

To: Cagen, Stuart Z SCC-HSE <stuart.cagen@shell.com>
From: Reese, John E SOPUS
</O=SHELL/OU=HUBCENTRAL/CN=CUSTOM RECIPIENTS
SHELL/CN=USI+RE09>
Cc:
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Subject: API Downstream Committee

Stuart: There is an API Downstream Committee meeting next week and I am preparing a briefing book for our representatives. The agenda contains an update item on "API Subscription Research and the Shanghai Health Study." As I understand it, this is an informational item and there is no specific action being requested from the Downstream Committee. I understand from David Steup that you participate in the research activities described below in API's write-up. Any comments? Anything that you would add? Anything that you think our representatives should advocate? If you could let me know by Monday morning that would be much appreciated. P.S. Thanks for your participation in the API Fuels Committee meeting the other day. I see that moving in the right direction.

Attachment 4

API SUBSCRIPTION RESEARCH AND THE SHANGHAI HEALTH STUDY

Subscription Research Programs are research projects that are funded outside of the regular API dues budget structure to conduct research of interest to the petroleum industry. These programs are designed to enable funding by both API members and non-members. Subscription research programs serve as a vehicle to conduct large, long-term research programs, which can be difficult to accomplish within the current API yearly budget cycle.

Previous and current subscription research program budgets have ranged from \$675K to \$30 million, and have been developed to conduct mandated and voluntary research initiatives. Mandated research is usually undertaken in response to EPA TSCA Section 4 Test Rules, with notable exceptions being the Clean Air Act Section 211b Fuel and Fuel Additive Testing Program and the Synthetic Based Drilling Muds Program, which are linked to EPA product registration and discharge permitting programs. Voluntary initiatives, such as the Mid-distillate Dermal Health Effects program and the White Oils and Waxes Food Use Safety program have been undertaken to develop data to prevent unnecessary restrictions on occupational or commercial use of products.

API administers these programs at cost to funding sponsors. Subscription research programs also offer an opportunity for API members to leverage funding with non-API member companies, since API membership is not a prerequisite for subscription research program participation.

The Shanghai Health Study is the most recent addition to the subscription

research programs administered by API.

Shanghai Health Study

Purpose: To gain an accurate understanding of the relationship between benzene exposure and the risk of certain hematopoietic (blood and blood forming organs) 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.

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 industry in achieving the highest product stewardship goals and in oversight of their risk management programs.

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 been troublesome for 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 (e.g. myelodysplastic syndrome, aplastic anemia). 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, Fudan University Medical Center (Shanghai) and Applied Health Sciences in the private sector.

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, independent, 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 (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 Review 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).
- └ Sponsors, Benzene Health Research Consortium

Major Sponsors: BP, ChevronTexaco, ConocoPhillips, ExxonMobil, Shell Chemical Company

Also Contributing: Marathon Ashland Petroleum and Marathon Oil

John E. Reese

Manager, Fuels Advocacy
Shell Oil Products US
910 Louisiana, Room 684
Houston, TX 77002
Phone: 713-241-6075
Fax: 713-241-1324
E-mail: jereese@ShellOPUS.com