

Benzene Task Force (BTF)
American Petroleum Institute
at
The Airlie Foundation
Warrenton, VA

Meeting Minutes - Subject to Approval

Wednesday, September 23, 1992

<u>Attendees</u>	<u>Affiliation</u>
Pat Beatty	Chevron
Mike Bird	Exxon
Rudy Breglia	BP
Peter Craig	Mobil
Cosmo DiPerna	Mobil
Bob Drew	API
Jennifer Galvin	Phillips
Chuck Lambert	Unocal
David Mongillo	API
Mary Paxton	API
Gerry Raabe	Mobil
Louise Scott	API
John Sepesi	Shell
Michael Wells	Amoco
Li Yang	ARCO
Lemone Yielding	U. of Texas

The Benzene Task Force (BTF) met from 1:00 to 3:30 following the workshop "Mechanisms of Benzene Toxicity as a Basis for Risk Assessment" (agenda and list of attendees attached). The purpose was to determine how the BTF's research budget should be allocated in light of the information and opinions that had been exchanged in the previous day and a half.

It was agreed that there was strong support for continued funding of Rich Irons' work at the University of Colorado on the specific targets among bone marrow cells for toxicity caused by benzene and its metabolites. Broadening of his work to include investigations involving human bone marrow in vitro, whole animal exposure, and human cancer chemotherapeutic agents was endorsed.

It was agreed that there are still gaps in our knowledge of benzene metabolism and kinetics. Lovelace/ITRI with Rogene Henderson as PI was deemed a more suitable institution to pursue this aspect of the research and cooperate with Irons in providing

him with tissues from treated animals. A proposal concerning biomarkers of benzene exposure has also been submitted by this researcher, and its support would forward the more long-term goals of developing reliable indicators of exposure and early signs that could aid in monitoring biological response. CIIT will be notified of this change.

The consensus was that the likelihood of identifying an animal model that could be used in illuminating the leukemogenic mechanism in humans was so remote that further allocation of funding to this objective would not be cost-effective for API.

Although it was granted that endpoints indicative of genotoxic activity have been observed in association with benzene exposure, it was generally agreed that their interpretability with respect to the carcinogenic process of primary concern is so uncertain that pursuit of this line of research would not be anticipated to have much impact on risk assessment for benzene.

It is possible that there are human subpopulations with special sensitivity to benzene's toxic effects. If so, this could effect risk assessment and regulation related to benzene. This concern makes genetic polymorphisms in factors that influence susceptibility and benzene's interaction with other possible exposures into areas that might merit support in the future.

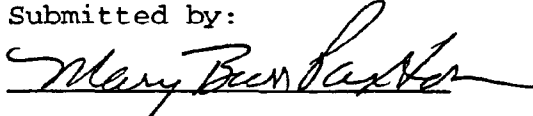
It was thought that Tony Cox's work on the BBRA model deserved continuing funding on the condition that he work closely with Irons and other benzene investigators. Efforts should be made, however, to make his reports and presentations more comprehensible to his audience.

On the short term, WSPA has just given Kenny Crump final direction on the elements to be included in his reanalysis of the Pliofilm cohort. His results should be forthcoming in about a month. After a review by the BTF's math and modeling subgroup, Crump will be asked to present his findings to the entire BTF, hopefully on a trip that can be coordinated with his making a similar presentation at EPA some time in November.

Kenny Crump indicated that he would feel increasingly justified in applying a non-linear model for low-dose extrapolation from the human data if the basic biology researchers continued to document the existence of non-linear components in the mechanisms defining leukemogenesis. He suggested focusing their research on the step(s) that are probably most non-linear, and so might impose a "functional threshold" on the process, rather than endeavoring to describe the entire pathway(s) in detail. In order to provide further justification for Crump's use of a non-linear model in the report to be presented to EPA (and also to ACGIH in the winter), the

staff will prepare a support document arguing, now primarily on a theoretical level, that non-linear elements occur and explaining how this non-linear effect is compounded by the multitude of biological processes intervening between benzene exposure and the production of a leukemia. Review of this document and the additional exemplary material will be sought from the researchers currently working on benzene for API.

Submitted by:

A handwritten signature in cursive script, reading "Mary Burr Paxton". The signature is written in dark ink and is positioned below the "Submitted by:" text.

Mary Burr Paxton, Ph.D.