

BENZIDINE-BASED DYES (Group 2A)

A. Evidence for carcinogenicity to humans (*inadequate*)

The epidemiological data were inadequate to evaluate the carcinogenicity of three benzidine-based dyes, Direct Black 38, Direct Blue 6 and Direct Brown 95, to humans. However, a study of silk dyers and painters who had had multiple exposure to benzidine-based and other dyes indicated that those exposures were strongly associated with the occurrence of bladder cancer¹.

B. Evidence for carcinogenicity to animals (*sufficient* for technical-grade Direct Black 38, technical-grade Direct Blue 6 and technical-grade Direct Brown 95)

Direct Black 38 was tested for carcinogenicity in mice by administration in drinking-water, producing liver and mammary tumours. Commercial Direct Black 38 produced hepatocellular carcinomas within 13 weeks after administration in the diet to rats and small numbers of carcinomas in the urinary bladder, liver and colon after administration to rats in drinking-water¹.

In a single study, commercial Direct Blue 6 produced hepatocellular carcinomas in rats within 13 weeks after its oral administration.

Commercial Direct Brown 95 produced neoplastic nodules in the livers of 4/8 female rats, and a hepatocellular carcinoma in one, after its oral administration in a single study

terminated after 13 weeks. The finding of preneoplastic lesions after such a short exposure prior indicates a carcinogenic effect similar to that of Direct Black 38 and Direct Blue 6¹.

C. Other relevant data

Benzidine-based dyes are structurally related to benzidine, exposure to which is causally associated with cancer in humans (see p. 123), and commercial material may contain small amounts of benzidine. Commercial Direct Black 38 may contain small quantities of 4-aminobiphenyl (see p. 91) and 2,4-diaminobenzene (the hydrochloride of which is chrysoidine [see p. 169])¹.

Benzidine has been detected in the urine of workers exposed to benzidine-based azo dyes. No data were available on the genetic and related effects of Direct Black 38, Direct Blue 6 or Direct Brown 95, in humans¹.

In experimental animals, Direct Black 38, Direct Blue 6 and Direct Brown 95 undergo reduction of the azo bonds with the appearance in the urine of benzidine and monoacetylbenzidine. The reductive cleavage of the azo bond has been attributed to the activities of intestinal microflora and/or liver azoreductases²

Direct Black 38 was mutagenic to bacteria. Urine from rodents treated with Direct Black 38 was mutagenic to bacteria in the presence of an exogenous metabolic system, and human intestinal microflora metabolized Direct Black 38 to highly mutagenic metabolites².

DNA adducts (including covalent binding products of benzidine) have been described in the livers of rats treated with Direct Blue 6 *in vivo*. Direct Blue 6 is mutagenic to bacteria only in the presence of an exogenous metabolic system and the cofactor flavine mononucleotide².

Direct Brown 95 induced unscheduled DNA synthesis in rat hepatocytes in an *in-vivo/in-vitro* assay but not in hepatocytes *in vitro*. It was mutagenic to bacteria in the presence of an exogenous metabolic system; this activity was enhanced by the cofactor flavine mononucleotide. The urine from rats treated with Direct Brown 95 was mutagenic to bacteria in the presence of an exogenous metabolic system².

References

¹IARC *Monographs*, 29, 295-310, 311-320, 321-330, 1982

²IARC *Monographs, Suppl. 6*, 275-281, 1987