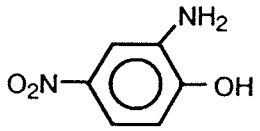
2-AMINO-4-NITROPHENOL

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Synonyms, structural and molecular data*

Chem. Abstr. Serv. Reg. No.: 99-57-0
Chem. Abstr. Name: 2-Amino-4-nitrophenol
Colour Index No.: 76530
Synonyms: 1-Amino-2-hydroxy-5-nitrobenzene; 1-hydroxy-2-amino-4-nitrobenzene; 2-hydroxy-5-nitroaniline; 4-nitro-2-aminophenol; *para*-nitro-*ortho*-aminophenol



$C_6H_6N_2O_3$ Mol. wt: 154.12

1.1.2 *Chemical and physical properties*

(*a*) *Description*: Yellow-brown to orange prisms (Lide, 1991)
(*b*) *Melting-point*: 143–145 °C (anhydrous) (Aldrich Chemical Co., 1992); 80–90 °C (hydrated) (Lide, 1991)
(*c*) *Spectroscopy data*: Infrared, ultraviolet and nuclear magnetic resonance spectral data have been reported (Pouchert, 1981, 1983; US National Toxicology Program, 1988; Sadtler Research Laboratories, 1980, 1991).
(*d*) *Solubility*: Soluble in ethanol, acetone, acetic acid and diethyl ether; sparingly soluble in water (US National Toxicology Program, 1988; Lide, 1991)
(*e*) *Octanol/water partition coefficient (P)*: 13.5 (Bronaugh & Congdon, 1984)

1.1.3 *Trade names, technical products and impurities*

Trade name: Rodol 42 (Jos. H. Lowenstein & Sons, 1991)

2-Amino-4-nitrophenol is available commercially with the following specifications: purity, 96% (min.); ash, 0.1% (max.); iron, 100 ppm (mg/kg) (max.); lead (see IARC, 1980a, 1987a), 5 ppm (mg/kg) (max.); and arsenic (see IARC, 1980b, 1987b), 2 ppm (mg/kg) (max.). It is also available in research quantities at purities ranging from 90 to > 99%

(Riedel-de-Haen, 1990; Heraeus, 1991; Jos. H. Lowenstein & Sons, 1991; Lancaster Synthesis, 1991; TCI America, 1991; Aldrich Chemical Co., 1992; Fluka Chemie AG, 1993).

1.1.4 *Analysis*

No data were available to the Working Group.

1.2 Production and use

1.2.1 *Production*

2-Amino-4-nitrophenol is produced by the reaction of 2,4-dinitrophenol with sodium sulfide (Farris, 1978). It was first synthesized by Agfa in 1898 (Society of Dyers and Colourists, 1971).

At present, approximately 150 kg of 2-amino-4-nitrophenol are used in hair colouring products in the USA annually, according to industry estimates. It is produced by one company each in Brazil, China, Czechoslovakia, France, Germany, India and the United Kingdom and by three companies in Japan (Chemical Information Services, 1991).

1.2.2 *Use*

2-Amino-4-nitrophenol is used as an intermediate in the manufacture of CI Mordant Brown 33 and CI Mordant Brown 1, which are used for dyeing leather, nylon, silk, wool and fur (US National Toxicology Program, 1988). It is also used in some countries as a dye in semi-permanent hair colour products to produce gold-blond shades. These products are generally shampooed into the hair, lathered and then allowed to remain in contact with the hair and scalp for 30–45 min. For this application, 2-amino-4-nitrophenol is mixed at levels up to 0.5% with a blend of several other dyes in a shampoo base to produce the final colour or tint (Frenkel & Brody, 1973; US National Toxicology Program, 1988). It has also been used in permanent hair colouring products.

1.3 Occurrence

1.3.1 *Natural occurrence*

2-Amino-4-nitrophenol is not known to occur as a natural product.

1.3.2 *Occupational exposure*

No data were available to the Working Group.

On the basis of a survey conducted in the USA between 1981 and 1983, the US National Institute for Occupational Safety and Health estimated that a total of 20 256 workers, including 17 049 women, were potentially exposed to 2-amino-4-nitrophenol in an estimated 2232 beauty shops (US National Library of Medicine, 1992).

1.3.3 *Other*

2-Amino-4-nitrophenol and 4-amino-2-nitrophenol are reportedly formed by environmental degradation (reduction) of 2,4-dinitrophenol, which is used as a fungicide on wood (Mitra & Vaidyanathan, 1982).

1.4 Regulations and guidelines

The use of 2-amino-4-nitrophenol in cosmetic products is prohibited in the European Economic Community (Commission of the European Communities, 1976, 1990, 1991).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

3.1 Oral administration

3.1.1 *Mouse*

Groups of 50 male and 50 female B6C3F$_1$ mice, seven to eight weeks of age, were administered 0, 125 or 250 mg/kg bw 2-amino-4-nitrophenol (98% pure) [impurities unspecified] by gavage in corn oil (10 ml/kg bw) on five days a week for up to 103 weeks. The mean body weight of low-dose females was up to 17% greater than that of the controls; the body weights of the other treated groups were comparable with those of vehicle controls. No significant difference in survival was observed at termination of the study in treated and control groups of either sex (males: control, 28/50; low-dose, 29/50 and high-dose, 23/50; females: control, 28/50; low-dose, 31/50; and high-dose, 30/50). The incidence of combined haemangiomas and haemangiosarcomas at all sites in high-dose male mice was significantly higher (5/50) than that in controls (0/50; $p < 0.05$, Fisher exact test); however, these tumours were not considered to be related to the treatment since their incidence in historical controls at the study laboratory was 16/149 (11 ± 10%) and that in all studies of the National Toxicology Program was 101/1743 (6 ± 5%) (US National Toxicology Program, 1988).

3.1.2 *Rat*

Groups of 50 male and 50 female Fischer 344/N rats, six weeks of age, were administered 0, 125 or 250 mg/kg bw 2-amino-4-nitrophenol (98% pure) [impurities unspecified] by gavage in corn oil (5 ml/kg bw) on five days a week for up to 103 weeks. Mean body weights of low-dose and high-dose males were 6 and 10% lower than those of controls, respectively; values for female rats were comparable to those of controls. Survival of high-dose males was significantly lower than that of controls ($p < 0.001$, Cox and Tarone's method); no significant difference was found for females. Survival at the end of the study was, in males, control, 32/50; low-dose, 24/50; high-dose, 10/50, and, in females, control, 25/50; low-dose, 27/50; high-dose, 31/50. Hyperplasia of the renal tubular epithelium was observed only in male rats (control, 1/50; low-dose, 4/48; high-dose, 5/50); the difference was not significant. Renal tubular-cell adenomas were also observed in treated males (control, 0/50; low-dose, 1/48; high-dose, 3/50); among male rats that lived beyond week 100, when the first renal tubular-cell tumour was observed, the incidence in high-dose animals (3/20) was

significantly higher than that in controls (0/39; $p = 0.035$, Fisher exact test). Two liver-cell neoplastic nodules and one hepatocellular carcinoma were observed in high-dose male rats. The historical incidence of neoplastic nodules or hepatocellular carcinomas at the study laboratory was 3/149 (2 ± 3%) and that of renal-cell adenomas, 0/149. In all studies of the National Toxicology Program, renal-cell adenomas occurred in 9/1695 (0.5 ± 0.9%) (US National Toxicology Program, 1988).

4. Other Relevant Data

4.1 Absorption, distribution, metabolism and exctretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Percutaneous absorption of ^{14}C-2-amino-4-nitrophenol (specific radioactivity, 10 mCi/mmol [65 μCi/mg]; purity, 98%) was studied *in vitro* by partitioning between excised human abdominal skin preparations and water. 2-Amino-4-nitrophenol appeared to bind to skin components (Bronaugh & Congdon, 1984).

Percutaneous absorption through the skin of Sprague-Dawley rats of each sex was examined following application of two hair dye formulations: formulation 1 contained 1.54% ^{14}C-2-amino-4-nitrophenol; formulation 2 contained 0.77% ^{14}C-2-amino-4-nitrophenol, 1,4-diaminobenzene (1,4-phenylenediamine), 2,4-diaminoanisole, oleic acid and isopropanol and was mixed with equal amounts of a 6% hydrogen peroxide solution. After one and five days, 0.21 and 0.36% of the radiolabel administered in formulation 1 and 1.12 and 1.67% of that administered in formulation 2 had been absorbed (calculated as combined radiolabel in urine, faeces, expired air and carcass, without treated skin area). Absorbed material was excreted predominantly in the urine within 24 h after the initial application (Hofer *et al.*, 1982).

Five days after oral administration by gavage of 2 ml ^{14}C-2-amino-4-nitrophenol (0.2% in saline), 68.3% ± 9.4 (SD) of the radiolabel had been excreted in the urine and 25.4% ± 6.9 in the faeces. Within 3 h, about 4% of the radiolabel was eliminated in the bile. Following subcutaneous injection of the same dose, 89% of the dose was eliminated after one day, predominantly in the urine (Hofer *et al.*, 1982). [The Working Group noted that metabolites were not identified in the urine, bile or faeces in either study.]

2-Amino-4-nitrophenol was the predominant metabolite formed enzymatically by nitroreduction following oral administration of 2,4-dinitrophenol (22.5 mg/kg bw) to ICR mice. It had an elimination half-time from the plasma of 46 h, while that of the isomer 4-amino-2-nitrophenol was 26 h (Robert & Hagardorn, 1985).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

The LD_{50} of 2-amino-4-nitrophenol in rats has been reported as 246 mg/kg bw after intraperitoneal injection (US National Toxicology Program, 1988) and 2400 mg/kg bw after oral administration (Lloyd *et al.*, 1977). The LD_{50} in mice after intraperitoneal injection was reported to be 143 mg/kg bw (Mikstacki, 1985).

During 15-day studies, groups of five Fischer 344/N rats and B6C3F_1 mice of each sex received 0, 313, 625, 1250, 2500 or 5000 mg/kg bw 2-amino-4-nitrophenol (purity, 98%) in corn oil by gavage. Reduced survival was observed in all animals that received 2500 or 5000 mg/kg; diarrhoea was observed in all treated rats except those receiving the lowest dose (US National Toxicology Program, 1988).

In 13-week studies, groups of 10 Fischer 344/N rats and B6C3F_1 mice of each sex received 2-amino-4-nitrophenol at doses of 0, 62.5, 125, 250, 500 or 1000 mg/kg bw by gavage in corn oil. Survival was reduced by the highest dose in both species. Diarrhoea was observed in rats that received 500 or 1000 mg/kg. Mild to severe mineralization of the renal cortex and mild to severe degeneration of the renal tubular epithelium were observed in male rats that received 500 or 1000 mg/kg and in females that received 1000 mg/kg. Degeneration and necrosis of the renal tubular epithelium, with some indication of regeneration, were observed in mice that received 1000 mg/kg (US National Toxicology Program, 1988).

In the two-year studies described above, nephropathy was present in nearly all exposed male rats and was presumed to have contributed to the reduced survival of those given 250 mg/kg. The more severe nephropathy was associated with a spectrum of non-neoplastic lesions characteristic of reduced renal function and renal secondary hyperparathyroidism, i.e., parathyroid hyperplasia, fibrous osteodystrophy, calcification of the heart and other organs (US National Toxicology Program, 1988).

2-Amino-4-nitrophenol was present at a low concentration in an oxidative hair colouring formulation evaluated in a 13-week study of dermal toxicity in rabbits (Burnett *et al.*, 1976, 0.4%) and in a semi-permanent formulation evaluated in a two-year feeding study in dogs (Wernick *et al.*, 1975; 0.05%), described in detail on p. 97. No treatment-related adverse effect was detected. [The Working Group noted that the dose of each component of the formulations was very low and unlikely to have been toxic.]

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

No data were available to the Working Group on the reproductive and developmental effects of 2-amino-4-nitrophenol alone. The compound was present at low concentrations in semi-permanent hair colouring formulations evaluated in a study of fertility and reproductive performance in rats and in studies of teratogenesis in rats and rabbits (Wernick

et al., 1975, 0.05%; see p. 99). It was also present (at 0.4%) in oxidative and semi-permanent formulations evaluated in a study of teratogenesis (Burnett *et al.*, 1976) and in a two-generation study of reproduction in rats (Burnett & Goldenthal, 1988) (see p. 100). No treatment-related adverse effect was detected. [The Working Group noted that the dose of each component of the formulations was very low and unlikely to have been toxic.]

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see also Table 1 and Appendices 1 and 2)

2-Amino-4-nitrophenol did not induce mutation in bacteriophage but was mutagenic to *Salmonella typhimurium*, to the fungus *Sordaria brevicollis* and at the *tk* locus in mouse lymphoma L5178Y cells. It induced sister chromatid exchange and chromosomal aberrations in cultured Chinese hamster ovary cells.

Neither micronuclei, chromosomal aberrations nor dominant lethal effects were induced in rodents exposed *in vivo*.

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 semi-permanent 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.

Table 1. Genetic and related effects of 2-amino-4-nitrophenol

Test system	Result		Dose[a] (LED/HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
BPF, Bacteriophage T4D, forward mutation	–	0	305.1000	Kvelland (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	500.0000	Shahin *et al.* (1982)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	1667.0000	Zeiger *et al.* (1987)[b]
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	500.0000	Shahin *et al.* (1982)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	1667.0000	Zeiger *et al.* (1987)[b]
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	500.0000	Shahin *et al.* (1982)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	1667.0000	Zeiger *et al.* (1987)[b]
SA8, *Salmonella typhimurium* TA1538, reverse mutation	0	+	10.0000	Ames *et al.* (1975)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	+	+	25.0000	Garner & Nutman (1977)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	+	(+)	25.0000	Shahin *et al.* (1982)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	(+)	5.0000	Shahin *et al.* (1982)
SA9, *Salmonella typhimurium* TA98, reverse mutation	(+)	+[c]	50.0000	Zeiger *et al.* (1987)[b]
PLM, *Sordaria brevicollis*, ascospore mutation	+	0	246.0000	Yu-Sun *et al.* (1981)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus	+	0	50.0000	US National Toxicology Program (1988)[b]
SIC, Sister chromatid exchange, Chinese hamster ovary cells *in vitro*	+	+	16.7000	US National Toxicology Program (1988)[b]
CIC, Chromosomal aberrations, Chinese hamster ovary cells *in vitro*	+	+	199.0000	US National Toxicology Program (1988)[b]
MVR, Micronucleus test, CFY rats bone-marrow cells *in vivo*	–		2500.0000 po × 2	Hossack & Richardson (1977)
CBA, Chromosomal aberrations, mouse bone-marrow cells *in vivo*	–		71.3500 ip	Mikstacki (1985)
CVA, Chromosomal aberrations, mouse Ehrlich ascites tumour cells *in vivo*	–		71.3500 ip	Mikstacki (1985)
DLR, Dominant lethal mutation, CD rats	–		20.0000 ip × 24	Burnett *et al.* (1977)

+, positive; (+), weakly positive; –, negative; 0, not tested

[a] In-vitro tests, μg/ml; in-vivo tests, mg/kg bw

[b] Results from two laboratories

[c] Hamster liver S9; negative result with rat liver S9

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[1]

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).*

6. References

Aldrich Chemical Co. (1992) *Aldrich Catalog/Handbook of Fine Chemicals 1992- 1993*, Milwaukee, WI, p. 75

Ames, B.N., Kammen, H.O. & Yamasaki, E. (1975) Hair dyes are mutagenic: identification of a variety of mutagenic ingredients. *Proc. natl Acad Sci. USA*, **72**, 2423–2427

Bronaugh, R.L. & Congdon, E.R. (1984) Percutaneous absorption of hair dyes: correlation with partition coefficients. *J. invest. Dermatol.*, **83**, 124–127

Burnett, C.M. & Goldenthal, E.I. (1988) Multigeneration reproduction and carcinogenicity studies in Sprague-Dawley rats exposed topically to oxidative hair-coloring formulations containing *p*-phenylenediamine and other aromatic amines. *Food Chem. Toxicol.*, **26**, 467–474

Burnett, C., Goldenthal, E.I., Harris, S.B., Wazeter, F.X., Strausburg, J., Kapp, R. & Voelker, R. (1976) Teratology and percutaneous toxicity studies on hair dyes. *J. Toxicol. environ. Health*, **1**, 1027–1040

Burnett, C., Loehr, R. & Corbett, J. (1977) Dominant lethal mutagenicity study on hair dyes. *J. Toxicol. environ. Health*, **2**, 657–662

Chemical Information Services (1991) *Directory of World Chemical Producers*, Dallas, TX, p. 39

Commission of the European Communities (1976) Council Directive 76/768/EEC of 27 July 1976. *Off. J. Eur. Commun.*, **L262**, 169–200

Commission of the European Communities (1990) Proposal for a Council Directive on the approximation of the laws of the Member States relating to cosmetic products of 15 November 1990. *Off. J. Eur. Commun.*, **C322**, 29–77

Commission of the European Communitites (1991) Commission Directive 91/184/EEC of 12 March 1991. *Off. J. Eur. Commun.*, **L91**, 59–62

Farris, R.E. (1978) Aminophenols. In: Mark, H.F., Othmer, D.F., Overberger, C.G., Seaborg, G.T. & Grayson, M., eds, *Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed., Vol. 2, New York, John Wiley & Sons, pp. 422–440

[1]For definition of the italicized terms, see Preamble, pp. 26–30.

Fluka Chemie AG (1993) *Fluka Chemika-BioChemika*, Buchs, p. 93

Frenkel, E.P. & Brody, F. (1973) Percutaneous absorption and elimination of an aromatic hair dye. *Arch. environ. Health*, **27**, 401–404

Garner, R.C. & Nutman, C.A. (1977) Testing of some azo dyes and their reduction products for mutagenicity using *Salmonella typhimurium* TA1538. *Mutat. Res.*, **44**, 9–19

Heraeus (1991) *Feinchemikalien Forschungsbedarf* (Refined chemicals and research supply), Karlsruhe, p. 70

Hofer, H., Schwach, G.W. & Fenzl, C. (1982) Percutaneous absorption of 2-amino-4-nitrophenol in the rat. *Food Chem. Toxicol.*, **20**, 921–923

Hossack, D.J.N. & Richardson, J.C. (1977) Examination of the potential mutagenicity of hair dye constituents using the micronucleus test. *Experientia*, **33**, 377–378

IARC (1980a) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 23, *Some Metals and Metallic Compounds*, Lyon, pp. 325–415

IARC (1980b) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 23, *Some Metals and Metallic Compounds*, Lyon, pp. 39–141

IARC (1987a) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Suppl. 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, pp. 230–232

IARC (1987b) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Suppl. 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, pp. 100–106

Jos. H. Lowenstein & Sons (1991) *Specifications: Rodol 42 (4-Nitro-2-aminophenol Pure)*, New York

Kvelland, I. (1985) Mutagenicity of five hair dyes in bacteriophage T4D. *Hereditas*, **102**, 151–154

Lancaster Synthesis (1991) *MTM Research Chemicals/Lancaster Catalogue 1991/92*, Windham, NH, MTM Plc, p. 69

Lide, D.R., ed. (1991) *CRC Handbook of Chemistry and Physics*, 72nd ed., Boca Raton, FL, CRC Press, p. 3–377

Lloyd, G.K., Liggett, M.P., Kynoch, S.R. & Davies, R.E. (1977) Assessment of the acute toxicity and potential irritancy of hair dye constituents. *Food Cosmet. Toxicol.*, **15**, 607–610

Mikstacki, A. (1985) Evaluation of mutagenicity of some aromatic amines, used as hair dyes, by chromosomal aberration tests *in vivo*. *Genet. pol.*, **26**, 109–116

Mitra, D. & Vaidyanathan, C.S. (1982) Comparative phytotoxicity of nitrophenolic soil pollutants and their microbial metabolites to the growth of cucumber (*Cucumis sativus* L.) seedlings. *Plant Soil*, **69**, 467–471

Pouchert, C.J. (1981) *The Aldrich Library of Infrared Spectra*, 3rd ed., Milwaukee, WI, Aldrich Chemical Co., p. 823

Pouchert, C.J. (1983) *The Aldrich Library of NMR Spectra*, 2nd ed., Vol. 1, Milwaukee, WI, Aldrich Chemical Co., p. 1166

Riedel-de Haen (1990) *Laboratory Chemicals 1990*, Seelze, p. 61

Robert, T.A. & Hagardorn, A.N. (1985) Plasma levels and kinetic disposition of 2,4-dinitrophenol and its metabolites 2-amino-4-nitrophenol and 4-amino-2-nitrophenol in the mouse. *J. Chromatogr.*, **344**, 177–186

Sadtler Research Laboratories (1980) *Sadtler Standard Spectra 1980*, Philadelphia, PA

Sadtler Research Laboratories (1991) *Sadtler Standard Spectra 1981–1991, Supplementary Index*, Philadelphia, PA

Shahin, M.M., Bugaut, A. & Kalopissis, G. (1982) Mutagenicity of aminonitrophenol compounds in *Salmonella typhimurium*: a study of structural–activity relationships. *Int. J. cosmet. Sci.*, **4**, 25–35

Society of Dyers and Colourists (1971) *Colour Index*, 3rd ed., Vol. 4, Bradford, Yorkshire, p. 4647

TCI America (1991) *Organic Chemicals 91/92 Catalog*, Portland, OR, p. 78

US National Library of Medicine (1992) *Registry of Toxic Effects of Chemical Substances* (RTECS No. SJ6300000), Bethesda, MD

US National Toxicology Program (1988) *Toxicology and Carcinogenesis Studies of 2-Amino-4-nitrophenol (CAS No. 99-57-0) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies)* (NTP Tech. Rep. No. 339; NIH Publ. No. 88-2595), Research Triangle Park, NC

Wernick, T., Lanman, B.M. & Fraux, J.L. (1975) Chronic toxicity, teratologic, and reproduction studies with hair dyes. *Toxicol. appl. Pharmacol.*, **32**, 450–460

Yu-Sun, C.C., Carter L.A., Sandoval, L. & Thompson, A. (1981) Mutagenicity of 4-nitroquinoline 1-oxide and three hair dye compounds in *Sordaria brevicollis*. *Neurospora Newslett.*, **28**, 22

Zeiger, E., Anderson, B., Haworth, S., Lawlor, T., Mortelmans, K. & Speck, W. (1987) *Salmonella* mutagenicity tests: III. Results from the testing of 255 chemicals. *Environ. Mutag.*, **9** (Suppl. 9), 1–110