

Shanghai Benzene Update November 2003

The objective of this memo is to provide an update on the Shanghai Benzene Study.

Additional and more detailed information can be found at

http://www.shanghaihealthstudy.org/Secured-Committee/SHS_Updates/SHS_Update.htm

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We anticipate providing internal updates on a quarterly basis, beginning in January 2004 as well as other communications on an as needed basis.

Background:

Shell Chemical is participating in a multi-stakeholder health study in Shanghai, China, which aims to better define the hazards and health risks from exposure to benzene. The project participants include a wide range of stakeholders including the Fudan University Medical Center, University of Colorado Health Sciences Center; Applied Health Sciences, Chinese public health agencies, Shanghai hospitals as well as several peer energy and chemical companies. This study, which is part of our commitment to product stewardship, will help clarify previous assumptions regarding benzene health risks, including some recent questions about benzene exposure related hazards... The study will examine past and current exposures in Shanghai-area manufacturing facilities (none are Shell facilities and the benzene used in these facilities are not associated with a Shell products). In order to accomplish the study goals, a state-of-the-art clinical and molecular laboratory was built on the Fudan Medical University campus to support the research project and the Shanghai medical community. Chinese technicians have been trained to operate the lab. This facility will remain at Fudan once the project is completed.

Current Status:

The Shanghai Health Study Launch Ceremony is scheduled for December 9th, 2003. As agreed with Shell China, Henry Wang, Corporate Planning Director for Shell China, will represent Shell at this event. Attendees will include Richard Spelman, Consul General of the US, and a Vice Mayor of Shanghai will be in attendance, along with Fudan University officials. The event will be open to all collaborators and participants in laboratory operations.

Annual Meeting:

The First Annual Meeting of the Shanghai Health Study was held August 25-27, 2003 at the Asilomar Conference Center in Monterey, California. The meeting was the first face-to-face gathering all the various groups involved with the study: the Principal Investigators (both Chinese and American research team members), Scientific and Ethical Review Panel members and the project sponsors. A summary of the meeting can be found at. http://www.shanghaihealthstudy.org/Secured-Committee/SHS_Updates/SHS_Update.htm

Project Status:

Study protocols have been reviewed and approved by University review boards as well as independent scientific and ethics review panel members. The clinical and molecular laboratory at Fudan University is completed and is fully functional. The study has begun accepting cases from referring hospitals. . While, the study is funded at a level below the original budget, it is expected that a scientifically rigorous study can be accomplished at the new funding level.

Financing:

The study was initiated with a recognized gap between the budget and the committed funds. Four of the original 5 sponsors have agreed to provide additional funding. The project is being re-scoped to meet the available committed funds. The project sponsors continue to seek additional funding support. Shell and other Consortium members have some recommendations for improving the oversight process including further document review and control of API management as well as a more rigorous approach towards project management; implementing cost management and controls.

Communications:

The Communications Committee has recommended that in order to ensure credibility a public website for the SHS should be maintained by Fudan University and/or the University of Colorado and Applied Health Services. The CC is in the process of determining the website capacity at both sites.

A final media plan will be presented at yearend to the Oversight Committee. In general, a proactive, low-profile media approach is recommended. A launch ceremony, scheduled for December 2003, will be held in Shanghai and. Henry Wang will attend this event on behalf of Shell. . APCO is providing consulting on public affairs strategy and plans for the study.

Other milestones have been identified such as annual study meetings, currently planned in California in 2004 and in Shanghai in 2005, a benzene toxicology workshop in Europe in 2004 and as well as a e planned Symposium on Benzene in 2005... These and other milestones present opportunities and/or challenges for the SHS and need further assessment as to appropriate communication regarding them.

The CC will meet with the University of Colorado press office to ensure SHS media protocol fully adopted and utilized by the participants in the study.

Stakeholder engagement with the scientific community, government, and NGOs will begin in the near future. We are currently finalizing the strategy and protocols for the engagement The Communication Committee budget may be reduced considerably to meet the reduced budget commitment. The regrets need to be identified.

S.H

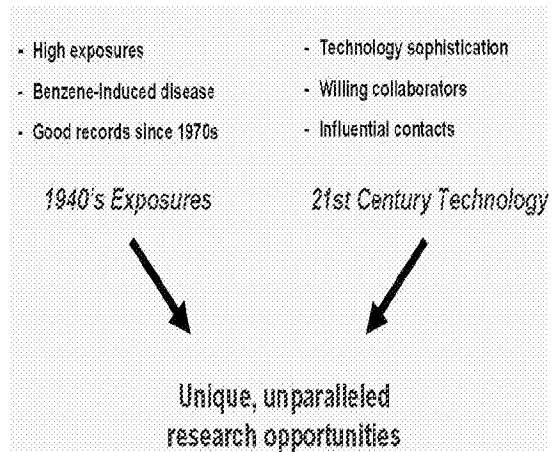
Proposed Studies on the Risk of Benzene-Induced Diseases in China

Page 1

Goal: To form a consortium to fund research on benzene-exposed workers in China.

Purpose: To gain an accurate understanding of the true relationship between benzene exposure and the risk of certain hematopoietic diseases. This study would 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.



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.
- **Ethical** - To address the ethical issues, the study protocols have all undergone a thorough analysis to ensure 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** - In order to address the realities of doing research in China, collaborators on these studies include researchers from the Medical School at Fudan University, and the Shanghai Municipal Centers for Disease Control and Prevention (responsible for occupational exposure monitoring and enforcement).

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.

The Studies: Three inter-related studies have been proposed for this project:

- **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.

