudan University, the Institute for Public Health Supervision, and the Shanghai Municipal Centers for Disease Control and Prevention (the latter two are responsible for occupational exposure monitoring and enforcement in Shanghai).

Equally critical is the Joint Sino-U.S. Clinical and Molecular Laboratory which was developed for this research project. This state-of-the-art clinical and molecular laboratory operates on the Fudan Medical University campus. It supports the research studies as well as providing diagnostic services for over 30 major hospitals in the Shanghai region. The facility will remain at Fudan once the project is completed. This sustainable technology transfer is an important aspect of the project design.

Conclusion: The project sponsors (listed below) are committed to seeing that the Shanghai Health Study is conducted openly and in a manner that assures the investigators' research independence in conducting the studies, analyzing the data, and publishing their conclusions. The sponsors' goal is for the results of the studies to become an important part of the body of scientific research on benzene.

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