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Sent: Monday, September 13, 2004 8:43 PM (GMT)
To: BHRC Oversight Committee (E-mail) <benzconsort-oc@listserve.api.org>; BHRC Technical Committee (E-mail) <benzconsort-tc@listserve.api.org>; BHRC Communications Committee (E-mail) <benzconsort-cc@listserve.api.org>
Subject: BHRC Communications Materials
Attach: 2004-09-13_shs_funding_questions.doc; 2004-09-09_shs_main_messages.doc; 2004-09-13_shs_overview.doc; 2004_Adaptable_Presentation.ppt

Dear BHRC Members:

Attached are updated communications documents for review and comment. Changes to these documents are noted to facilitate your review.

1) SHS Funding Questions - Changes to reflect membership funding changes, project budget, timeline, etc.

2) SHS Main Messages - Change to the end of the document on projected end date.

3) SHS Overview - Change to timing and budget portion of document. Contact information changed to include all Oversight members.

4) 2004 SHS Adaptable Presentation

- Changed diagram (old on showed cases going to IPHS and exposure information come back from them)
- Deleted slide listing hospitals and used "about 30" as the number
- Deleted slide on funding structure and indicated \$500k provided membership benefits
- Anticipate completion and publications by 2007
- Updated SRP/ERP slides
- Updated the format of Master document to resemble SHS website

Please review and provide comments by Oct 11th.

Best regards,
Matt

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SHANGHAI HEALTH STUDY

The Shanghai Health Study

Sponsored by:

Benzene Health Research Consortium

SHANGHAI HEALTH STUDY

Presentation Topics

- Shanghai Health Study Overview
- Shanghai Solutions
- Benzene Basics
- Current Benzene Science
- Shanghai Health Study Elements
- Shanghai Health Study Sponsors
- Shanghai Health Study Funding Structure
- Terms, Sources and Resources

SHANGHAI HEALTH STUDY

What is the Shanghai Health Study?

- Clinical study to investigate the potential causes and development of lympho-hematopoietic diseases (lymphoid organs, blood and bone marrow) as potentially related to benzene
- Project of
 - Fudan University Medical Center
 - University of Colorado Health Sciences Center
 - Applied Health Sciences
 - Chinese public health agencies
 - Shanghai hospitals

SHANGHAI HEALTH STUDY

Shanghai Health Study Purpose

- To gain a quantifiable understanding of the relationship between benzene exposure and potential associated cancer risks
 - Researchers using cutting-edge technologies to advance the understanding of benzene-induced disease

SHANGHAI HEALTH STUDY

Understanding Benzene: Current Science

Benzene Is . . .

- A constituent of crude oil and a chemical building block
- A recognized human carcinogen:
 - Acute Myelogenous Leukemia (AML)
- Tightly regulated although worldwide standards vary
- What is not currently known:
 - benzene's impact on a molecular level;
 - the "threshold" exposure level;
 - whether and how associated cancers or other related diseases may be caused; and
 - the role of genetic susceptibility

Benzene Toxicity

- The effects of exposure to any hazardous substance depend on:
 - dose,
 - duration,
 - other exposures,
 - personal traits and habits,
 - genetic susceptibility
- Co-exposure to other chemicals can also influence toxicity

Why is Understanding Benzene Important?

- Benzene exposure is universal
- Advancing current scientific understanding of benzene exposure would be a significant contribution to health and to worker safety
- Understanding health effects of low-level benzene exposures would advance benzene science

SHANGHAI HEALTH STUDY

Why Shanghai?

- Unique Study Environment
 - Databases documenting exposure
 - Exposure across industries
 - Range of exposure levels
- Committed Collaborators
 - Government
 - University and hospital based researchers
 - Community hospitals
 - Shanghai Municipal Center for Disease Control and Prevention
 - Institute for Public Health Supervision

Unparalleled Collaboration

- “This study is an enormous collaborative effort, unlike anything American and Chinese researchers have ever done.”
 - Dr. Richard Irons, PhD, SHS principal investigator, professor and director of the University of Colorado’s Molecular Toxicology and Environmental Health Sciences Program

Shanghai Health Study Background

- Most environmental and occupational standards for benzene are based on mathematical extrapolations of cancer risk from high-level exposures to environmental concentrations
- These extrapolations are based on almost no knowledge of how benzene functions at a molecular level in humans

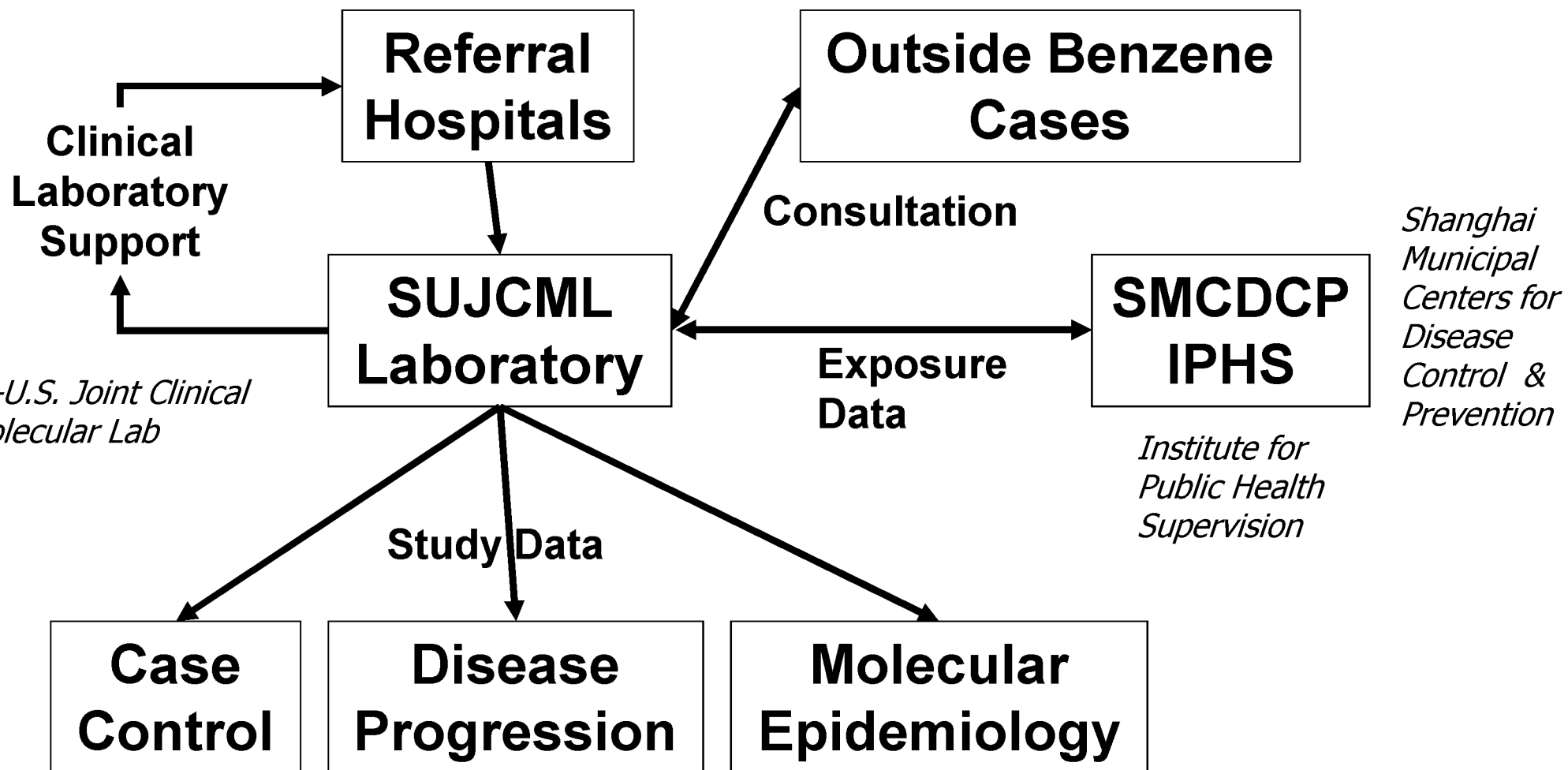
Difficulties in Past Benzene Research

- Animal models do not replicate human benzene-related diseases
- Retrospective research
 - Review case files of people who have died
 - Rely on inexact diagnoses
 - Accuracy of reconstructed exposure data
 - Guess at lifestyle and dietary habits

How is the SHS Distinct?

- Prospective research
 - Patients at participating hospitals suspected of having a lymphoid, blood or bone marrow disease will be referred to the SHS
 - Patients' diets, environmental exposures and family histories will be recorded
 - Patient disease progression followed at supporting hospitals

SHANGHAI HEALTH STUDY



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How is the SHS Distinct?

- Study will be able to examine primary diagnostic and medical data in real time
- First-hand exposure reports are more reliable than second-hand or reconstructed information
- State-owned databases document worker histories

Shanghai Health Study Purpose

- Designed to provide mechanistic data on AML development in humans
- Goal to identify a more reliable basis for the extrapolation of leukemia risk associated with low-level benzene exposure

SHANGHAI HEALTH STUDY

Shanghai Solutions

- Unique Study Environment
- Unparalleled Collaboration
- Shanghai Health Study Genesis
- Rare Opportunity
- Shanghai Health Study Partners
- Shanghai Health Study Hospital Partners
- Sino-U.S. Joint Clinical & Molecular Lab

Unique Study Environment: Shanghai

- Robust data set
 - State-maintained benzene exposure and health effects databases documented from 1970s
 - Benzene related health effects are #2 in reported chronic occupational health hazards in China in 2001 (*Source: Ministry of Public Health*)
 - Large range of exposure levels from a variety of occupational sources
- Regulatory authorities interest in improving benzene exposure regulation and enforcement

Unique Study Environment: Shanghai

- China interested in scientific basis for improved worker-safety regulations
 - Chinese occupational standards based on measurable human health effects
- Chinese Occupational Diseases Protection Law (*effective May 1, 2002*)
 - Increases worker protections
 - Specifies company role regarding worker health problems resulting from occupational exposures
 - Benzene receiving additional scrutiny

SHANGHAI HEALTH STUDY

Unique Study Environment: Shanghai

- High interest in collaborating on research
 - Technology transfers
 - International health standards
 - State-of-the-art lab/ equipment
 - Shanghai hematology/pathology communities support and expertise
- Strong research program supports China's regulatory understanding and objectives

SHANGHAI HEALTH STUDY

Unique Study Environment: Shanghai

- Fudan University Medical Center
 - Research partnership with a leading research university
- Community participation
 - About 30 hospitals refer patients to the SHS
 - Shanghai Municipal Center for Disease Prevention and Control
 - Shanghai Institute for Public Health and Supervision

SHANGHAI HEALTH STUDY

SHS Genesis

- NCI/CAPM study in Shanghai
 - Retrospective study published 1997
 - Raised new questions on effects of low-level benzene exposure
- Assessed feasibility of building on Shanghai experience
 - Respected scientific collaborators
 - Well-documented occupational exposure levels across variety of industries
 - Detailed health and historical records
 - Sufficient incidences of disease
 - Conclusion: full study feasible
- Three distinct, highly integrated studies designed

Rare Opportunity

- Unique data set
- Technological advances
- Early, consistent detection and diagnosis of leukemias and related diseases in Shanghai
- Identification of more sensitive benzene exposure biological markers
- Convergence of company and local Shanghai research interests

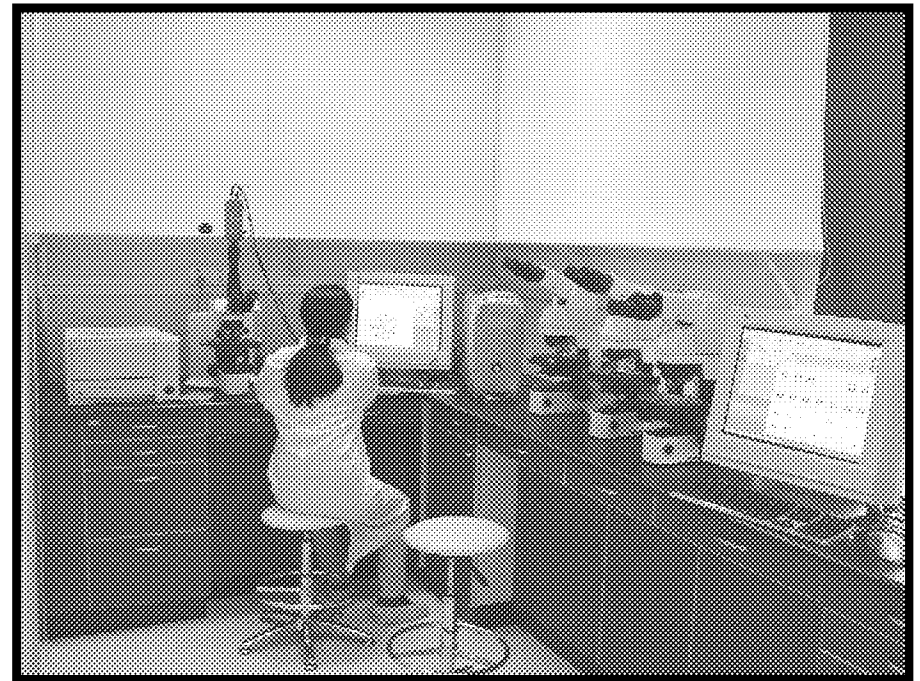
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Shanghai Partners

- Fudan University Medical Center
- Institute for Public Health Supervision
Shanghai Public Health Bureau
- Shanghai Hematology Society
- Shanghai Pathology Society
- Shanghai Municipal Centers for Disease
Control and Prevention
- About 30 Shanghai-area hospitals

SHANGHAI HEALTH STUDY

Sino-U.S. Joint Clinical and Molecular Laboratory



Benzene Basics

- What is Benzene
- Benzene Uses

What is Benzene?

- A colorless, volatile, flammable liquid with a sweet aromatic odor;
- A natural component of many substances including crude oil;
- A by-product of combustion;
- A chemical building block; and
- One of top-20 most-produced U.S. chemicals

Benzene Uses

- Benzene is a basic petrochemical building block, widely used in the manufacture of products such as:
 - Dyes and laundry detergents
 - Lubricants
 - Nylon and synthetic fibers (carpet, clothing)
 - Pharmaceuticals
 - Pesticides
 - Plastics and resins
 - Some types of rubbers (tires)

Benzene Uses

- Element of crude oil; found in small amounts in petroleum products
- As a chemical building block, is transformed in the manufacturing process
- Eliminated as an unconverted additive to solvents and adhesives

SHANGHAI HEALTH STUDY

Existing Benzene Knowledge

- Conclusions pre-1997
- U.S. Regulatory Interpretation
- Recent Epidemiological Studies
- Challenges
- Observations on Existing Science

Epidemiology Conclusions pre-1997

- Acute Myelogenous Leukemia (AML) associated with benzene
 - No risk at exposures < 1ppm
 - Clear risk at exposures > 20 ppm
 - Insufficient data at 1-20 ppm to assess risk
- Some steps are not dose-dependent and are governed by a threshold mechanism
- All steps required for induction of cancer have not been determined

U.S. Regulatory Interpretation

- Regulatory decisions based on no-threshold assumption
- More research needed to assess threshold assumption

Research Challenges

- Accounting for multiple exposures
- Addressing confounding factors
- Exposure estimates
- Accuracy of medical diagnosis
- Analysis of results (case numbers, exposure range, etc.)

Recent Epidemiological Studies

- National Cancer Institute Shanghai Study (NCI) – case-control study published in 1997
 - Benzene associated with AML and Non Hodgkin's Lymphoma (NHL): unusual association with a non-AML cancer
 - Study design did not add to understanding of threshold (lowest exposure group was 10 ppm or less)

Recent Epidemiological Studies

- Australian Institute of Petroleum's (AIP) Health Watch Study – case-control study released in 2001
 - Association with all leukemias, including chronic lymphocytic leukemia
 - No association with NHL or multiple myeloma

Observations on Current Science

- No definitive epidemiological evidence to define a threshold
- NCI and AIP studies conflict with earlier studies by associating benzene exposure with non-AML cancers
- SHS designed to quantitatively address these issues

SHANGHAI HEALTH STUDY

SHS Elements

- Case Control Study
- Disease Progression Study
- Molecular Epidemiology
- Quality Science
- Scientific Review Panels
- Current Status
- Scientific and Ethical Reviews
- Projected Timeline

Specific Study Goals

- Understand relationship, if any, between benzene exposure and development of specific hematopoietic diseases: AA, MDS, AML and NHL
 - Causation of specific diseases/subtypes
 - Mechanism of disease progression
 - Dose-response relationships
 - Identification of cofactors and confounders
 - Identification of biomarkers of exposure and disease progression

Study #1 - Case Control Study

- Prospective epidemiology study to determine risk of AML, and potentially NHL, among benzene exposed workers
- Data collected will allow analysis of potential other causal factors for NHL
- Estimate 4 to 5 years to obtain 450 AML and 450 NHL patients into study
- Improved exposure assessment based on historical and concurrent workplace monitoring and questionnaire

Study #2 - Disease Progression

- Prospective study on relationship of non-cancer bone marrow disease and benzene-induced AML
 - Is benzene-induced AML different from spontaneous AML by unique cellular markers?
 - Does AML involve a progression through one or more non-cancer states?
- Research methods: medical profile developed by questionnaire and interview, work history used for exposure reconstruction, blood and urine analyzed for biomarkers of benzene exposure

Study #3 – Molecular Epidemiology

- Prospective study of establish quantitative relationship between exposure and effect
 - Do low benzene exposures cause blood effects?
 - Is there an association of blood effects and genetic susceptibility?
 - Do biomarkers of exposure accurately reflect workplace exposures?
- Healthy workers at sites with varying levels of benzene exposure will participate; extensive lab work, including genetic tests, will be conducted

Quality Science

- Protocols approved by external Institutional Review Boards (IRB's)
 - Govern use of human subjects
 - U.S. and China independently
- Shanghai Health Study panels
 - International Ethics Expert Panel
 - International Scientific Expert Panel
 - 10 members
 - 6 scientific disciplines
 - Involved during entire project

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Scientific Review Panels

Cancer Mechanisms	Dr. Jerry M. Rice, (Chair), Georgetown University Medical Center Dr. Helmut Greim, Technical University of Munich
Epidemiology	Dr. Harvey Checkoway, University of Washington
Biostatistics	Dr. Howard Rockette, University of Pittsburgh
Exposure Assessment	Dr. John Cherrie, Institute of Occupational Medicine Dr. Robert F. Herrick, Harvard School of Public Health
Hematology	Dr. Richard Larson, University of Chicago School of Medicine Dr. Mark Minden, University of Toronto
Genetic Toxicology	Dr. Li Guilan, Chinese Center of Disease Control and Prevention
Occupational Health	Dr. Richard Albertini, University of Vermont

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Ethics Review Panels

Bioethics	Dr. Jerry M. Rice (Chair), Georgetown University Medical Center Dr. Juhana Idanpaan-Heikkila (Co-Chair), Council for International Organization of Medical Sciences (CIOMS) Dr. Ellen Clayton, Vanderbilt University Dr. Paul Lombardo, University of Virginia Dr. Xu Zong-Liang, Fudan University
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Current SHS Status

- State-of-the-art laboratory constructed on Fudan University campus
 - Built according to international standards
 - Lab will support the project, Shanghai medical community and remain at Fudan
- Technology transfers
 - Chinese staff receiving training at University of Colorado
 - U.S. researchers working with Chinese colleagues and government officials on methodologies, questionnaires, processes, etc.

Scientific and Ethical Review Status

- Fudan University IRB – final approval Nov 01
- External International Scientific Review Panel – final approval Jan 02
- External Ethics Review Panel – final approval Feb 02
- University of CO IRB – final approval May 02
- Applied Health Sciences – final approval 02

SHS Projected Timeline

- Questionnaire development, pilot testing in progress, 2002
- Key laboratory personnel trained, 2002
- Laboratory complete, 2003
- Laboratory opening, summer 2003
- Case recruitment began – 4th quarter, 2003
 - 1600 benzene exposed workers, 400 controls
 - Time necessary to identify qualified patients
 - Length of study may be extended if required
- Research, analysis expected 2003-2007
- Results published as studies completed

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SHS Sponsors

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Who is Sponsoring the SHS?

- A consortium of petroleum and chemical companies concerned about understanding the human health effects of benzene
 - BP, ChevronTexaco, ConocoPhillips, ExxonMobil, Shell Chemical with additional funding from Marathon Ashland
 - Other participants welcome
 - Project Administrator: American Petroleum Institute

Why Industry Sponsors?

- SHS goal to provide an accurate understanding of how benzene works on a molecular level in humans
 - Advanced understanding of benzene-induced disease could lead to development of effective disease prevention strategies
 - Would allow a more finely calibrated assessment of potential health effects
 - Provide best protection for workers and public

Why Industry Sponsors?

- Worldwide, benzene occupational exposure regulatory standards vary widely
 - 0.5ppm in Malaysia; 1.0ppm in U.S.; 10ppm in Japan
 - American Conference of Governmental Industrial Hygienists recommends 0.5ppm
- Industry has long sponsored benzene research

SHS Funding Structure

SHS Funding Structure

- \$21.08 million program total for all costs over approximately 5 years needed to complete study.
- Costs highest during first years (laboratory construction and equipment, training).
- Minimum contribution of \$500k for full membership and participation

SHS Funding Structure

- Direct costs
 - Data collection and analysis with procedures to protect privacy;
 - Procedures and training for data collection in participating clinics;
 - Constructing, training, staffing state-of-the-art hematology laboratory;
 - Laboratory operations for research and clinical tests; and
 - Operations for 5 years estimated to identify study cases
- Administrative costs
 - Internal and external communications and coordination;
 - API project administration, travel; off-site meetings

Conclusions

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Conclusions

- PRESENTER: SELECT AUDIENCE
 - General
 - Recruitment – Funding
 - Recruitment – Technical

SHANGHAI HEALTH STUDY

Conclusions

- Study will advance benzene science
- Sponsors funding study
 - Product stewardship
 - Corporate social responsibility goals
- Anticipate completion and major publications by 2007
- Results will add to accepted body of scientific research on benzene
 - Referenced by government, industry decision-makers

Additional Sponsors Needed

- Responsibility to understand the health impacts of your products
- Commitment to worker health, safety
- Need for most advanced science possible

SHANGHAI HEALTH STUDY

Terms, Sources and Resources

Terminology

- AA
- AML
- Biomarker
- Epidemiology
- Histology
- NHL

SHANGHAI HEALTH STUDY

Acronyms

- API – American Petroleum Institute
- AIP – Australia Institute of Petroleum
- IRB – Institutional Review Board
- CAPM – Chinese Academy of Preventive Medicine
- IPHS – Institute for Public Health Supervision (China)
- NCI – National Cancer Institute (U.S.)
- SUJCML – Sino-U.S. Joint Clinical and Molecular Lab
- SMCDPC – Shanghai Municipal Center for Disease Control and Prevention
- USEPA – U.S. Environmental Protection Agency

SHANGHAI HEALTH STUDY

Sources

- American Council of Government Industrial Hygienists
- Agency for Toxic Substances and Disease Registry ToxFAQs, U.S. Department of Health and Human Services
- American Petroleum Institute
- International Agency for Research on Cancer
- United States Environmental Protection Agency
- University of Colorado Cancer Center, Denver, CO

SHANGHAI HEALTH STUDY

For More Information

- Template: Add your contact information here.
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SHANGHAI HEALTH STUDY

For More Information

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SHANGHAI HEALTH STUDY

Overview

Purpose: To gain an accurate understanding of the 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 could also lead to improved, health-based regulatory (e.g., ambient air, water & occupational) standards worldwide, by providing the regulatory and scientific communities with additional information for more accurate assessment of the risks from exposure to benzene.

A unique set of circumstances in Shanghai enabled investigators to launch this meaningful benzene research. These include a database of occupational exposures, and qualified co-investigators influential in local scientific medical, and regulatory establishments. Therefore, questions that have complicated benzene health risk assessment for decades may be addressed in Shanghai.

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

- Case-Control Study - A hospital-based case control study investigating 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 the AML response.
- Disease Progression Study - A hospital/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 - Investigating 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 for benzene-induced disease in individuals.

Benefits: Information gained from this project may have 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 made 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 (Institutional Review Board or IRB) both in the US and China.

SHANGHAI HEALTH STUDY

Overview

- 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, including for example insuring 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 informed consent. An Ethics Panel is part of the oversight for the project. It includes bioethicists from the U.S., China and Europe.
- 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).

Costs: The estimated costs for the project were derived after careful consideration of all of the technical, ethical, and political issues. (inflation has been incorporated into the estimate).

Item	Cost Estimate
Case-Control Study	\$2,283,095
Disease Progression & Molecular Epid. Studies	\$15,921,428
Fudan University	\$230,000
Total Research Costs	\$18,434,523
Scientific Review Panel	\$300,000
Ethics Review Panel	\$64,000
External Pathology & Cytogenetics Workgroups	\$0
Total Panel Costs	\$364,000
Outside Counsel	\$100,000
Public Affairs	\$550,000
QA/QC Activities	\$100,000
UCHSC Interest	(\$100,000)
Contingency	\$390,272
Miscellaneous Costs	\$1,040,272
Subtotal	\$19,838,795
Administrative Overhead (5%)	\$1,245,205
GRAND TOTAL	\$21,084,000

Funding: Funding for the project is being provided by a consortium of interested oil and chemical companies. It is anticipated to take five years to complete the project. The costs will be highest in the first years of the project.

For More Information: Please contact any one of the following individuals.

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SHANGHAI HEALTH STUDY

Main Messages

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 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 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 impact 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 cancer or other related diseases may be caused, the interactions that may occur between benzene and genetic material, and the role biomarkers may play in adding to existing 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 program has met the rigorous requirements of three separate Independent Review Boards; the research program has also attained the approval of two separate and independent scientific and ethical review panels. Finally, the research also meets the Council for International Organizations of Medical Sciences (CIOMS) guidelines for medical research involving human subjects. The scientific and ethical review panels will remain involved as consultants throughout the project; permission to adjust the research protocols in any way also requires prior review and approval from each institution's Independent Review Board.

Study sponsors are committed to seeing that the Shanghai Health Study in as open a manner as possible consistent with ensuring the investigators' research independence in conducting the study, analyzing the data, and publishing their conclusions. The sponsors' goal is for the study to contribute to the accepted body of scientific research on benzene consulted by decision makers in government and industry.

A state-of-the-art clinical and molecular laboratory is being built on the Fudan Medical University campus. The laboratory supports 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. The unique 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-U.S. benzene research and analysis is projected to take about five years. Results will be published, with final publications anticipated in 2007/8.

Shanghai Health Study

Background Information

Q: Who are the funders?

A: Current funders (as of Oct. 2002):

- BP
- ChevronTexaco
- ConocoPhillips
- ExxonMobil
- Shell Chemical
- Additional funding from Marathon

The American Petroleum Institute is the project administrator.

Q: How were the funders selected?

A: A consortium of petroleum and chemical companies are sponsoring the SHS as part of their ongoing individual product stewardship and corporate responsibility programs. Others with a similar interest in the health effects of benzene are welcome to join the consortium.

Q: How much will the SHS cost?

A: \$21.08 million program total for all costs including:

- operations for five years estimated to identify case studies;
- staff training, data collection, and analysis;
- study revisions recommended by the scientific and ethics panels;
- patient privacy protections;
- constructing a state-of-the-art laboratory at Fudan University in China;
- and
- laboratory operations for research and clinical tests.
 - The on-site lab provides cutting edge technologies and diagnostic capabilities without necessitating shipping human tissue samples to the U.S. for testing.

Q: Are funding shares equal? If not, how they are allocated?

A: Funding shares for start-up were determined by size and sector. Currently, a contribution of \$500,000 provides full membership benefits (see table at end of document).

Q: Apart from financial commitments, if our organization were to join, what are the membership requirements?

A: Current members can serve on three separate committees –communications, oversight or technical. The oversight committee makes budgeting, resource and other major decisions; the technical committee follows progress of the research;

and the communications committee helps with external communications about the project.

Q: Would it be possible to join the SHS as a partial member? If so, how would that be decided?

A: The Oversight Committee would need to consider that request. Marathon has been admitted as a partial member. They are invited to participate in the Annual Meeting and receive the investigator's periodic updates.

Q: Why are petroleum and petrochemical companies the only funders?

A: The petrochemical industry has long taken a lead role in researching benzene health effects. However, any interested company or group is invited to participate.

Q: Wouldn't the American Petroleum Institute and their European counterpart (CONCAWE) be a logical source for additional funds?

A: All of the current funders are API and CONCAWE members. For a variety of reasons, member companies often fund and manage major research initiatives in a separate resource consortium rather than through the association. However, the sponsors do think the project should be of interest to other companies, industries and sectors and would like to see funding diversified.

Q: Were other funders solicited?

A: Yes and active outreach continues.

Q: If they said no, why should I be interested?

A: Each company has to set its own priorities and interests. And I can't address the decisions other companies have made. Obviously, since my company is funding the project (*ALT for API staff: since I'm closely involved with..*) we think it is important for understanding the health effects of benzene, which is an important part of our product stewardship responsibilities.

Q: Why are the original project supporters seeking additional funding?

A: We believe this project is of general interest to all companies who produce or handle benzene. We'd like to see as many of them as possible them directly involved.

Q: What is the benefit to me to join the study at this point? Won't the study be conducted anyway?

A: Study sponsorship allows you the opportunity to engage in constructive dialogue on these issues with the people actively searching for worker safety solutions. It will help ensure your company has a solid understanding of the project, beyond the summaries presented in the anticipated peer-reviewed publication of the study

results. And it will clearly demonstrate to your employees, customers and shareholders that you agree you have a responsibility to actively study and understand your products.

Q: Your company was involved in designing the project; at this point my company wouldn't have input to the research. So why should we join now?

A: First, the research was designed by Drs. Richard Irons and Otto Wong. Sponsoring companies established an Ethics Review Board and a Scientific Review Panel, both of which had extensive input to the project. These bodies endorsed the study design. While the initial sponsors had a lot to do with that process, they did not control the study design. As a result, we think we will make a sound contribution to the science of benzene health effects.

[As appropriate, repeat reasons for joining.]

Q: Is there a role for non-government and/ or government organizations in the SHS?

A: We would welcome the opportunity to brief others on the project and to keep in touch with them on future progress.

Approved Sponsorship Privileges for New Funding Sponsors		
Privileges	<\$500,000	\$500,000
Oversight Committee	X	1 share Participant
Technical Committee	Observer	Participant
Budget Committee	X	Participant
Communications Committee	Invite to participate	Participant
SRP/ERP	X	X
Study Updates	√	√
Website access	√	√
Financial Reports	√	√
Identified as sponsor on publications, posters and meeting presentations	Second tier acknowledgement: “With additional funding by . . .”	Full
Annual Meeting	Observer	Participant