

To: Mallett, Anthony AK SC-CHSE-TM
<Anthony.K.Mallett@OPC.shell.com>; Hill, Patsy PM SCC
<PH197432@MSXSOPC.SHELL.COM>
From: Gingell, Ralph R SCC
</O=SHELL/OU=MSXSOPC/CN=RECIPIENTS/CN=RG724048>
Cc: Owen, David DE SC-CHSE-DO
<David.E.Owen@OPC.shell.com>
Bcc:
Received Date: 2000-03-30 20:20:07 GMT
Subject: FW: BZ/Shanghai materials

Tony: information from Exxon on the proposed China Benzene study; Shell Chemical is invited by API to become part of a consortium to fund this study.

-----Original Message-----

From: arschna [SMTP:arschna@erenj.com]
Sent: Wednesday, March 29, 2000 7:54 AM
To: 'Gingell, Ralph (Shell Chemical)'
Cc: 'Beatty, Patrick (Chevron)'; 'Vail, Jim (API consultant)'
Subject: BZ/Shanghai materials

Ralph - as you requested --- attached are some materials regarding the proposed Shanghai studies. The first document was presented by Mike Redemer of Texaco at the IPIECA meeting last month, Pat Beatty wrote it.

The second is an updated presentation that I wrote at the conclusion of a study planning meeting last year at EBSI. Subsequently, Gerry Raabe presented it to an IPIECA group. I've modified it slightly to reflect some re-alignment of the projects.

Hopefully, this will help you see where we're coming from. Feel free to talk to Pat, me, or Jim if you need anything clarified.

Rob

A. Robert Schnatter
Room LF-252
ExxonMobil Biomedical Sciences, Inc.
1545 Rte 22 East, PO Box 971
Annandale, NJ 08801-0971
908-730-1101
908-730-1192(fax)
732-437-4702(pager)



BZCHINA22500.ppt (62 KB)



IPIECA_Benzene.doc (27 KB)

Attachments:

BZCHINA22500.ppt
IPIECA_Benzene.doc

INTERNATIONAL LEVERAGED RESEARCH PROPOSAL

Project Description (1-2 sentences):

The proposed research is an investigation of the effects and dose response of hematological effects of benzene exposure in a population of workers in Shanghai , China (PRC). It is intended as a scientific response to findings from a nationwide study of benzene exposed workers in over 50 industries by researchers from the United States National Cancer Institute and the Chinese Academy of Preventative Medicine. The research includes a case control study of Non-Hodgkin's lymphoma (NHL) and acute myelogenous leukemia (AML), an investigation of the role of non-cancer diseases such as aplastic anemia and myelodysplastic syndrome in the progression to AML, and a determination of the dose response relationship between benzene exposure and biomarkers of both exposure and effect.

Background -- Describe the Significant Issue(s) of Concern to Global Petroleum Industry that the Research Would Affect:

- The expected health effects of ambient air concentrations of benzene currently drive calls for the reformulation of motor gasoline that would have massive financial impacts on petroleum refiners.
- Concerns about localized impacts of benzene exposure are the basis for initiatives to control emissions from stationary sources such as refineries and marketing facilities.
- Benzene is a major determinant of the extent of required cleanup of many petroleum-contaminated media such as soil and water.

Project Value – How Will Research Results Enhance Industry’s Ability To Achieve Objectives On Issue Of Global Impact And Concern:

The planned research is expected to:

- Provide strong scientific support for the lack (or presence) of a risk of leukemia or other hematological disease at current ambient benzene concentrations to the general population.
- Establish that adherence to current occupational exposure limits (in the range of 1-5 ppm) do not (or does) create a significant risk to workers exposed to benzene.

The planned research may establish:

- That there is an absolute threshold for benzene-induced hematological disorders below which there is no effect.
- The extent to which “sensitive subpopulations” based upon age, genetic or other factors either do or do not exist.

Project Selectivity – Describe The Data Gaps The Research Would Fill, The Absence Of Other Sources Of The Data, And Its Applicability World Wide:

The data gaps that would be filled include:

- Clarification of the identity of hematological cancers caused by benzene exposure. (The NCI/CAPM study suggested that Non-Hodgkin’s lymphoma may be caused by occupational benzene exposure).
- The role of non-cancer diseases such as myelodysplastic syndrome and aplastic anemia in the development of acute myelogenous leukemia.
- The shape of the dose response relationship (including a possible threshold) of various hematological disorders and benzene exposure.
- Clarification of the similarities between benzene-induced leukemia to other established secondary AMLs, e.g., subsequent to alkylation chemotherapy.
- Clarification of the quantitative relationship between benzene exposure and potential biomarkers of exposure, e.g., metabolites and biomarkers of effect, e.g., chromosomal abnormalities.

Uniqueness of data source:

Shanghai represents the unique situation of a large number of workers with documented exposures to benzene at levels that have not existed in Western Europe or North America since the 1940's or 50s. These exposures are combined with a computerized database of worker exposure and hematological monitoring data extending back to the mid 1980's. In Shanghai there exists the infrastructure of a modern medical school and hospitals as well as a government agency (the Shanghai Center for Disease control and Prevention) that maintains the above database and has the authority to conduct industrial hygiene monitoring at occupational sites.

**Project Details – Scope and Potential Project Managers/Researchers:
The project has three components:**

- 1). A case control study of Non-Hodgkin's lymphoma and AML investigating the hypothesis that there is a relationship between benzene exposure and NHL and or AML. NHLs will be analyzed by subtype and for viral status to determine potential confounders if the relationship reported by the NCI is replicated.
- 2.) A determination of the relationship between and involvement of diseases such as myelodysplastic syndrome or aplastic anemia and acute myelogenous leukemia.
- 3.) An investigation of the quantitative relationship between benzene exposure and potential biomarkers of exposure and effect in a focused population of benzene-exposed shoe manufacturing workers.

Primary participants include:**Epidemiology:**

Otto Wong, D.Sc. – Applied Health Sciences

Robert Schnatter, Ph.D.– Exxon Biomedical Sciences Inc.

Hua Fu – Deputy Dean, Shanghai Medical University School of Public Health

Hematology/Molecular Biology:

Richard Irons, Ph.D. – University of Colorado Health Sciences Center
Guowei Lin - Director, Center of Clinical Epidemiology, Hua Shan Hospital

Industrial Hygiene:

Wei Lu – Deputy Director General, Shanghai Municipal Center for Disease Control and Prevention.
Thomas Armstrong – Exxon Biomedical Sciences Inc.

Project Cost -- Describe the Projected Duration and Cost (annual/total):

The project as described is expected to require a total of \$6.5 +/- \$0.5MM over a period of 5 years. Although this annualizes to \$1.3MM/year the total cost would be front loaded with \$2.2MM expected in the first year to cover initial costs of establishing laboratory facilities in Shanghai and higher than average travel expenses for initiation of activities.