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Joint Sino-US Shanghai Health Study

As part of their ongoing individual product stewardship and safety and health programs, a consortium of petroleum and chemical companies is sponsoring a scientifically rigorous, unique research project to further the current understanding of the human health effects of benzene.

The research project's purpose is to gain a more refined understanding of the relationship between benzene exposure and associated cancer risks. The studies will utilize cutting edge, state-of-the-art technologies to advance the scientific knowledge of benzene-induced disease and potential prevention strategies.

This new approach to better define the risks from benzene exposure could underpin future decisions on health-based air, water and occupational standards for benzene worldwide. While benzene is recognized as a human carcinogen, what is not understood is how these cancers or other related diseases may be caused, the interactions that may occur between benzene and genetic material, and the role biomarkers may be able to play in adding to our knowledge.

The study is a project of Fudan University Medical Center, the University of Colorado Health Sciences Center, and Applied Health Sciences (an independent U.S. research firm). Other key participants in China include the Shanghai Municipal Center for Disease Prevention and Control and the Shanghai Institute for Public Health and Supervision. The research protocols were subjected to independent reviews by outside experts, including reviews of their consistency with international ethical standards and reviews by an expert scientific panel. The research protocols have been approved by independent review boards at Fudan University, the University of Colorado, and Applied Health Sciences.

A state-of-the-art clinical and molecular laboratory is being built on the Fudan Medical University campus. The lab will support the research project and the Shanghai medical community and will remain at Fudan once the project is completed. This sustainable technology transfer is an important aspect of the project design.

The data from a wide range of benzene exposures in Shanghai, China provides a rare opportunity to conduct meaningful research on the health effects of human exposure to benzene. This strong historical database combined with cooperation of local regulatory authorities and the partnership with scientists in Shanghai form the basis for an exciting scientific collaboration. The joint Sino-US benzene research and analysis is projected to take about five years; results will be published upon project conclusion.

Shanghai Health Study Overview

Purpose: To gain an accurate understanding of the true relationship between benzene exposure and the risk of certain hematopoietic diseases. This study is an important element in the product stewardship programs of participating companies. It can also lead to improved benzene-driven, health-based regulatory (e.g., ambient air, water & occupational) standards worldwide, by providing the regulatory and scientific communities with information for more accurate assessment of the risks from exposure to benzene.

A unique set of circumstances exists at this point in time in Shanghai to conduct meaningful benzene research. These include a database of occupational exposures in a different regulatory environment, and willing and qualified co-investigators influential in local scientific medical, and regulatory establishments. Therefore, questions that have plagued benzene health risk assessment for decades appear to be answerable in Shanghai.

The Studies: The program involves three inter-related studies:

- Case-Control Study - A hospital-based case control study to investigate the potential relationship between benzene exposure and both Non-Hodgkins Lymphoma (NHL) and Acute Myelogenous Leukemia (AML), including an attempt to quantify the potency of benzene for the AML response.
- Disease Progression Study - A hospital/clinic-based investigation of the relationship between non-cancer diseases of the bone marrow and AML (cancer) to determine if effects on bone marrow progress through non-cancer stages to an ultimate leukemia. This study would also attempt 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 - Investigate if there is a quantitative relationship between benzene exposure and potential early indicators of both exposure and effect in a focused population of workers.

The investigators are leading experts in their fields, coming from such well-known institutions as the University of Colorado Health Sciences Center and Fudan University Medical Center. The combined studies apply cutting-edge, 21st century technologies in ways that will not only advance our understanding of benzene-induced disease, but may also identify potential prevention strategies benzene-induced disease in individuals.

Benefits: Information gained from this project will have a direct relevance for worldwide regulatory standards designed to protect workers and the general population from benzene-induced disease. These include air and water quality standards, as well as hazardous waste and site remediation standards. These studies will assist contributing companies in achieving the highest product stewardship goals and in oversight of their risk management programs.

Challenges: The proposed studies meet several technical, ethical, and cultural/political challenges.

- Technical - In order to stand up to scientific scrutiny, studies must be large, well-managed, and incorporate the latest 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 make up of leading experts from a number of fields relevant to these studies has reviewed and endorsed the research protocols. Additionally, the protocols have been reviewed by Use of Human Subjects Committees (IRB) both in the US and China.
- Ethical - To address the ethical issues, the study protocols have all undergone a thorough analysis to ensure that they meet international standards for research involving humans, including that the subjects and participating communities benefit from having participated in

the study; that confidentiality is preserved, and that researchers are working with local regulatory authorities to improve worker safety. An Ethics Panel is part of the oversight for the project and includes a Chinese bioethicist.

- Cultural/Political – A key to this 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).

Funding: Funding for the project will be handled by a consortium of interested stakeholders, with shares determined by size of the benzene related operations of the contributing organization. The proposed funding formula was devised based on the assumption that most of the support will come from the petroleum and petrochemical industries. It is anticipated to take five years to complete the project, and that the costs will be highest in the first years of the project.

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