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Foreword

# International Symposium on the Evaluation of Butadiene and Chloroprene Health Risks

**Abstract**

These proceedings represent nearly all the platform and poster presentations given during the International Symposium on Evaluation of Butadiene and Chloroprene Health Risks, held in Charleston, South Carolina, USA, on September 20–22, 2005. The Symposium was attended by 78 participants representing private industry (37), academia (21), government (11), not-for-profit organizations (5), and consulting (4). The program followed the format of previous symposia on butadiene, chloroprene, and isoprene in London UK (2000) and butadiene and isoprene in Blaine, Washington USA (1995). This format enabled the exchange of significant new scientific results and discussion of future research needs. Isoprene was not evaluated during the 2005 Symposium because of lack of new data. For background information, the reader is referred to the proceedings of the London 2000 meeting for a thorough historical perspective and overview of scientific and regulatory issues concerning butadiene, chloroprene, and isoprene [Chem.-Biol. Interact. (2001) 135–136:1–7]. The Symposium consisted of seven sessions: (1) Introduction and Opening Remarks, (2) Butadiene/styrene-butadiene rubber (SBR)—Process Overview, Exposure and Health Effects/Human Studies; (3) Chloroprene—Process Overview, Exposure and Health Effects/Human Studies; (4) Mode of Action/Key Events; (5) Risk Assessment; (6) Poster Presentations; and (7) Panel Discussion and Future Directions. The Symposium concluded with a discussion by all participants of issues that arose throughout the course of the Symposium. The Proceedings of the Symposium published in this Special Issue are organized according to the Sessions outlined above. The purpose of this foreword is to summarize the presentations and their key findings and recommend future research directions for each chemical.


*Keywords:* 1,3-Butadiene; Beta-chloroprene; Exposure; Rat; Mouse; Humans; Epidemiology; Toxicology; Metabolism; Pharmacokinetics; DNA and hemoglobin adducts; Mode of action; Key events; Risk assessment; Research needs

## 1. Overview

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### *1.1. 1,3-Butadiene*

#### *1.1.1. Introduction*

1,3-Butadiene (BD) is an important industrial chemical used as a monomer in the production of synthetic rubber [2]. BD has been the subject of considerable research regarding metabolism, toxic effects and carcinogenicity to experimental animals, as well as in epidemiological and molecular epidemiological studies of workers exposed to BD during its production and use in synthetic rubber manufacturing. Although many questions remain, the burgeoning mechanistic data generated from research on BD have contributed significantly to improved understanding of the mechanisms underlying the carcinogenicity of BD in laboratory animals. Evaluations of carcinogenic hazard to humans and assessments of risk from exposures to BD have been conducted by a number of national and international agencies, both in North America (e.g. the US Environmental Protection Agency (EPA) and the US National Toxicology Program (NTP) and in Europe (e.g. the International Agency for Research on Cancer (IARC)). Mechanistic information has played a major role in these evaluations. Moreover, research strategies developed during the last decade for understanding mechanisms of BD carcinogenicity have been shown to be applicable to the BD congeners, chloroprene and isoprene.

#### *1.1.2. Epidemiology*

The investigators from the University of Alabama at Birmingham (UAB) presented findings based on an additional 10 years of mortality follow-up (through 1998) for the male SBR worker cohort [3]. There was a clear exposure–response trend for all leukemias combined in relation to both cumulative and peak exposures to BD. The UAB investigators also conducted analyses using the new WHO disease classification scheme for leukemias and lymphomas. Based on this WHO classification, myeloid neoplasms were most strongly associated with peak exposures, while lymphoid neoplasms showed an opposite pattern, i.e. a stronger association with cumulative versus peak exposure to BD.

Overall, the UAB findings represent the effect of BD exposure in the presence of styrene and other SBR chemicals (e.g. dimethyldithiocarbamate, DMDTC). The UAB investigators ruled out styrene as an independent risk factor for leukemia, but because of the high correlation between BD and styrene exposure in the cohort, a possible role for styrene as a co-exposure factor could not be ruled out. Similar conclusions were reached for DMDTC, except that it was less clear as to whether or not DMDTC exposure is associated independently with leukemia. Finally, it was suggested that the mortality results for workers in the polymer and monomer industries may be more similar than previously thought for leukemia among those employed prior to 1950.

Mortality results for female workers employed in the SBR industry from 1944 to 1991 were to be presented at the Symposium. However, results were unavailable due to delays in obtaining mortality follow-up information at the Canadian plant. The UAB investigators anticipate approximately 30–35 lymphohematopoietic cancer deaths among about 5000 female SBR workers; this study will contribute significant new information, once completed [4].

The UAB investigators also presented results from a comparison of estimated versus measured BD exposure concentrations at the Canadian Sarnia plant (a latex operation) [5]. This plant had collected data from a number of industrial hygiene measurements for BD from the late 1970s onward. The results indicated that, before 1984, estimated concentrations were lower than measured concentrations, whereas after 1984 an opposite pattern was observed (i.e. estimated concentrations came out higher than the measured concentrations). There was reasonably good agreement between measured versus estimated BD exposures at lower concentrations across time, but at higher exposures the estimates tended to be less than the measured values.

Tsai [6] reported on the investigation of hematological parameters in BD monomer workers at two Shell facilities in Texas. These workers were exposed to BD concentrations of 4.55 ppm during 1979–1996 and 0.25 ppm from 1997 to 2003. These data showed no increase in adverse hematological parameters in relation to BD exposure. These findings are consistent with those of other studies of hematological parameters in BD-exposed workers reported in the literature.

Several studies of BD concentrations in ambient air in Texas, USA [7] and in Japan [8] were presented. These studies showed trends towards decreasing ambient BD concentrations over time, with current concentrations in the ppb range. Additionally, the Texas Commission on Environmental Quality (TCEQ) presented an analysis of mortality (1993–2002) and cancer incidence (1995–2001) patterns in several areas of Texas with sources of BD emission and elevated BD ambient air concentrations [7]. These results showed no increase in cancer incidence or mortality, with the exception of a