DISPERSE YELLOW 3

Disperse Yellow 3 was evaluated by a previous working group (IARC, 1975)[1]. Since that time, new data have become available, and these have been incorporated into the monograph and taken into consideration in the present evaluation.

1. Chemical and Physical Data

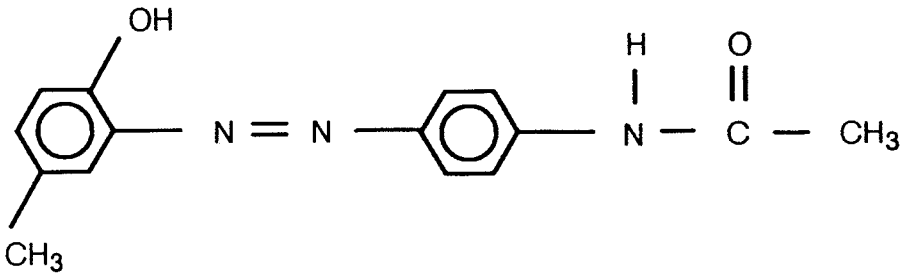
Disperse Yellow 3 is produced and used as a mixture of chemicals (see section 1.4). Sections 1.1-1.3 give the chemical and physical characteristics of the principal colour component or of the dye.

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 2832-40-8
(Replaced CAS Reg. Nos 12227-01-9, 12238-70-9 and 66057-65-6)
Chem. Abstr. Name: Acetamide, N-{4-[(2-hydroxy-5-methylphenyl)azo]phenyl}-
IUPAC Systematic Names: 4′-[(6-Hydroxy-*meta*-tolyl)azo]acetanilide; CI Disperse Yellow 3
Colour Index No.: 11855
Synonyms: 4-Acetamido-2′-hydroxy-5′-methylazobenzene; CI Solvent Yellow 77; CI Solvent Yellow 92; CI Solvent Yellow 99; 4′-[(2-hydroxy-5-methylphenyl)azo]acetanilide; 4′-(6-hydroxy-*meta*-tolylazo)acetanilide

[1]The earlier evaluation of the carcinogenicity of this compound was based on the results of a study in experimental animals by Boyland *et al.* (1964), which was subsequently found to concern an isomer of Disperse Yellow 3.

1.2 Structural and molecular formulae and molecular weight of the principal component



$C_{15}H_{15}N_3O_2$ Mol. wt: 269.30

1.3 Chemical and physical properties of Disperse Yellow 3

(*a*) *Melting-point*: Decomposes at 192-195°C (National Toxicology Program, 1982); 195°C (Patterson & Sheldon, 1960)

(*b*) *Spectroscopy data*: Infrared (prism [1452A]; prism-FT [969A]) and ultraviolet spectral data have been reported (Pouchert, 1981; National Toxicology Program, 1982; Pouchert, 1985).

(*c*) *Solubility*: Soluble in acetone, ethanol and benzene (Society of Dyers and Colourists, 1971a); soluble in water at 1.5-6.1 mg/l at 60°C (Patterson & Sheldon, 1960)

1.4 Technical products and impurities

Trade Names: Acetamine Yellow CG; Acetate Fast Yellow G; Acetoquinone Light Yellow 4JLZ; Altco Sperse Fast Yellow GFN New; Amacel Yellow G; Atrisil Direct Yellow G; Atrisil Yellow G; Atrisil Yellow 2GN; Calcosyn Yellow GCN; Celliton Discharge Yellow GL; Celliton Fast Yellow G; Celliton Fast Yellow GA; Celliton Fast Yellow GA-CF; Celliton Yellow G; Celutate Yellow GH; Cibacet Yellow GBA; Cibacet Yellow 2GC; Cilla Fast Yellow G; Diacelliton Fast Yellow G; Disperse Yellow G; Disperse Yellow Z; Dispersol Fast Yellow G; Dispersol Printing Yellow G; Dispersol Yellow A-G; Dispersyl Fast Yellow J; Durgacet Yellow G; Durosperse Yellow G; Eastone Yellow GN; Esteroquinone Light Yellow 4JL; Fenacet Fast Yellow G; Hispacet Fast Yellow G; Hisperse Yellow G; Interchem Acetate Yellow G; Interchem Hisperse Yellow GH; Intrasperse Yellow GBA; Intrasperse Yellow GBA Extra; Kayalon Fast Yellow G; Kayaset Yellow G; KCA Acetate Fast Yellow G; Lurafix Yellow 142; Microsetile Yellow GR; Miketon Fast Yellow G; Nacelan Fast Yellow CG; Navicet Yellow G; Navilene Yellow G; Novalon Yellow 2GN; Nyloquinone Yellow 4J; Ostacet Yellow P2G; Palacet Yellow GN; Palanil Yellow G; Pamacel Yellow G-3; Perliton Yellow G; Reliton Yellow C; Resiren Yellow TG; Safaritone Yellow G; Serinyl Hosiery Yellow GD; Seriplas Yellow GD; Serisol Fast Yellow GD; Setacyl Yellow G; Setacyl Yellow 2GN; Setacyl Yellow P 2GL; Silotras Yellow TSG; Sumiplast Yellow FC; Supracet Fast Yellow G; Synten Yellow 2G; Terasil Yellow GBA Extra; Terasil Yellow 2GC; Tertranese Yellow N-2GL; Transetile Yellow P-GR; Tuladisperse Fast Yellow 2G; Vonteryl Yellow G; Vonteryl Yellow R; Yellow Reliton G; Yellow Z

Analysis of a commercial batch of Disperse Yellow 3 before formulation indicated approximately 87.6% dyestuff, 7% water, 4% sodium chloride and 1% sodium carbonate. Several impurities were detected but were not identified (National Toxicology Program, 1982). In commercial formulations, the dyestuff content is approximately 42-44%.

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

Disperse Yellow 3 was first prepared by Fischer and Müller (1926) by coupling diazotized 4-acetamidoaniline with *para*-cresol, but it is not known whether this is the method used for commercial production.

Large-scale production of Disperse Yellow 3 in the USA was first reported in 1941 (US Tariff Commission, 1945). US production of Disperse Yellow 3 in 1972, 1975, 1979 and 1980 was 1280, 1420, 1460 and 930 tonnes, respectively (US Tariff Commission, 1974; US International Trade Commission, 1977, 1980, 1981). Separate figures were not reported after 1980. Production of all Disperse Yellow dyes ranged from a low of approximately 760 tonnes in 1985 to a high of approximately 1490 tonnes in 1983 (US International Trade Commission, 1983-1988).

As many as 11 companies may manufacture this dye in western Europe, with an estimated annual total production of 1 million kg. Production of Disperse Yellow 3 by three Japanese manufacturers was 82 tonnes 1972 and 44 tonnes in 1973 (IARC, 1975). This dye is also manufactured in India.

(*b*) *Use*

Disperse Yellow 3 is a monoazo pigment dye of low aqueous solubility, used to colour nylon, polyvinyl chloride and acrylic fibres, wools and furs, cellulose acetate, polystyrene and other thermoplastics. Finished products containing this material include clothing, hosiery and carpeting (Society of Dyers and Colourists, 1971b; Foussereau *et al.*, 1972; National Toxicology Program, 1982).

(*c*) *Regulatory status and guidelines*

No regulatory standard or guideline has been established for Disperse Yellow 3.

2.2 Occurrence

(*a*) *Natural occurrence*

Disperse Yellow 3 is not known to occur as a natural product.

(*b*) *Occupational exposure*

Approximately 17 000 workers were estimated to be potentially exposed to Disperse Yellow 3 in the USA in 1972-74 (National Institute for Occupational Safety and Health, 1977).

(*c*) *Water and sediments*

Disperse Yellow 3 was identified in wastewater and mud samples from the Coosa River Basin, Atlanta, GA, USA. The Coosa River Basin and its tributaries carry approximately 50% of all carpet dyeing wastewater in the USA. Concentrations of Disperse Yellow 3 in samples of waste treatment plant influents and effluents ranged from none detected to 436 ppb (μg/l). Concentrations in mud samples ranged from 140 to 455 ppb (μg/kg; Tincher & Robertson, 1982).

(*d*) *Other*

Disperse Yellow 3 was identified in dichloromethane extracts of 51 out of 52 beige stockings and pantihose collected in Belgium, France, the Federal Republic of Germany, Italy, Portugal, Romania and the UK (Berger *et al.*, 1984).

2.3 Analysis

Selected methods for the analysis of Disperse Yellow 3 are given in Table 1.

Table 1. Methods for the analysis of Disperse Yellow 3

Sample matrix	Sample preparation[a]	Assay procedure[a]	Limit of detection	Reference
Air	Collect on filter; extract with solvent; separate by TLC	Spectrophotometry	0.5 mg/m^3	Zenina *et al.* (1986)
Wastewater	Adsorb on macroreticular resin; recover by backwashing with solvents	HPLC	0.1 ppm (mg/l)	Tincher & Robertson (1982)
Hosiery	Extract with dichloromethane; evaporate; dissolve in dichloromethane	TLC	Not reported	Berger *et al.* (1984)
Dye lots	Extract with hexane/-ethanol; evaporate; dissolve in dichloromethane	TLC	Not reported	Foussereau & Dallara (1986)
Hand skin wash-off samples	Extract with ethanol/water; concentrate; resuspend with solvent; separate by TLC	Spectrophotometry	Not reported	Zenina *et al.* (1986)
Dyestuffs	Extract with solvent	TLC	Not reported	Foussereau *et al.* (1972)

[a]Abbreviations: TLC, thin-layer chromatography; HPLC, high-performance liquid chromatography

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

Oral administration

Mouse: Groups of 50 male and 50 female B6C3F$_1$ mice, six weeks of age, were fed diets containing 2500 or 5000 mg/kg Disperse Yellow 3 (87.6% dye [impurities unspecified]) for 103 weeks and were observed for two additional weeks. Groups of 50 male and 50 female mice served as untreated controls. All animals were killed at 111 weeks of age. Mean body weights of mice of each sex tended to be lower those of than controls; survival was comparable in all groups. The incidence of hepatocellular adenomas was significantly ($p < 0.001$, Cochran-Armitage test) increased in treated females: controls, 0/50; low-dose, 6/50; high-dose, 12/50. The incidence of hepatocellular carcinomas was also increased in treated females, but not significantly (control, 2/50; low-dose, 4/50; high-dose, 5/50). A significantly ($p = 0.019$, Cochran-Armitage test) increased incidence of alveolar/bronchiolar adenomas was observed in male mice: control, 2/50; low-dose, 6/49; high-dose, 9/49; and a significant ($p = 0.032$, Cochran-Armitage test) increase in the incidence of malignant lymphomas was observed in female mice (control, 10/50; low-dose, 16/50; high-dose, 19/50; National Toxicology Program, 1982).

Rat: Groups of 50 male and 50 female Fischer 344/N rats, six weeks of age, were fed diets containing 5000 or 10 000 mg/kg of diet Disperse Yellow 3 (87.6% dye [impurities unspecified]) for 103 weeks and were observed for one additional week. Groups of 50 male and 50 female rats served as untreated controls. All animals were killed at 111 weeks of age. Mean body weights of treated rats of each sex were lower than those of controls; survival in male and female treated rats was significantly longer than that in corresponding controls. A significant ($p = 0.014$, Cochran-Armitage test) increase in the incidence of neoplastic nodules in the liver [adenomas (Maronpot *et al.*, 1986)] was observed in treated males: controls, 1/49; low-dose, 15/50; high-dose, 10/50. The incidence of foci of altered hepatocytes in males, predominantly composed of vacuolated, clear and eosinophilic cells, was dose-related (controls, 1/49; low-dose, 4/50; high-dose, 17/50). Stomach tumours were also observed in treated males, with one adenocarcinoma and a sarcoma in a high-dose male and one squamous-cell papilloma, one fibrosarcoma, one adenoma and one mucinous adenocarcinoma in animals in the low-dose group. This incidence was not significantly higher than that in controls. Analysis by a survival-adjusted test did not change the results (National Toxicology Program, 1982).

3.2 Other relevant biological data

(*a*) *Experimental systems*

(i) *Absorption, distribution, excretion and metabolism*

No data were available to the Working Group.

(ii) *Toxic effects*

In 14-day studies in which Disperse Yellow 3 was incorporated into the diet of Fischer 344 rats and B6C3F$_1$ mice, rats died at concentrations of 50 000 ppm (mg/kg) and higher, and mice at a concentration of 100 000 ppm. Splenic enlargement was noted in mice given 25 000 ppm and more (National Toxicology Program, 1982).

Of Fischer 344 rats and B6C3F$_1$ mice fed Disperse Yellow 3 (1250 to 20 000 ppm) in the diet for 13 weeks and then killed, 1/10 high-dose female rats died; no other death appeared to be related to treatment. Weight gains were depressed in rats and mice receiving diets containing 10 000 ppm or more. In rats, proliferative lesions of the thyroid follicular cells were observed as well as vacuolar degeneration of the pars distalis of the pituitary gland, haemosiderosis in the spleen and pigment deposition in the kidney. In mice, haemosiderosis of the renal tubular epithelium and spleen and cytoplasmic swelling of centrilobular hepatocytes were related to treatment (National Toxicology Program, 1982).

(iii) *Effects on reproduction and prenatal toxicity*

No data were available to the Working Group.

(iv) *Genetic and related effects*

Disperse Yellow 3 was mutagenic to several frame-shift mutants of *Salmonella typhimurium* in the presence and absence of an exogenous metabolic system from Aroclor 1254-induced rat liver or Syrian hamster liver; however, it was not mutagenic to strain TA1535 (Cameron *et al.*, 1987; Zeiger *et al.*, 1988). In one of the studies, it was mutagenic to TA100 only in the presence of a metabolic system from Syrian hamsters (Cameron *et al.*, 1987).

Disperse Yellow 3 was reported to cause unscheduled DNA synthesis in primary cultures of rat hepatocytes [details not given] (Tennant *et al.*, 1987a). In one study, it was weakly mutagenic at the TK locus in mouse lymphoma cells in culture in the absence of an exogenous metabolic system (Cameron *et al.*, 1987); in another, it was mutagenic in the presence of an exogenous metabolic system (McGregor *et al.*, 1988). It induced sister chromatid exchanges, but not chromosomal aberrations in the Chinese hamster CHO cell line in the absence of an exogenous metabolic system from Aroclor 1254-induced rat liver (Tennant *et al.*, 1987b).

(*b*) *Humans*

(i) *Absorption, distribution, excretion and metabolism*

No data were available to the Working Group.

(ii) *Toxic effects*

Textiles coloured with dyes containing Disperse Yellow 3 caused allergic, contact-type dermatitis (Dobkevitch & Baer, 1947; Cronin, 1968; Foussereau *et al.*, 1971, 1972; Conde-Salazar *et al.*, 1984). Skin tests with isolated dyes indicated that Disperse Yellow 3 is a contact allergen (Cronin, 1968; Kousa & Soini, 1980; Hausen & Schulz, 1984).

(iii) *Effects on reproduction and prenatal toxicity*

No data were available to the Working Group.

(iv) *Genetic and related effects*

No data were available to the Working Group.

3.3 Case reports and epidemiological studies of carcinogenicity to humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Exposure data

Disperse Yellow 3 is a monoazo pigment dye which has been produced in significant quantities since the 1940s to colour fabrics and plastics. There is potentially widespread exposure to Disperse Yellow 3 because of its use in clothing, hosiery and carpets. No data on occupational exposure levels were available.

4.2 Experimental carcinogenicity data

Disperse Yellow 3 was tested for carcinogenicity by oral administration in one strain of mice and in one strain of rats. In female mice, it produced increases in the incidences of hepatocellular tumours and malignant lymphomas; in male mice, the incidence of alveolar/bronchiolar adenomas was increased. In rats, it produced an increase in the incidence of hepatocellular adenomas in males.

4.3 Human carcinogenicity data

No data were available to the Working Group.

4.4 Other relevant data

In a single study, Disperse Yellow 3 induced sister chromatid exchange but not chromosomal aberrations in Chinese hamster cells in culture. It was mutagenic to mouse cells in culture. Disperse Yellow 3 was mutagenic to bacteria in the presence and absence of an exogenous metabolic system.

Summary table of genetic and related effects of Disperse Yellow 3

Nonmammalian systems													**Mammalian systems**																													
Proka-ryotes		Lower eukaryotes				Plants			Insects				*In vitro*														*In vivo*															
													Animal cells								Human cells								Animals							Humans					
D	G	D	R	G	A	D	G	C	R	G	C	A	D	G	S	M	C	A	T	I	D	G	S	M	C	A	T	I	D	G	S	M	C	DL	A	D	S	M	C	A
	+													+	+[1]		−[1]																									

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbols indicate the consensus of the Working Group with regard to the results for each endpoint:

\+ considered to be positive for the specific endpoint and level of biological complexity

+[1] considered to be positive, but only one valid study was available to the Working Group

−[1] considered to be negative, but only one valid study was available to the Working Group

4.5 Evaluation[1]

There is *limited evidence* for the carcinogenicity of Disperse Yellow 3 in experimental animals.

No data were available from studies in humans on the carcinogenicity of Disperse Yellow 3.

Overall evaluation

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

5. References

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[1]For description of the italicized terms and criteria for making the evaluation, see Preamble, pp. 25-29.

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