Documents of International Meetings and Activities

International Workshop on Toxicology of Benzene, Paris: 9th – 11th November 1976

The International Workshop on the Toxicology of Benzene was held in Paris from 9th to 11th November 1976 under the auspices of the Permanent Commission and International Association on Occupational Health and more specifically organised by its Scientific Committee on Permissible Limits for Airborne Potentially Toxic Chemicals in Working Areas. The organising Committee consisted of Professor Rene Truhaut, Chairman of the Scientific Committee, Professor E. C. Vigliani, Dr. Robert Murray, and Dr. H.G.S. van Raalte.

49 representatives from 16 different countries together with representatives of ILO and WHO participated in the Workshop. Their names are given in Appendix I.

The object of the Workshop was to discuss available information in the fields of experimental toxicology and epidemiology related to benzene exposure with special emphasis on dose-response relationships in workers, particularly with regard to long-term effects of low levels of exposure. The question of exposure of the general population was also mentioned.

Prior to the Workshop the Chairman had circulated a number of documents presented at the ILO meeting of experts on benzene (1967), the report of that meeting, the Convention and Recommendation concerning Protection against Hazards of Poisoning Arising from Benzene adopted by the ILO in 1971 and the IARC Monograph on Benzene. The papers presented at the Workshop were precirculated and covered the following topics:

- metabolism and toxicity of benzene in animals and man
- chromosomal changes in benzene exposure in animals and man
- epidemiological studies of benzene workers
- the scientific/pragmatic basis for the establishment of guidelines for benzene exposure.
- methods of biological monitoring for benzene

The problems of sampling and analysis of air and biological materials were not examined by the Workshop.

A full list of the contributions is given in Appendix 2. The authors of the papers presented at the Workshop were invited to publish them in a journal of their own choice mentioning the fact of their presentation at the Workshop.

Reprints may be requested from:
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Production and Use of Benzene

The situation concerning the production and use of benzene has been well covered by the report of the ILO Expert Committee and the IARC Monograph. Nevertheless it was apparent that the production of benzene as a raw material for chemical synthesis e.g. of styrene, continues to increase, and that benzene, as a natural constituent of crude petroleum, is still in many countries a component of motor spirit. The manufacture and transport of large quantities of benzene therefore entails the risk of exposure and consequently continuing care and vigilance to minimise exposure of those engaged in process work, transport and maintenance.

Benzene Metabolism, Distribution and Elimination

The following summary of the work reported at the Workshop is not intended to be an exhaustive review of all the available knowledge of benzene metabolism, distribution and elimination, but it represents a consensus of the present state of knowledge.

Qualitatively the metabolites of benzene recovered from urine are the same regardless of the route of administration. These include phenol (free and conjugated), catechol, and depending upon dose and species, hydroquinone, tri-hydroxylated benzenes, mercapturic acid and muconic acid. In most studies, both in man and in animals, 20–40% of the administered dose is recovered in urine. An exception to this is a report by Sherwood who observed that 60–70% of benzene inhaled is excreted in urine as conjugated phenols after exposures of one to eight hrs. Except for small amounts of phenyl-glucuronide excreted in bile, the remainder of the administered benzene is exhaled in the breath.

Benzene Metabolism in Vitro

The liver is the organ most active in the metabolism of benzene in vitro. Differential centrifugation of liver homogenate demonstrates that the benzene — metabolizing enzyme system is localised in the microsomal fraction. It has been shown that benzene hydroxylase belongs to the group of mixed function oxidases. The mechanism by which benzene is hydroxylated is shown in Figure 1.

Distribution of Benzene

Benzene is distributed in the body primarily in tissues and organs with a high fat content. Fat and bone marrow display high levels of benzene, spleen and blood relatively low levels, while intermediate levels are seen in liver. In contrast, the metabolites of benzene are low in blood, fat and spleen. Higher levels are observed in liver but the highest levels are seen in the bone marrow.