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Occupational Exposures of Hairdressers and Barbers and Personal Use of Hair Colourants; Some Hair Dyes, Cosmetic Colourants, Industrial Dyestuffs and Aromatic Amines

Summary of Data Reported and Evaluation

N,N-Dimethylaniline

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OCCUPATIONAL EXPOSURES OF HAIRDRESSERS AND BARBERS AND PERSONAL USE OF HAIR COLOURANTS
Occupation as a hairdresser (Group 2A)
Personal use of hair colourants (Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 43)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Since the early twentieth century, hairdressers have made use of a wide range of products, including hair colourants and bleaches, shampoos and conditioners, hair styling preparations and nail and skin care products. Several thousand chemicals are found in formulations of these products. Barbers generally cut only men's hair and make limited use of some of the above products, such as hair dyes, in their work.

Hair colourants are classified as permanent (primarily aromatic amines and aminophenols with hydrogen peroxide), semi-permanent (nitro-substituted aromatic amines, aminophenols, aminoanthraquinones and azo dyes) and temporary (high-molecular-weight or insoluble complexes and metal salts, such as lead acetate). The numerous individual chemicals used in hair colourants have varied over time. Only permanent and semi-permanent hair colourants are used to a significant extent by hairdressers, while consumers at home use any of the three types.

Hairdressers may also be exposed to volatile solvents, propellants and aerosols (from hair sprays), formaldehyde (an antibacterial agent), methacrylates (in nail care products) and trace quantities of nitrosamines, which have been reported in many hair care products.

It is estimated that there are several million hairdressers and barbers worldwide. Few exposure measurements are available. Approximately 35% of women and 10% of men in Europe, Japan and the USA use hair colourants.

5.2 Human carcinogenicity data

There is consistent evidence from five (all from Europe) of the six large cohort studies of an excess risk for cancer of the urinary bladder in male hairdressers and barbers. The increase was significant in three studies, and the overall risk relative to that in the general population amounted to about 1.6. In 12 case-control studies, male hairdressers and barbers had an overall relative risk of about 1.2; smoking was adjusted for in three of these case-control studies, conducted in North America, and these did not show an overall excess risk. The risk for cancer of the urinary bladder was less consistently increased in corresponding studies in women: positive results were obtained in five cohort studies and negative results in three; none was significant. An overall relative risk for lung cancer of about 1.3 was seen among male and female hairdressers in cohort studies. One case-control study from Australia found a significant excess risk for non-Hodgkin's lymphoma among female hairdressers; a nonsignificant excess of this malignancy was noted in one cohort study from Denmark in men and women and in one case-control study from the USA in men.

One cohort study, from Finland, found a significant excess risk for ovarian cancer; two other studies, in the USA and Japan, found nonsignificant risks, and a fourth, in Switzerland, showed no effect. Excess risks were seen among male hairdressers for cancers of the buccal cavity and pharynx and prostate in one study from Switzerland; increased risks for cancers at these sites were not reported in another cohort study, from the United Kingdom.

Personal use of hair colourants has been studied in seven case-control studies of cancer of the urinary bladder. Overall, these do not indicate an excess risk; however, one study from Denmark found an association with personal use of brilliantine, although it had methodological limitations. Following a report in 1976 of an excess of breast cancers among hair dye users in New York, USA, six case-control studies and one cohort study examined this subject. None found evidence of a significant excess among hair dye users overall. One case-control study of non-Hodgkin's lymphoma from Iowa and Minnesota showed a significantly increased risk among male users of hair colouring products. A second case-control study, from Nebraska, showed an excess risk for this malignancy among female users of hair colourants but showed no excess among a smaller number of male users. The case-control study from Nebraska also found a significant excess of multiple myeloma among female users of permanent hair dyes, and another study from Iowa reported a nonsignificant excess of this malignancy in male users of hair colourants. One cohort study in the USA showed no excess risk among hair dye users for all lymphomas combined. One case-control study of neuroblastoma and one of Wilms' tumour showed significantly increased risks for the offspring of mothers who had used hair dyes during pregnancy. Single studies have reported significant excess risks for Hutchinson's melanotic freckle, Hodgkin's disease, leukaemia, malignant tumours of the brain and cancers of the salivary gland, cervix and lower female genital tract. Other studies showed no such excesses.

The higher prevalence of smokers reported among male hairdressers and barbers in some studies is consistent with the overall excess of lung cancer but cannot readily explain the magnitude of the increase in risk for cancer of the urinary bladder in the European cohort studies. In particular, studies in Switzerland and Denmark have shown significant excesses of cancer of the urinary bladder unaccompanied by appreciable excesses of lung cancer, which further weigh against smoking as the sole explanation for the overall excess. Specific exposures of hairdressers and barbers have not been evaluated in epidemiological studies.

5.3 Animal carcinogenicity data

Various commercially available hair dye formulations and various laboratory preparations of hair dyes were tested for carcinogenicity in mice or rats by skin application in many studies and by subcutaneous injection in a single study in rats. In one study by skin application in rats, a particular formulation was associated with an increased incidence of pituitary adenomas in females. The other studies either showed no increased incidence of tumours at any site or were inadequate for evaluation.

5.4 Other relevant data

Contact dermatitis is a common clinical dermatological problem in hairdressers. Because hairdressers use a wide variety of multicomponent chemical products, it is difficult to determine the specific etiology of their dermatitis, although cutaneous nickel allergy and atopic status have been suggested to play a role. Moreover, many of the products used contain both irritants and sensitizers. Pulmonary toxicity has been associated with the use of hair lacquer by consumers and hairdressers.

No study has reported a significant excess of congenital malformations, early or late fetal death or low birth weight among the offspring of male or female barbers or hairdressers.

No increase was observed in chromosomal aberration frequencies in the lymphocytes of humans exposed to commercial hair colourants which included hydrogen peroxide application. In this and another study, no increase in sister chromatid exchange frequency was found.

A number of different commercial permanent and semipermanent hair colourants were tested for their mutagenic activity *in vitro*. Many were mutagenic to bacteria. Less than half of the preparations applied to rats resulted in the excretion of bacterial mutagens in urine. Application of a semipermanent and an oxidation dye colourant topically to male rats had no effect on the reproductive performance of the treated rats and did not induce heritable translocations, as judged by a mating protocol.

5.5 Evaluation

There is *limited evidence* that occupation as a hairdresser or barber entails exposures that are carcinogenic.

There is *inadequate evidence* that personal use of hair colourants entails exposures that are carcinogenic.

Overall evaluations

Occupation as a hairdresser or barber entails exposures that are *probably carcinogenic (Group 2A)*.

Personal use of hair colourants *cannot be evaluated as to its carcinogenicity (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

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CI ACID ORANGE 3
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 121)
CAS No.: 6373-74-6
Chem. Abstr. Name: 5-[(2,4-Dinitrophenyl)amino]-2-(phenylamino)benzene-sulfonic acid, monosodium salt

5. Summary of Data Reported and Evaluation

5.1 Exposure data

CI Acid Orange 3 is used to a limited extent as a dye in semi-permanent hair colouring products and in the dyeing of textiles.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

CI Acid Orange 3 was tested for carcinogenicity by gavage in one study in mice and in one study in rats. In mice, there was no significant increase in the incidence of tumours. A significant increase in the incidence of transitional-cell carcinomas of the renal pelvis was observed in female rats given the high dose. The data on high-dose male rats could not be evaluated owing to their poor survival.

5.4 Other relevant data

CI Acid Orange 3 caused renal toxicity in rats and mice. It was mutagenic to bacteria.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of CI Acid Orange 3.

There is *limited evidence* in experimental animals for the carcinogenicity of CI Acid Orange 3.

Overall evaluation

CI Acid Orange 3 is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- Acid Fast Yellow AG
- Acid Fast Yellow E 5R
- Acid Leather Light Brown G
- 2-Anilino-5-(2,4-dinitroanilino)benzenesulfonic acid, monosodium salt
- Acid Orange 3

- Acid Yellow E
- Airedale Yellow E
- Amido Yellow E
- Amido Yellow EA
- Amido Yellow EA-CF
- Anthralan Yellow RRT
- CI No. 10385
- Coranil Brown H EPS
- Derma Fur Yellow RT
- Derma Yellow P
- Dimacide Yellow N-5RL
- Duasyn Acid Yellow RRT
- Elbenyl Orange A-3RD
- Erio Fast Yellow AE
- Erio Fast Yellow AEN
- Erio Yellow AEN
- Erionyl Yellow E-AEN
- Fast Light Yellow E
- Fenalan Yellow E
- Heliacid Light Yellow 4R
- Intranyl Orange T-4R
- Kiton Fast Yellow A
- Lanaperl Yellow Brown GT
- Light Fast Yellow ES
- Lissamine Fast Yellow AE
- Lissamine Fast Yellow AES
- Lissamine Yellow AE
- Multacid Yellow 3R
- Multicuer Brown MPH
- Nailamide Yellow Brown E-L
- Nylocrom Yellow 3R
- Nylomine Acid Yellow B-RD
- Nylosan Yellow E-3R
- Polan Yellow E-3R
- Sellacid Yellow AEN
- Sodium 4-(2,4-dinitroanilino)diphenylamine-2-sulfonate
- Solanile Yellow E
- Sulfacid Light Yellow 5RL
- Superian Yellow R
- Tectilon Orange 3GT
- Tertracid Light Yellow 2R
- Unitertracid Light Yellow RR
- Vondacid Fast Yellow AE
- Vondacid Light Yellow AE
- Xylene Fast Yellow ES

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HC BLUE No. 1
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 129)
CAS No.: 2784-94-3
Chem. Abstr. Name: 2,2'-([4-(Methylamino)-3-nitrophenyl]imino)bis(ethanol)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

HC Blue No. 1 was used as a semipermanent hair dye until the mid-1980s, when its production and use were discontinued.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

HC Blue No. 1 was tested for carcinogenicity by administration in the diet in two studies in mice, one of which was restricted to females, and in one study in male and female rats. In one study in male and female mice and in several experiments in the study of females, it significantly increased the incidence of hepatocellular adenomas and/or carcinomas in mice of each sex and increased the incidence of thyroid follicular-cell adenomas in males. An increase in the combined incidence of pulmonary adenomas and carcinomas was seen in female but not in male rats.

5.4 Other relevant data

Commercial samples of HC Blue No. 1 bound to DNA and induced mutation in bacteria. They induced DNA damage, gene mutation and chromosomal anomalies and inhibited intercellular communication in cultured mammalian cells.

Purified samples of HC Blue No. 1 did not bind to DNA or induce mutation in bacteria. They did not induce mitotic recombination in yeasts and did not induce mutation in insects. They induced DNA damage, sister chromatid exchange and, weakly, gene mutation but not chromosomal aberrations in cultured mammalian cells. DNA damage was not induced in cultured human cells (HeLa). Micronuclei were induced in the bone marrow of female mice of one strain exposed *in vivo*.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of HC Blue No. 1.

There is *sufficient evidence* in experimental animals for the carcinogenicity of HC Blue No. 1.

Overall evaluation

HC Blue No. 1 is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- N^4,N^4-Bis(2-hydroxyethyl)-N^1-methyl-2-nitro-*para*-phenylenediamine
- HC Blue 1
- HC Blue Number 1
- 2,2'-([4-(Methylamino)-3-nitrophenyl]imino)di(ethanol)

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HC BLUE No. 2
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 143)
CAS No.: 33229-34-4
Chem. Abstr. Name: 2,2'-([4-([2-Hydroxyethyl]amino)-3-nitrophenyl]imino)bis(ethanol)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

HC Blue No. 2 is used as a semi-permanent hair dye.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

HC Blue No. 2 was tested for carcinogenicity by administration in the diet in one study in mice and in one study in rats. No significant increase in tumour incidence was observed in either species, but the data on female mice could not be adequately evaluated.

5.4 Other relevant data

HC Blue No. 2 induced gene mutation in bacteria. It induced DNA damage, gene mutation and sister chromatid exchange but not chromosomal aberrations or inhibition of intercellular communication in cultured mammalian cells. Micronuclei were not induced in the bone marrow of mice exposed *in vivo*.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of HC Blue No. 2.

There is *inadequate evidence* in experimental animals for the carcinogenicity of HC Blue No. 2.

Overall evaluation

HC Blue No. 2 is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- HC Blue 2
- HC Blue Number 2
- 2,2'-([4-([2-Hydroxyethyl]amino)-3-nitrophenyl]imino)di(ethanol)
- N^1,N^4,N^4-Tris(2-hydroxyethyl)-2-nitro-*para*-phenylenediamine

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HC RED No. 3
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 153)
CAS No.: 2871-01-4
Chem. Abstr. Name: 2-[(4-Amino-2-nitrophenyl)amino]ethanol

5. Summary of Data Reported and Evaluation

5.1 Exposure data

HC Red No. 3 is used as a semipermanent hair dye.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

HC Red No. 3 was tested for carcinogenicity by gavage in one study in mice and in one study in rats. There was a significant increase in the incidence of hepatocellular adenomas and carcinomas combined in male mice administered the high dose; poor survival precluded evaluation of the females. No increase in the incidence of treatment-related tumours was seen in rats of either sex.

5.4 Other relevant data

HC Red No. 3 was mutagenic to bacteria.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of HC Red No. 3.

There is *inadequate evidence* in experimental animals for the carcinogenicity of HC Red No. 3.

Overall evaluation

HC Red No. 3 is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- 2-(4-Amino-2-nitroanilino)ethanol
- HC Red 3
- HC Red Number 3
- 4-(2-Hydroxyethyl)amino-3-nitroaniline
- N^1-(2-Hydroxyethyl)-2-nitro-*para*-phenylenediamine

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HC YELLOW No. 4
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 159)
CAS No.: 59820-43-8
Chem. Abstr. Name: 2-[(2-[2-Hydroxyethoxy]-4-nitrophenyl)amino]ethanol

5. Summary of Data Reported and Evaluation

5.1 Exposure data

HC Yellow No. 4 is used as a semipermanent hair dye.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

HC Yellow No. 4 was tested for carcinogenicity by administration in the diet in one study in mice and in one study in rats. No significant increase in tumour incidence was found in mice. The incidence of adenomas of the pituitary gland was increased in male rats but not in females.

5.4 Other relevant data

HC Yellow No. 4 induced gene mutation in bacteria and in insects. Chromosomal aberrations were not induced in insects, and equivocal results for this end-point were obtained in cultured mammalian cells. Sister chromatid exchange was induced in mammalian cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of HC Yellow No. 4.

There is *inadequate evidence* in experimental animals for the carcinogenicity of HC Yellow No. 4.

Overall evaluation

HC Yellow No. 4 is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- *N*,*O*-Di(2-hydroxyethyl)-2-amino-5-nitrophenol
- HC Yellow 4
- 2-[3-Nitro-6-(*beta*-hydroxyethylamino)phenoxy] ethanol

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2-AMINO-4-NITROPHENOL
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 167)
CAS No.: 99-57-0
Chem. Abstr. Name: 2-Amino-4-nitrophenol

5. Summary of Data Reported and Evaluation

5.1 Exposure data

2-Amino-4-nitrophenol is used as an intermediate in the manufacture of certain azo dyes. It is also used in semipermanent hair colouring products and has been used in permanent hair colours.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

2-Amino-4-nitrophenol was tested for carcinogenicity by gavage in one study in mice and one study in rats. No significant increase in the incidence of tumours was observed in mice or in female rats. The incidence of renal-cell adenomas was increased in male rats.

5.4 Other relevant data

2-Amino-4-nitrophenol caused renal toxicity in rats and mice. The effect occurred at a lower dose in male than in female rats.

2-Amino-4-nitrophenol induced mutation in bacteria, fungi and cultured mammalian cells and sister chromatid exchange and chromosomal aberrations in cultured mammalian cells. It did not induce micronuclei, chromosomal aberrations or dominant lethal mutation in rodents exposed *in vivo*.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of 2-amino-4-nitrophenol.

There is *limited evidence* in experimental animals for the carcinogenicity of 2-amino-4-nitrophenol.

Overall evaluation

2-Amino-4-nitrophenol is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- 1-Amino-2-hydroxy-5-nitrobenzene
- CI No. 76530
- 1-Hydroxy-2-amino-4-nitrobenzene
- 2-Hydroxy-5-nitroaniline
- 4-Nitro-2-aminophenol
- *para*-Nitro-*ortho*-aminophenol
- Rodol 42

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2-AMINO-5-NITROPHENOL
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 177)
CAS No.: 121-88-0
Chem. Abstr. Name: 2-Amino-5-nitrophenol

5. Summary of Data Reported and Evaluation

5.1 Exposure data

2-Amino-5-nitrophenol is used as an intermediate in the manufacture of certain azo dyes. It is also used in semi-permanent and permanent hair colouring products.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

2-Amino-5-nitrophenol was tested for carcinogenicity by gavage in one study in mice and one study in rats. In mice, no significant increase in tumour incidence was observed in the low-dose groups; data on the high-dose groups could not be evaluated owing to high mortality rates. An increased incidence of pancreatic acinar-cell tumours was observed in male rats.

5.4 Other relevant data

Oral treatment with 2-amino-5-nitrophenol was associated with inflammation of the lower intestinal tract in mice and rats.

2-Amino-5-nitrophenol induced gene mutation in bacteria and gene mutation, sister chromatid exchange and chromosomal aberrations in cultured mammalian cells. It did not induce dominant lethal mutation in rats.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of 2-amino-5-nitrophenol.

There is *limited evidence* in experimental animals for the carcinogenicity of 2-amino-5-nitrophenol.

Overall evaluation

2-Amino-5-nitrophenol is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- CI No. 76535
- 3-Hydroxy-4-aminonitrobenzene
- 2-Hydroxy-4-nitroaniline
- 3-Nitro-6-aminophenol
- 5-Nitro-2-aminophenol
- Rodol YBA
- Ursol Yellow Brown A

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1,4-DIAMINO-2-NITROBENZENE
(2-Nitro-*para*-phenylenediamine)
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 185)
CAS No.: 5307-14-2
Chem. Abstr. Name: 2-Nitro-1,4-benzenediamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

1,4-Diamino-2-nitrobenzene is used in permanent and semi-permanent hair dye formulations and for dyeing fur.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

1,4-Diamino-2-nitrobenzene was tested for carcinogenicity by oral administration in the diet in one study in mice and in one study in rats. An increased incidence of liver-cell tumours was observed in female mice. No increase in the incidence of tumours was observed in male mice or in rats.

5.4 Other relevant data

1,4-Diamino-2-nitrobenzene induced gene mutation in bacteria and in cultured mammalian cells. It did not induce gene mutation, mitotic crossing over or gene conversion in yeasts. It induced chromosomal aberrations, sister chromatid exchange and cell transformation in cultured mammalian cells and chromosomal aberrations in human lymphocytes *in vitro*. Equivocal responses were obtained for DNA damage induction in cultured rodent cells.

There was no evidence for induction of sister chromatid exchange, micronuclei, chromosomal aberrations or dominant lethal mutation in rodents dosed *in vivo*.

1,2,4-Triaminobenzene, a metabolite of 1,4-diamino-2-nitrobenzene, was mutagenic to bacteria.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of 1,4-diamino-2-nitrobenzene.

There is *limited evidence* in experimental animals for the carcinogenicity of 1,4-diamino-2-nitrobenzene.

Overall evaluation

1,4-Diamino-2-nitrobenzene is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluation: Suppl. 7 (1987) (p. 61)

Synonyms

- 4-Amino-2-nitroaniline
- CI No. 76070
- CI Oxidation Base 22
- 2,5-Diaminonitrobenzene
- Durafur Brown 2R
- Fouramine 2R
- Fourrine 36
- Fourrine Brown 2R
- 2-Nitro-4-aminoaniline
- 2-Nitro-1,4-benzenediamine
- 2-Nitro-1,4-diaminobenzene
- 2-Nitro-1,4-phenylenediamine
- Nitro-*para*-phenylenediamine
- *ortho*-Nitro-*para*-phenylenediamine
- NPD
- Ursol Brown RR
- Zoba Brown RR

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D&C RED No. 9 (CI Pigment Red 53:1) (Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 203)
CAS No.: 5160-02-1
Chem. Abstr. Name: 5-Chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl benzenesulfonic acid, barium salt (2:1)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

D&C Red No. 9 (a certified grade of CI Pigment Red 53:1) is used in lipsticks, mouthwashes, dentifrices and drugs in some countries. CI Pigment Red 53:1 has been used extensively since the 1940s as a pigment in printing inks, coated papers, crayons, rubber and baking enamels.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

D&C Red No. 9 was tested for carcinogenicity by administration in the diet in one study in mice and in two studies in rats and by skin painting in one study in mice. In one study, it produced splenic sarcomas in male rats and increased the incidence of neoplastic liver nodules in animals of each sex. No treatment-related increase in the incidence of tumours was observed in mice.

5.4 Other relevant data

D&C Red No. 9 caused splenic toxicity in rats and mice.

D&C Red No. 9 was inactive in all studies in which it was tested, including assays for gene mutation in bacteria and in cultured mammalian cells, DNA damage in cultured mammalian cells and in rodents *in vivo*, sister chromatid exchange and chromosomal aberrations in cultured mammalian cells and micronucleus formation in the bone marrow of rats treated orally.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of D&C Red No. 9.

There is *limited evidence* in experimental animals for the carcinogenicity of D&C Red No. 9.

Overall evaluation

D&C Red No. 9 is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluation: Suppl. 7 (1987) (p. 61)

Synonyms

- CI No. 15585:1
- CI Pigment Red 53, Ba salt
- CI Pigment Red 53, barium salt (2:1)
- D and C Red No. 9
- Pigment Red 53:1
- Lake Red C
- Red Lake C

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MAGENTA AND CI BASIC RED 9
Manufacture of magenta (Group 1)
CI Basic Red 9 (Group 2B)
Magenta containing CI Basic Red 9 (Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 215)

Magenta I
CAS No.: 632-99-5
Chem. Abstr. Name: 4-[(4-Aminophenyl)(4-imino-2,5-cyclohexadien-1-ylidene)methyl]-2-methylbenzenamine, monohydrochloride

Magenta II
CAS No.: 26261-57-4
Chem. Abstr. Name: 4-[(4-Aminophenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl]-2-methylbenzenamine, monohydrochloride

Magenta III
CAS No.: 3248-91-7
Chem. Abstr. Name: 4-[(4-Amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl]-2-methylbenzenamine, monohydrochloride

CI Basic Red 9
CAS No.: 569-61-9
Chem. Abstr. Name: 4-[(4-Aminophenyl)(4-imino-2,5-cyclohexadien-1-ylidene)methyl]-benzenamine, monohydrochloride

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Magenta and CI Basic Red 9, a common constituent of magenta, were first produced commercially in the late nineteenth century in Germany. As the industry developed in the early twentieth century, it converted in some countries, such as Italy and the United Kingdom, from production of magenta (prepared from a mixture of aniline and *ortho*-toluidine) to production of magenta III (prepared from *ortho*-toluidine without aniline).

Magenta and CI Basic Red 9 have been used to dye textile fibres, in the preparation of pigments for printing inks and in other specialty applications, such as biological stains.

5.2 Human carcinogenicity data

Two small cohorts of workers engaged in the manufacture of magenta were studied in the United Kingdom and Italy. Marked excesses of cancer of the urinary bladder were identified. Although efforts were made to exclude workers exposed to 2-naphthylamine and benzidine, both cohorts may also have been exposed to aromatic amines present as intermediates and suspected to be urinary bladder carcinogens, such as *ortho*-toluidine.

5.3 Animal carcinogenicity data

No adequate study was available to evaluate the carcinogenicity in experimental animals of magenta or of

magenta I, magenta II or magenta III.

CI Basic Red 9 was tested for carcinogenicity in one study in mice and in one study in rats by oral administration in the diet and in one study in rats by subcutaneous administration. After oral administration, the compound induced hepatocellular carcinomas in male and female mice and in male rats; adrenal gland phaeochromocytomas in female mice; benign and malignant skin tumours in male rats; and subcutaneous fibromas, thyroid gland follicular-cell tumours and Zymbal gland carcinomas in male and female rats. Subcutaneous administration to rats resulted in a high incidence of local sarcomas.

5.4 Other relevant data

CI Basic Red 9 lowers thyroxin levels and caused hypertrophy of the thyroid in rats and mice.

CI Basic Red 9 induced DNA damage in bacteria, but conflicting results were obtained in assays for gene mutation. Mitotic recombination was not induced in yeast. In cultured mammalian cells, there was no induction of sister chromatid exchange or chromosomal aberrations, but DNA damage and cell transformation were induced; assays for gene mutation gave inconsistent results.

5.5 Evaluations

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

There is *inadequate evidence* in humans for the carcinogenicity of CI Basic Red 9.

There is *sufficient evidence* that the manufacture of magenta entails exposures that are carcinogenic.

There is *sufficient evidence* in experimental animals for the carcinogenicity of CI Basic Red 9.

There is *inadequate evidence* in experimental animals for the carcinogenicity of magenta.

Overall evaluation

The manufacture of magenta *entails exposures that are carcinogenic (Group 1)*.

CI Basic Red 9 is *possibly carcinogenic to humans (Group 2B)*.

Magenta containing CI Basic Red 9 is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluation: Magenta: Suppl. 7 (1987) (p. 238)

Synonyms for 4-[(4-Aminophenyl)(4-imino-2,5-cyclohexadien-1-ylidene)methyl]-2-methylbenzenamine, monohydrochloride

- Aizen Magenta
- Astra Fuchsine B
- Basic fuchsin
- Basic fuchsine
- Basic magenta
- Basic Magenta E 200

- Basic Violet 14
- C-WR Violet 8
- Calcozine Fuchsine HO
- Calcozine Magenta RTN
- Calcozine Magenta XX
- Cerise B
- CI Basic Violet 14
- CI Basic Violet 14, monohydrochloride
- CI No. 42510
- Diabasic Magenta
- Diamond Fuchsine
- Fuchsin
- Fuchsine
- Fuchsine A
- Fuchsine CS
- Fuchsine G;
- Fuchsine HO
- Fuchsine N
- Fuchsine RTN
- Fuchsine SBP
- Fuchsine Y
- Magenta DP
- Magenta E
- Magenta G
- Magenta I
- Magenta PN
- Magenta S
- Magenta Superfine
- Orient Basic Magenta
- 12418 Red
- Rosaniline
- Rosaniline chloride
- Rosaniline hydrochloride
- Rosanilinium chloride

Synonyms for 4-[(4-Aminophenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl]-2-methylbenzenamine, monohydrochloride

- Dimethyl fuchsin
- Magenta II

Synonyms for 4-[(4-Amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl]-2-methylbenzenamine, monohydrochloride

- Basic Violet 2
- CI Basic Violet 2
- CI No. 42520
- Isorubine
- Magenta III
- Neofuchsine
- New fuchsine
- New magenta
- Trimethyl fuchsin

Synonyms for 4-[(4-Aminophenyl)(4-imino-2,5-cyclohexadien-1-ylidene)methyl]-benzenamine, monohydrochloride

- Basic fuchsin
- Basic parafuchsine
- Basic Red 9
- Basic rubine
- Calcozine Magenta N
- CI Basic Red 9
- CI Basic Red 9, monohydrochloride
- CI No. 42500
- Fuchsine DR 001
- Fuchsine SP
- Fuchsine SPC
- *para*-Fuchsin
- *para*-Fuchsine
- *para*-Magenta
- Orient Para Magenta Base
- Parafuchsin
- Parafuchsine
- Pararosaniline
- Pararosaniline chloride
- Pararosaniline hydrochloride
- *para*-Rosaniline hydrochloride

Last updated 08/22/1997

CI DIRECT BLUE 15
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 235)
CAS No.: 2429-74-5
Chem. Abstr. Name: 3,3'-[(3,3'-Dimethoxy[1,1'-biphenyl]-4,4'-diyl) bis(azo)]bis[5-amino-4-hydroxy-2,7-naphthalenedisulfonic acid], tetrasodium salt

5. Summary of Data Reported and Evaluation

5.1 Exposure data

CI Direct Blue 15, a bis-azo dye derived from 3,3'-dimethoxybenzidine, is used mainly for dyeing textiles and paper. The technical grade contains about 50% of pure dye, in addition to inorganic salts and a mixture of about 35 organic compounds, including 3,3'-dimethoxybenzidine.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

Technical-grade CI Direct Blue 15 was tested for carcinogenicity in one study in rats by administration in the drinking-water. It produced benign and malignant tumours of the skin, Zymbal gland, liver, small intestine and oral cavity as well as leukaemia in animals of each sex, of the large intestine and preputial gland in males and of the uterus and clitoral gland in females.

5.4 Other relevant data

CI Direct Blue 15 caused renal and hepatic toxicity in rats. Reductive cleavage of the azo bonds to yield 3,3'-dimethoxybenzidine was demonstrated *in vivo*.

CI Direct Blue 15 induced mutation in bacteria under conditions that favour reduction. Neither sister chromatid exchange nor chromosomal aberrations were induced in cultured mammalian cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of CI Direct Blue 15.

There is *sufficient evidence* in experimental animals for the carcinogenicity of technical grade CI Direct Blue 15.

Overall evaluation

CI Direct Blue 15 is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- Airedale Blue D
- Aizen Direct Sky Blue 5B
- Aizen Direct Sky Blue 5BH
- Amanil Sky Blue
- Atlantic Sky Blue A
- Atul Direct Sky Blue
- Azine Sky Blue 5B
- Belamine Sky Blue A
- Benzanil Sky Blue
- Benzo Sky Blue A-CF
- Benzo Sky Blue S
- Cartasol Blue 2GF
- Chloramine Sky Blue A
- Chloramine Sky Blue 4B
- Chrome Leather Pure Blue
- CI No. 24400
- Cresotine Pure Blue
- Diacotton Sky Blue 5B
- Diamine Blue 6B
- Diamine Sky Blue
- Diaphtamine Pure Blue
- Diazol Pure Blue 4B
- Diphenyl Brilliant Blue
- Diphenyl Sky Blue 6B
- Direct Blue 10G
- Direct Blue 15
- Direct Blue HH
- Direct Pure Blue
- Direct Pure Blue M
- Direct Sky Blue
- Direct Sky Blue A
- Direct Sky Blue 5B
- Enianil Pure Blue AN
- Fenamin Sky Blue
- Hispamin Sky Blue 3B
- Kayafect Blue Y
- Kayaku Direct Sky Blue 5B
- Mitsui Direct Sky Blue 5B
- Naphtamine Blue 10G
- Niagara Blue 4B
- Niagara Sky Blue
- Nippon Direct Sky Blue
- Nippon Sky Blue
- Nitto Direct Sky Blue 5B
- Oxamine Sky Blue 5B
- Paper Blue S
- Phenamine Sky Blue A
- Pontamine Sky Blue 5BX
- Shikiso Direct Sky Blue 5B
- Sky Blue 4B
- Sky Blue 5B
- Tertrodirect Blue F
- Vondacel Blue HH

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CI ACID RED 114
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 247)
CAS No.: 6459-94-5
Chem. Abstr. Name: 8-[(3,3'-Dimethyl-4'-[(4-[([4-methylphenyl]sulfonyl)oxy]phenyl)azo][1,1'-biphenyl]-4-yl)azo]-7-hydroxy-
1,3-naphthalenedisulfonic acid, disodium salt

5. Summary of Data Reported and Evaluation

5.1 Exposure data

CI Acid Red 114, a bis-azo dye derived from 3,3'-dimethylbenzidine, is used to dye wool, silk, jute and leather.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

CI Acid Red 114 was tested for carcinogenicity in one study in rats by administration in the drinking-water. It increased the incidences of benign and malignant tumours of the skin, Zymbal gland and liver in male and female rats, and of the clitoral gland, lung, oral cavity and small and large intestine in female rats.

5.4 Other relevant data

Reductive cleavage of the azo bonds to yield 3,3'-dimethylbenzidine was demonstrated *in vivo*.

CI Acid Red 114 induced gene mutation in bacteria under reducing conditions. It did not induce gene mutation in insects or sister chromatid exchange or chromosomal aberrations in cultured mammalian cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of CI Acid Red 114.

There is *sufficient evidence* in experimental animals for the carcinogenicity of CI Acid Red 114.

Overall evaluation

CI Acid Red 114 is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- Acid Leather Red BG
- Acid Red 114
- Amacid Milling Red PRS
- Benzyl Fast Red BG
- Benzyl Red BR
- CI Acid Red 114, disodium salt
- CI No. 23635
- Elcacid Milling Fast Red RS
- Erionyl Red RS
- Fenafor Red PB
- Folan Red B
- Intrazone Red BR
- Kayanol Milling Red RS
- Leather Fast Red B
- Levanol Red GG
- Midlon Red PRS
- Milling Fast Red B
- Milling Red B
- Milling Red BB
- Milling Red SWB
- Polar Red RS
- Sandolan Red N-RS
- Sella Fast Red RS
- Sulphonol Red R
- Suminol Milling Red RS
- Supranol Fast Red 3G
- Supranol Fast Red GG
- Supranol Red PBX-CF
- Supranol Red R
- Telon Fast Red GG
- Tertracid Milling Red B
- Vondamol Fast Red RS

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CI PIGMENT RED 3
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 259)
CAS No.: 2425-85-6
Chem. Abstr. Name: 1-[(4-Methyl-2-nitrophenyl)azo]-2-naphthalenol

5. Summary of Data Reported and Evaluation

5.1 Exposure data

CI Pigment Red 3, one of the most widely used red pigments, is found in paints, inks, plastics, rubber and textiles.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

CI Pigment Red 3 was tested for carcinogenicity by administration in the diet in one study in mice and in one study in rats. In male mice, it induced follicular-cell adenomas of the thyroid and renal-cell adenomas. There was an increased incidence of adrenal phaeochromocytomas in male rats and of hepatocellular adenomas in female rats.

5.4 Other relevant data

CI Pigment Red 3 did not induce gene mutation in bacteria or sister chromatid exchange or chromosomal aberrations in cultured mammalian cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of CI Pigment Red 3.

There is *limited evidence* in experimental animals for the carcinogenicity of CI Pigment Red 3.

Overall evaluation

CI Pigment Red 3 *cannot be classified as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- Accosperse Toluidine Red XL
- ADC Toluidine Red B
- Atlasol Spirit Red 3
- CI No. 12120

- CP Toluidine Toner A 2989
- CP Toluidine Toner A 2990
- CP Toluidine Toner Dark RS 3340
- CP Toluidine Toner Deep X 1865
- CP Toluidine Toner Light RS 3140
- CP Toluidine Toner RT 6101
- CP Toluidine Toner RT 6104
- Calcotone Toluidine Red YP
- Carnelio Helio Red
- Chromatex Red J
- Dainichi Permanent Red 4R
- D&C Red No. 35
- D and C Red No. 35
- Deep Fastona Red
- Duplex Toluidine Red L 20-3140
- Eljon Fast Scarlet PV Extra
- Eljon Fast Scarlet RN
- Enialit Light Red RL
- Fast Red A
- Fast Red AB
- Fast Red J
- Fast Red JE
- Fast Red R
- Fastona Red B
- Fastona Scarlet RL
- Fastona Scarlet YS
- Graphtol Red A 4RL
- Hansa Red B
- Hansa Red G
- Hansa Scarlet RB
- Hansa Scarlet RN
- Hansa Scarlet RNC
- Helio Fast Red BN
- Helio Fast Red RL
- Helio Fast Red RN
- Helio Red RL
- Helio Red Toner
- Hispalit Fast Scarlet RN
- Independence Red
- Irgalite Fast Red P 4R
- Irgalite Fast Scarlet RND
- Irgalite Red PV 2
- Irgalite Red RNPX
- Irgalite Scarlet RB
- Isol Fast Red HB
- Isol Fast Red RN 2B
- Isol Fast Red RN 2G
- Isol Fast Red RNB
- Isol Fast Red RNG
- Isol Toluidine Red HB
- Isol Toluidine Red RN 2B
- Isol Toluidine Red RN 2G
- Isol Toluidine Red RNB
- Isol Toluidine Red RNG
- Japan Red 221
- Japan Red No. 221
- Kromon Helio Fast Red
- Kromon Helio Fast Red YS
- Lake Red 4R

- Lake Red 4RII
- Lithol Fast Scarlet RN
- Lutetia Fast Red 3R
- Lutetia Fast Scarlet RF
- Lutetia Fast Scarlet RJN
- 1-(4-Methyl-2-nitrophenylazo)-2-naphthol
- Monolite Fast Scarlet CA
- Monolite Fast Scarlet GSA
- Monolite Fast Scarlet RB
- Monolite Fast Scarlet RBA
- Monolite Fast Scarlet RN
- Monolite Fast Scarlet RNA
- Monolite Fast Scarlet RNV
- Monolite Fast Scarlet RT
- 1-[(2-Nitro-4-methylphenyl)azo]-2-naphthol
- 1-(*ortho*-nitro-*para*-tolylazo)-2-naphthol
- No. 2 Forthfast Scarlet
- Oralith Red P 4R
- Permanent Red 4R
- Pigment Red 3
- Pigment Red RL
- Pigment Scarlet
- Pigment Scarlet B
- Pigment Scarlet N
- Pigment Scarlet R
- Polymo Red FGN
- Recolite Fast Red RBL
- Recolite Fast Red RL
- Recolite Fast Red RYL
- Sanyo Scarlet Pure
- Sanyo Scarlet Pure No. 1000
- Scarlet Pigment RN
- Segnale Light Red 2B
- Segnale Light Red B
- Segnale Light Red BR
- Segnale Light Red C 4R
- Segnale Light Red RL
- Seikafast Red 4R4016
- Siegle Red 1
- Siegle Red B
- Siegle Red BB
- Silogomma Red RLL
- Silosol Red RBN
- Silosol Red RN
- Siloton Red BRLL
- Siloton Red RLL
- Symuler Fast Red 4R100
- Symuler Fast Scarlet 4R
- Syton Fast
- Scarlet RB
- Syton Fast Scarlet RD
- Syton Fast Scarlet RN
- Tertropigment Red HAB
- Tertropigment Scarlet LRN
- Toluidine red
- Toluidine Red 10451
- Toluidine Red 3B
- Toluidine Red 4R
- Toluidine Red BFB

- Toluidine Red BFGG
- Toluidine Red D28-3930
- Toluidine Red Light
- Toluidine Red M 20-3785
- Toluidine Red R
- Toluidine Red RT 115
- Toluidine Red Toner
- Toluidine Red XL 20-3050
- Toluidine Toner
- Toluidine Toner Dark 5040
- Toluidine Toner HR-X 2700
- Toluidine Toner HR-X 2741
- Toluidine Toner Keep HR-X 2742
- Toluidine Toner L 20-3300
- Toluidine Toner RT 252
- Versal Scarlet PRNL
- Versal Scarlet RNL
- Vulcafor Scarlet A

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4,4'-METHYLENEBIS(2-CHLOROANILINE) (MOCA) (Group 2A)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 271)
CAS No.: 101-14-4
Chem. Abstr. Name: 4,4'-Methylenebis(2-chlorobenzenamine)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

4,4'-Methylenebis(2-chloroaniline) (MOCA) was introduced in the mid-1950s in the production of high-performance polyurethane mouldings. It is used in many countries, with a total worldwide production of several thousand tonnes per year; it is used as a curing agent for roofing and wood sealing in Japan and the Far East. There was considerable occupational exposure by cutaneous absorption in the early years of use of MOCA, as revealed by urine analysis, but exposure has decreased with the implementation of control measures. Extensive environmental contamination is known to have occurred in a large area surrounding at least one factory, prior to the introduction of controls.

5.2 Human carcinogenicity data

Three asymptomatic cases of cancer of the urinary bladder (two in men under the age of 30 among 552 workers) were identified in a factory where MOCA was produced and where screening for this cancer was undertaken in a subgroup. Although this finding suggests an excess, expected numbers could not be calculated.

5.3 Animal carcinogenicity data

MOCA was tested for carcinogenicity by oral administration in the diet in mice in one study, in rats of each sex in two studies, in male rats in a further two studies using normal and low-protein diets and in capsules in female dogs. It was also tested by subcutaneous administration to rats in one study. Oral administration of MOCA increased the incidence of liver tumours in female mice. In a series of experiments in which rats were fed either standard or low-protein diets, it induced liver-cell tumours and malignant lung tumours in males and females in one study, a few liver-cell tumours in male rats in another, lung adenocarcinomas and hepatocellular tumours in males and females in a third and malignant lung tumours, mammary gland adenocarcinomas, Zymbal gland carcinomas and hepatocellular carcinomas in a fourth. Oral administration of MOCA to female beagle dogs produced transitional-cell carcinomas of the urinary bladder and urethra. Subcutaneous administration to rats produced hepatocellular carcinomas and malignant lung tumours.

5.4 Other relevant data

MOCA forms adducts with DNA, both *in vitro* and *in vivo*. One of the two major adducts, *N*-(deoxyadenosin-8-yl)-4-amino-3-chlorobenzyl alcohol, was found in rat tissues; it also cochromatographed with a DNA adduct from urothelial cells recovered from the urine of a worker in the polyurethane industry who was accidentally exposed to a high dose of MOCA. An increased frequency of sister chromatid exchange was seen in a small number of workers exposed to MOCA.

MOCA induced DNA damage in prokaryotes, cultured mammalian and human cells and in animals treated *in vivo*. Gene mutation was induced in bacteria and cultured mammalian cells, but not in yeast. Equivocal results for mitotic recombination were obtained in yeasts. Aneuploidy was induced in yeast and sister chromatid exchange, transformation and inhibition of intercellular communication in cultured mammalian cells.

Micronuclei were induced in the bone marrow of mice treated *in vivo*, and sister chromatid exchange was induced in the bone marrow of rats treated *in vivo*.

MOCA is comprehensively genotoxic. Furthermore, (i) rats, dogs and humans metabolize MOCA to *N*-hydroxy-MOCA by hepatic cytochromes P450; (ii) DNA adducts are formed by reaction with *N*-hydroxy-MOCA, and MOCA is genotoxic in bacteria and mammalian cells; (iii) the same major MOCA-DNA adduct is formed in the target tissues for carcinogenicity in animals (rat liver and lung; dog urinary bladder) as that found in urothelial cells from a man with known occupational exposure to MOCA.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of 4,4'-methylenebis(2-chloroaniline) (MOCA).

There is *sufficient evidence* in experimental animals for the carcinogenicity of 4,4'-methylenebis(2-chloroaniline) (MOCA).

Overall evaluation

4,4'-Methylenebis(2-chloroaniline) (MOCA) is *probably carcinogenic to humans (Group 2A)*.

Overall evaluation 2A and not 2B on the basis of supporting evidence from other relevant data.

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluation: Suppl. 7 (1987) (p. 246)

Synonyms

- Bisamine A
- Bisamine S
- Bis(4-amino-3-chlorophenyl)methane
- Bis(3-chloro-4-aminophenyl)methane
- Cuamine M
- Cuamine MT
- Curalin M
- Curalon M
- Curene 442
- Diamet Kh
- 3,3'-Dichloro-4,4'-diaminodiphenylmethane
- LD 813
- MBOCA
- Methylenebis(3-chloro-4-aminobenzene)
- 4,4'-Methylenebis(*ortho*-chloroaniline)
- Millionate M
- Quodorole

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para-CHLOROANILINE
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 305)
CAS No.: 106-47-8
Chem. Abstr. Name: 4-Chlorobenzenamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

para-Chloroaniline is used as an intermediate in the manufacture of dyes, pigments, agricultural chemicals and pharmaceuticals. It is a persistent environmental degradation product of some herbicides and fungicides.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

para-Chloroaniline was tested for carcinogenicity in mice and rats by administration in the diet and by gavage. It produced haemangiosarcomas in male and female mice in different organs after administration in the diet. It induced haemangiosarcomas of the spleen and liver and hepatocellular adenomas and carcinomas in male mice after administration by gavage. It induced sarcomas of the spleen and splenic capsule in male rats in both studies.

5.4 Other relevant data

para-Chloroaniline causes methaemoglobinaemia and is metabolized similarly in humans and experimental animals.

para-Chloroaniline induced DNA damage in bacteria, but conflicting results were obtained for gene mutation. Gene mutation but not mitotic recombination was induced in fungi. Gene mutation, sister chromatid exchange and chromosomal aberrations were induced in cultured mammalian cells, while conflicting data were obtained for cell transformation.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of *para*-chloroaniline.

There is *sufficient evidence* in experimental animals for the carcinogenicity of *para*-chloroaniline.

Overall evaluation

para-Chloroaniline is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- 4-Aminochlorobenzene
- *para*-Aminochlorobenzene
- 1-Amino-4-chlorobenzene
- 4-Amino-1-chlorobenzene
- 4-Chloro-1-aminobenzene
- 4-Chloroaniline
- 4-Chlorophenylamine
- *para*-Chlorophenylamine

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2,6-DIMETHYLANILINE (2,6-XYLIDINE)
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 323)
CAS No.: 87-62-7
Chem. Abstr. Name: 2,6-Dimethylbenzenamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

2,6-Dimethylaniline is used as a chemical intermediate in the manufacture of pesticides, dyestuffs, antioxidants, pharmaceuticals and other products. It is a metabolite of the xylidine group of anaesthetics, including, for example, lidocaine, and is produced by the reduction of certain azo dyes by intestinal microflora. It may also enter the environment through degradation of certain pesticides.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

2,6-Dimethylaniline was tested for carcinogenicity in one study in rats by pre- and postnatal administration in the diet. It induced adenomas and carcinomas as well as several sarcomas in the nasal cavity. It also produced subcutaneous fibromas and fibrosarcomas in both males and females and increased the incidence of neoplastic nodules in the livers of female rats.

5.4 Other relevant data

Methaemoglobinaemia has been observed in humans and animals exposed to 2,6-dimethylaniline. The metabolism of 2,6-dimethylaniline in humans and rats appears to be similar and gives rise to a characteristic haemoglobin adduct in both species.

2,6-Dimethylaniline gave conflicting results for gene mutation in bacteria. Sister chromatid exchange and chromosomal aberrations were induced in cultured mammalian cells. The compound bound covalently to DNA in rat tissues but did not induce micronuclei in the bone marrow of mice treated *in vivo*.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of 2,6-dimethylaniline.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 2,6-dimethylaniline.

Overall evaluation

2,6-Dimethylaniline is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- 1-Amino-2,6-dimethylbenzene
- 2-Amino-1,3-dimethylbenzene
- 2-Amino-1,3-xylene
- 2-Amino-*meta*-xylene
- 2,6-Dimethylphenylamine
- *ortho*-Xylidine
- 2,6-*meta*-Xylidine
- 2,6-Xylylamine

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N,*N*-DIMETHYLANILINE
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 57 (1993) (p. 337)
CAS No.: 121-69-7
Chem. Abstr. Name: *N*,*N*-Dimethylbenzenamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

N,*N*-Dimethylaniline is used as an intermediate in the manufacture of dyes and other products and as a solvent for special purposes, a rubber vulcanizing agent and a stabilizer. It has been detected in ambient water and soil in the vicinity of industrial facilities.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

N,*N*-Dimethylaniline was tested for carcinogenicity in one study in mice and in one study in rats by gavage. It increased the incidence of forestomach papillomas in female mice. A few splenic sarcomas were observed in treated male rats.

5.4 Other relevant data

The metabolism of *N*,*N*-dimethylaniline has been studied in many species and in human tissues. It involves enzymatic *N*-demethylation, *N*-oxidation and ring hydroxylation. Aniline is a major metabolite. Chronic methaemoglobinaemia and erythrocyte haemolysis, with concomitant splenomegaly and other pathological lesions characteristic of aniline, were observed in mice and rats treated with *N*,*N*-dimethylaniline.

N,*N*-Dimethylaniline did not induce gene mutation in bacteria or DNA damage in cultured mammalian cells. It induced gene mutation, sister chromatid exchange and chromosomal aberrations in cultured mammalian cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of *N*,*N*-dimethylaniline.

There is *limited evidence* in experimental animals for the carcinogenicity of *N*,*N*-dimethylaniline.

Overall evaluation

N,*N*-Dimethylaniline is *not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- (Dimethylamino)benzene
- *N*,*N*-dimethylaminobenzene
- Dimethylaniline
- Dimethylphenylamine
- *N*,*N*-Dimethylphenylamine

Last updated 08/22/1997