資料２－２

トルエンの発がん性等に関する主な外国機関の報告書（抜粋）

1　　US.NTP（1990）

2　　IARC　（1999）

3　　US.EPA　（2005）

NTP (1990), *NTP TECHNICAL REPORT ON THE TOXICOLOGY AND CARCINOGENESIS STUDIES OF TOLUENE (CAS NO. 108-88-3) IN F344/N RATS AND B6C3Fi MICE (INHALATION STUDIES)*, pp.14-15

Toluene is rapidly metabolized primarily in the liver (SRI, 1980; Slooff and Blokzijl, 1988). In rats, rabbits, and humans, 25%-40%of an oral or inhaled dose is excreted unchanged in exhaled air, and 608-758 of the dose is converted to ben- zoic acid and excreted in urine, primarily as hip-puric acid; smaller amounts are excreted as the sulfate or glucuronide conjugate of benzoic acid (Figure 1) (von Oettingen et al., 1942a; Srbova and Teisinger, 1952; Smith et al., 1954; El Masry et al., 1956; Daly et al., 1968; Bakke and Scheline, 1970; Angerer, 1976; Pfaffli et al., 1979;Toftgard and Gustafsson, 1980;Van Doorn et al., 1980;Woiwode and Drysch, 1981;Baelum et al., 1987).

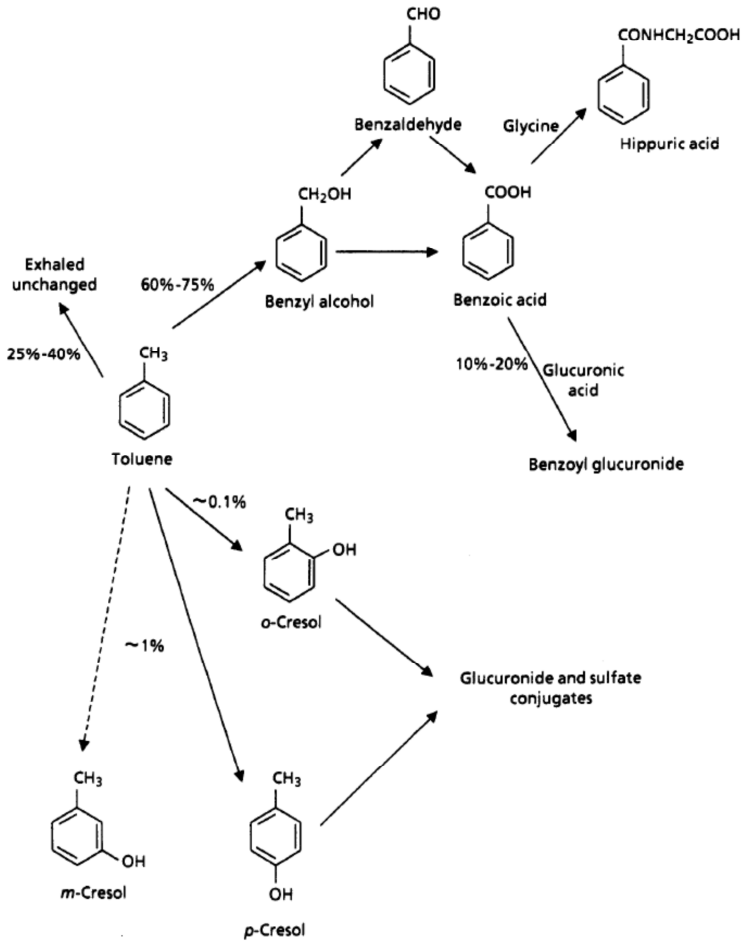

FIGURE 1. METABOLISM OF TOLUENE IN HUMANS AND ANIMALS
(taken from IPCS, 1985, and modified)

IARC (1999), "TOLUENE," in *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 71*, pp.855

5.2 Human carcinogenicity data

Toluene was mentioned as an exposure in eight studies. Two were community-based case–control studies, one of which involved brain cancer and one involved several types of cancer. Of the six industry-based studies, three were analysed as cohort studies and three were configured as nested case–control studies of one or a few types of cancer. In two of the studies, that of shoe-manufacturing workers in the United States and particularly that of Swedish rotogravure printers, it was believed that toluene was the predominant exposure; in the other studies, there were probably concomitant exposures. Cancers of most sites were not significantly associated with toluene exposure in any study. Stomach cancer mortality was significantly elevated in the Swedish rotogravure printers study, it was slightly, though not significantly, elevated in two other studies, and it was not associated at all in a fourth. Rates of lung cancer were significantly elevated in the cohort of shoe manufacturers and in the Swedish cohort of rotogravure printers, but was not associated at all in two other studies. Colorectal cancer was significantly elevated in the Swedish rotogravure printers study and in the Canadian case–control study, and colon cancer was nonsignificantly elevated in the shoe manufacturers cohort. While results on leukaemias and lymphomas generally showed no association, these were based on small numbers.

Considering the multiple exposure circumstances in most studies and the weak consistency of findings, these results are not strong enough to conclude that there is an association.

5.3 Animal carcinogenicity data

Toluene was tested for carcinogenicity by inhalation exposure in one study in mice and in one study in rats. No significant increase in the incidence of tumours was observed.

Repeated application of toluene to the skin of mice did not result in an increased incidence of skin tumours.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of toluene.

There is *evidence suggesting lack of carcinogenicity* of toluene in experimental animals.

Overall evaluation

Toluene is *not classifiable as to its carcinogenicity to humans (Group 3).*

US.EPA (2005), in *TOXICOLOGICAL REVIEW OF TOLUENE (CAS No. 108-88-3)*, pp.86

5.3. CANCER ASSESSMENT

Under the Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005), there is inadequate information to assess the carcinogenic potential of toluene because studies of humans chronically exposed to toluene are inconclusive, toluene was not carcinogenic in adequate inhalation cancer bioassays of rats and mice exposed for life (CIIT, 1980; NTP, 1990; Huff, 2003), and increased incidences of mammary cancer and leukemia were reported in a lifetime rat oral bioassay at a dose level of 500 mg/kg-day but not at 800 mg/kg-day (Maltoni et al., 1997).

Toluene has generally not been genotoxic in short-term testing protocols. A quantitative assessment of carcinogenic potential was not performed.