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TO:	D. Poller	REFERENCE:	95MR 307
FROM:	B. R. Friedlander	SUBJECT:	National Cancer Institute (NCI) Trip Report (2/13/95)

Tom Armstrong, Michael Bird, Stevan Phillips, Rob Schnatter and I met with members of the National Cancer Institute (NCI) on February 13th, 1995. The purpose of the meeting was to discuss with NCI investigators their studies of workers exposed to benzene in the Peoples Republic of China and for us to describe some of the work with which Exxon is involved in Canada, the UK and Australia.

We are monitoring the NCI studies because of their potential impact concerning health risks at low benzene exposures and their interaction with key activities currently underway within and outside Exxon. These activities include the IP Epidemiology Study, the European Union Benzene Risk Assessment and the IOL Worker Study. The EBSI team summarized our work on benzene using materials previously cleared for release.

The NCI epidemiology efforts consist of a large cohort study followed by a "nested case-control" assessment. The cohort study compares the health experience over time of a large group of workers believed to have had substantial exposure to benzene to a set of controls whose history and available work records suggest an absence of occupational benzene exposure. The case-control study focuses on individuals with or without the disorders of concern (e.g., certain leukemias, aplastic anemia, etc.) and assesses the relationship of having those disorders with specific exposure attributes (e.g., concentrations, durations, and frequency of benzene exposure).

The cohort study is very large and complicated with over 75,000 benzene exposed workers and about 36,000 non-benzene controls. The study covers 12 Chinese cities, nearly 700 factories, multiple job categories and several industries. Petroleum industry workers are not significantly represented in the study. Painters, chemical manufacturing, and rubber industry workers appeared to comprise the largest of the groups studied.

The benzene exposure concentrations found were quite high. In the 1950s and 1960s, jobs such as rubber gluers and drip painters were reported to have hourly exposures sometimes exceeding 100 ppm. Average daily exposures exceeded 50 ppm for those workers and between 10 and 50 ppm for most others exposed. The exposure "data" are derived from a mix of actual measurement data in about 40% of categories, and the residual 60% are based on best industrial hygiene judgments. Little information was provided at the meeting as to the quality or validation of the exposure data.

While their studies are still in early stages, some initial results have been reported from the cohort study. In addition to increases in acute myelogenous leukemia (a known target site), excesses were also noted for several other diseases of the blood-forming system such as non-Hodgkins lymphoma, lymphoid leukemia, and aplastic anemia. Also, there appears to be an increase in some solid tumors. The case-control studies may provide further insight into these results, some of which (e.g., solid tumors, lymphomas, etc.) appear to conflict with other published findings.

Although motivated investigators from the NCI, the Chinese Academy of Preventive Medicine, and consulting organizations are participating in the research, several important methodological issues could influence study quality and conclusions:

1. Accuracy of benzene exposure data - Much of the exposure data has been estimated based on "best judgements". Quality assurance of analytical measurements needs verification. We infer from our discussions with the NCI scientists that benzene exposures experienced by the workers in the previous decades may have been even higher than those reported.
2. Assessment of other exposures - Exposure to other agents, including carcinogens, needs more detailed consideration. Workers likely had significant exposures to other chemical and physical agents. The study impact of such exposures and life style factors such as smoking, diet, and dwellings (radiation, asbestos, and PAH issues) need further assessment to more fully define the role of benzene in the reported disorders.
3. Case ascertainment and verification - At least one incentive exists for more complete reporting (or over-reporting) of leukemia in benzene workers than in other members of the population. If leukemia occurs in benzene-exposed workers, compensation payments are made to the family. Thus, a potential bias exists for leukemia to be reported preferentially for benzene workers compared to study "controls". Hematologic malignancies were verified by clinical, laboratory and pathologic data review, thus making this study's results incomparable to most other published studies.
4. Accuracy of diagnoses of solid tumors - Many of the solid lung tumors reported were based only on chest x-ray results. Without a confirmation from biopsy, autopsy or cytology, tuberculosis (a common disorder in China) could often be misdiagnosed as lung cancer. The potential for this issue to create misleading results needs to be assessed.

In summary, the NCI China program is the world's largest health study of heavily exposed benzene workers. There are many issues surrounding the study, e.g., accuracy and completeness of exposure information, reliability of disease reporting, effect of lifestyle factors, etc. which may confound interpretation of results. However, a key point is that the reported health findings to date are in workers exposed to high concentrations of benzene. The NCI studies do not directly address the low dose exposure region of current regulatory and risk assessment interest. However, because future interpretations or findings could imply lower dose effects and impact policy, it is important that we continue to monitor these studies. NCI will present some of its results in the June Benzene Conference at Rutgers University and anticipates publications in late 1995 or early 1996.

Additional details are available upon request.

BRF:jmk

cc: T. W. Armstrong, J. G. Bell, M. G. Bird, J. L. Cox, G. F. Egan,
A. M. Goldstein, M. Harrison, D. R. Hudgins, A. M. Katz, T. J. McDonagh,
R. D. Phillips, S. C. Phillips, J. T. Sanderson, A. R. Schnatter,
F. R. Smith, C. V. Want, C. M. Yarborough

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