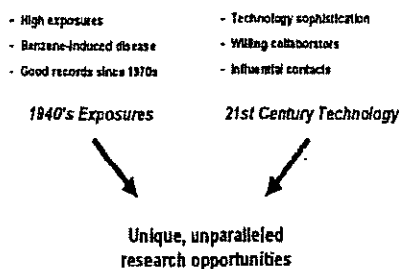


Proposed Studies on the Risk of Benzene-Induced Diseases in China

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 disease. This study would lead to improved benzene-driven, health-based regulatory standards by providing the regulatory and scientific communities with information for more accurate assessment of the risks from exposure to benzene.

Opportunities: A unique set of opportunities exists at this point in time in Shanghai to conduct meaningful benzene research, including high occupational exposures that do not exist anywhere in the West, willing co-investigators influential in local scientific, medical, and regulatory establishments. Therefore, questions that have plagued and confounded 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 changing the existing benzene risk assessment paradigm.
- **Ethical** - To address the ethical issues, the study protocols have all undergone a thorough analysis to ensure that the subjects are appropriately compensated for their participation; that both the subjects and communities benefit from having participated in the study; and that worker safety will improve. 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, the Shanghai Municipal Centers for Disease Control (responsible for occupational exposure monitoring and enforcement).

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Benefits of Extensive Collaboration

CHINESE PERSPECTIVE

- Imports from the West:
 - > Study Methods Expertise
 - > Leading Technology & Know-How
- Enhances Professional Advancement - Publications
- Broadens Training Opportunities
- Allows Greater Autonomy in Future

U.S. PERSPECTIVE

- Required to Navigate Socio-Political Infrastructure
- Ensures Adequate Participation
- Enhances Study Impact, Relevance
- Improves Business-Regulatory Interface in China

Benefits:

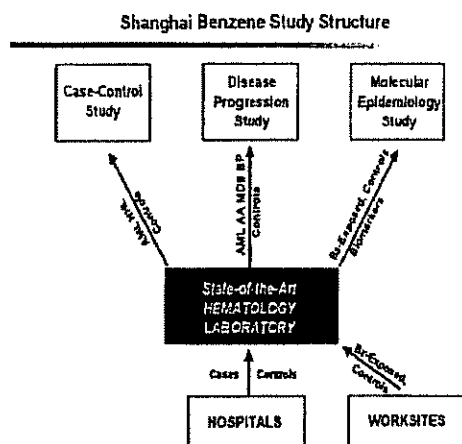
Information gained from this project will have a direct, cross-media impact upon regulatory standards designed to protect workers and the general population from benzene-induced disease. These include air and water quality standards, as well as hazardous waste and site remediation standards. The information gained from these studies will assist contributing companies in achieving product stewardship goals and will be useful in defending the industry's risk reduction programs. Additional benefits from this collaborative approach are outlined below.

2/16/2001

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

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 these "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 benzene exposed workers.

Total Cost Estimate (2001 U.S. Dollars)	
Seed Monics	\$500,000
Study Costs	
Case-Control Study	\$1,761,000
Disease Progression Study	\$3,494,000
Molecular Epidemiology Study	\$3,275,000
Hematological Laboratory in Shanghai	\$8,340,000
External Communications	\$1,000,000
Other Costs (Administrative, Travel, Ethics Panel, Scientific Oversight Panel)	\$1,341,000
GRAND TOTAL	\$19,713,000

Costs: The estimated costs for the project were derived after careful consideration of all of the technical, ethical, and political issues. Therefore, the estimated costs are fairly stable and are not anticipated to

2/16/2001

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increase by much (inflation has been incorporated into the estimate).

Funding: Funding for the project will be handled by a consortium of interested stakeholders, with shares determined by size 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.

Example Funding for One Share By Project Year*

Study Year	Percent of Costs	Cost Per Share
1	30	\$422,400
2	25	\$352,000
3	15	\$211,200
4	15	\$211,200
5	15	\$211,200
Total:		\$1,408,000

*Assumes that there are a total of 14 shares at approximately \$1,408,000 per share. Costs per share may increase or decrease (i.e., total number of shares).

Proposed Funding Formula Share Determination

Shareholder Category	Shares
U.S. Refiner (based on U.S. refinery capacity)*	
Small ($\leq 500,000$ bbl/day)	1
Medium ($>500,000$ and $\leq 1,500,000$ bbl/day)	2
Large ($> 1,500,000$ bbl/day)	3
Non-U.S. Refiners (no U.S. refineries)	1
Free-Standing Chemical Co. (No refineries)	2
Upstream Company (No refineries)	1
Other (trade association, government, NGO)	Negotiable

*U.S. refinery capacity will be determined based upon refinery ownership as of October 1, 2000. Capacity will be as Journal's 2000 Pennwell Directory.

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