

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 and thus the beginning of an unusual cooperative research partnership involving leading researchers from the U.S. and China, facilities at Fudan University, a network of Shanghai hospitals, and involving U.S. oil and chemical company support. This study, to further examine the potential health effects of benzene and other causal agents, has been underway since then, with data collection scheduled for completion late next year (2006).

Purpose: The 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). This study is an important element in the product stewardship programs of the sponsor companies.

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 inter-related studies:

- Case-Control Study - A hospital-based case control study investigating the potential relationship between exposures to benzene and other variables and both Non-Hodgkins Lymphoma (NHL) and Acute Myelogenous Leukemia (AML).
- 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 progress through non-cancer stages to an ultimate leukemia. This study is also attempting to define the shape of the dose response for possible “precursor” diseases and could result in characterization of unique identifiers of benzene-induced AML.
- Molecular Epidemiology Study – An investigation of whether there is a quantitative relationship between benzene exposure and potential early 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, and at the same time look into whether there may be suggestions on potential additional prevention strategies for benzene-induced disease in individuals. The investigators are leading experts in their fields. The three Principal Investigators are Dr. Fu Hua with Fudan University, Dr. Richard Irons with the University of Colorado Health Sciences Center, and Dr. Otto Wong with Applied Health Sciences (an independent U.S. research firm).

Benefits: These studies will further assist contributing companies in their continuing efforts to achieve the highest product stewardship goals and in oversight of their risk management programs. These programs address worker protection, air and water quality, hazardous waste, and other product and operations standards. In addition, the studies may contribute to analyses conducted when governments debate future regulatory standards.

Challenges: The studies met several technical and ethical challenges.

- **Technical** - In order to stand up to rigorous scientific standards, studies must pass scientific scrutiny, be well-managed, and incorporate the best technology. State-of-the-art research is absolutely necessary to make real progress in developing sound benzene risk assessments. To that end, a Scientific Review Panel made up of leading experts from a number of fields relevant to these studies was assembled. They reviewed, commented on, and after revisions, endorsed the research protocols. Additionally, the protocols also met the rigorous requirements of three separate Use of Human Subjects Committees (Institutional Review Board or IRB), two in the US and one in China. The Scientific Review Panel has also met with the lead investigators annually to hear about progress and provide their perspectives on issues that arise. They will remain available to the investigators throughout the research program.
- **Ethical** - To address ethical issues posed by the study, the protocols have undergone a thorough analysis to ensure that they meet international standards for research involving humans (guidelines established by the Council for International Organizations of Medical Sciences or CIOMS), including for example ensuring that the subjects and the communities benefit from participating in the study; that confidentiality is preserved; and that participants are fully informed about the research to give their consent. An Ethics Panel is part of the oversight for the project. It includes bioethicists from the U.S., China and Europe. This panel also consults with the key investigators during the course of the 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 study sponsors (listed below) are committed to seeing that the Shanghai Health Study is conducted in as open a manner as possible, and ensures the investigators' research independence in conducting the study, analyzing the data, and publishing their conclusions. The sponsors' goal is for the study to become part of the accepted body of scientific research on benzene.

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