

**SUMMARY OF PEER REVIEW COMMENTS ON THE
TOXICOLOGY AND CARCINOGENESIS STUDIES OF BENZENE
(July 27, 1984 Meeting)**

On July 27, 1984, the draft Technical Report on the toxicology and carcinogenesis studies of benzene received peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

The draft Technical Report on the toxicology and carcinogenesis studies of benzene was initially evaluated by the Peer Review Panel on October 28, 1983. The interpretative conclusions on the carcinogenesis results were accepted by the Panel at that time; however, approval of the full Technical Report was deferred to allow for complete analyses of the hematologic data and inclusion of reportable findings into the report, and to allow for editorial tightening and incorporation of a number of suggested changes.

In the current review, Dr. Friess, a principal reviewer, again agreed with the conclusions. He noted that the conclusions relating to the hematologic findings, especially the dose-related lymphocytopenia and associated leucocytopenia, and suggested they be added to the conclusions on carcinogenicity. Dr. J. Huff, NTP, said this would be done.

As a second principal reviewer, Dr. Davis said some comment should be made on the use of corn oil as the vehicle in view of the possible cocarcinogenicity of corn oil. Dr. E. McConnell, NTP, pointed out that NTP is investigating the mechanism for these apparent effects (pancreatic lesions) associated with corn oil gavage (Boorman and Eustis, 1984). Dr. Huff said a manuscript (Haseman et al., 1985) had been accepted for publication regarding the incidence of neoplasms in untreated and corn oil gavage controls; where relevant, this reference would be cited in appropriate technical reports. In essence, he said that the historical control data on Fischer 344 (F344/N) rats and B6C3F₁ mice from the National Toxicology Program were examined to determine if animals receiving corn oil by gavage showed tumor incidences that differed from those in untreated control animals. Analyses of these data were adjusted for interlaboratory variability, time-related trends, and supplier effects. Two significant effects were found: male F344/N vehicle control rats receiving corn oil by gavage showed a significantly higher ($P < 0.05$) incidence of pancreatic acinar cell adenomas and a significantly lower ($P < 0.001$) incidence of leukemia (primarily mononuclear cell leukemia) than did the corresponding untreated controls. The increased incidences of pancreatic acinar cell adenomas observed in corn oil gavage male rats were associated with elevated body weights observed in these animals relative to those observed in untreated controls. Little difference in tumor incidence between corn oil gavage and untreated controls was observed in female F344/N rats and male and female B6C3F₁ mice. Dr. Davis said more mention should be given to the extensive epidemiologic studies on benzene.

As a third principal reviewer, Dr. Van Ryzin said the Technical Report was complete.

There was some discussion about the relevance of the gavage route versus other routes by which human exposure is more likely to occur, especially inhalation and dermal routes. Mr. Beliczky asked that a comment be included on skin absorption as an important route of entry. He referred to a study by the National Institute for Occupational Safety and Health which measured skin absorption in hairless mice. Dr. Tannenbaum stated that the route of administration can have a major influence on

the tumorigenicity of a chemical. Dr. Huff noted that Dr. C. Maltoni had demonstrated positive effects for benzene by both the inhalation and olive oil gavage exposure routes. Mr. Beliczky said that human risk assessments have been performed for benzene and should be referenced. Dr. Huff responded that additional references would be included on epidemiologic studies and situations of risk assessment.

Dr. Friess moved that the Technical Report on the toxicology and carcinogenesis studies of benzene be accepted with revisions as suggested. Mr. Beliczky seconded the motion, and the report was approved by nine affirmative votes. There was one absention (Dr. Kociba).