BENZOYL PEROXIDE

Data were last reviewed in IARC (1985) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

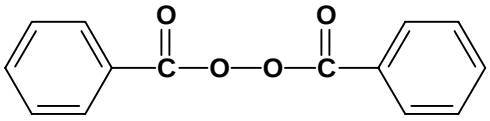
Chem. Abstr. Serv. Reg. No.: 94-36-0

Chem. Abstr. Name: Dibenzoyl peroxide

IUPAC Systematic Name: Benzoyl peroxide

Synonyms: Benzoic acid, peroxide; benzoperoxide; benzoyl superoxide; diphenylglyoxal peroxide

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_{14}H_{10}O_4$ Relative molecular mass: 242.22

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: White granular crystalline solid with a faint odour of benzaldehyde (American Conference of Governmental Industrial Hygienists, 1991; Budavari, 1996)

(*b*) *Boiling-point*: May explode when heated (Budavari, 1996; Lide, 1997)

(*c*) *Melting-point*: 105°C (Lide, 1997)

(*d*) *Solubility*: Slightly soluble in water; soluble in acetone, diethyl ether, ethanol, and most other organic solvents (American Conference of Governmental Industrial Hygienists, 1991; Budavari, 1996; Lide, 1997)

(*e*) *Vapour pressure*: < 13 Pa at 20°C (American Conference of Governmental Industrial Hygienists, 1991)

(*f*) *Reactivity:* Highly flammable and explosive (American Conference of Governmental Industrial Hygienists, 1991)

(*g*) *Conversion factor:* $mg/m^3 = 9.91 \times ppm$

1.2 Production and use

Production of benzoyl peroxide in the United States in 1982 was 2300 tonnes. Information available in 1995 indicated that it was produced in 16 countries (Chemical Information Services, 1995).

Benzoyl peroxide is used as an initiator for polymerization of acrylates (including dental cements and restoratives) and other polymers; as a bleaching agent for flour, fats, oils, waxes and milk used in the preparation of certain cheeses; in pharmaceuticals for the topical treatment of acne; in rubber curing; and as a finishing agent for some acetate yarns (Anon., 1984; Lewis, 1993; Medical Economics Co., 1996; United States Food and Drug Administration, 1997).

1.3 Occurrence

1.3.1 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (NOES, 1997), approximately 90 000 workers in the United States were potentially exposed to benzoyl peroxide (see General Remarks).

Occupational exposures to benzoyl peroxide may occur in its production and use in the plastics, rubber and pharmaceutical industries, and in food processing.

1.3.2 *Environmental occurrence*

No data on the environmental occurrence of benzoyl peroxide were available to the Working Group. General population exposures may occur as a result of its use in pharmaceutical and dental formulations.

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 5 mg/m^3 as the 8-h time-weighted average threshold limit value for occupational exposures to benzoyl peroxide in workplace air. Similar values have been used as standards or guidelines in many countries (International Labour Office, 1991).

No international guideline for benzoyl peroxide in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

The potential carcinogenicity of exposure to benzoyl peroxide has been reviewed (Binder *et al.*, 1995; Kraus *et al.*, 1995).

Among a small factory population, two cases of lung cancer were found in men (one 40-year-old smoker and one 35-year-old nonsmoker) who were involved primarily in the production of benzoyl peroxide but were also exposed to benzoyl chloride (see this volume) and other chemicals (IARC, 1985).

In a study based on the Los Angeles County, United States, Cancer Surveillance Program, white male chemists with malignant melanoma and with other cancers (used as controls) were interviewed (Wright *et al.*, 1983). Four of the seven chemists with malignant melanoma gave a history of exposure to benzoyl peroxide (among many other chemicals) and none of the nine controls.

In a pilot case–control study of malignant melanoma in England (Cartwright *et al*., 1988), 159 cases aged less than 45 years and seen between 1984 and 1986 were compared with 213 controls matched for general practitioner, sex and age. The risk ratio between past acne and malignant melanoma was 1.1 (95% confidence interval (CI), 0.7–1.9). The risk ratio between use of benzoyl peroxide and malignant melanoma was 0.5 (95% CI, 0.2–1.5).

A population-based case–control study of acne treatments as risk factors for skin cancer of the head and neck was carried out in the Province of Saskatchewan, Canada (Hogan *et al.*, 1991). The study was specifically designed to cover the age group who may have used benzoyl peroxide from the time it was marketed in Canada (1966). With interviews conducted in 1989, women aged 10–56 and men aged 10–51 years were included. Cases were identified from the files of the Saskatchewan cancer registry, and confirmed as being resident in Saskatchewan at the time of diagnosis and at the time of study. Four age- and sex-matched controls per case were identified from the files of the Saskatchewan Medicare Plan. All subjects were asked to complete a self-administered mailed questionnaire, that requested information on risk factors for skin cancer and all acne medications used. A list of 33 widely-used acne medications (including trade names) was supplied to facilitate recall of use at any time in the past. The response rate for the 964 cases was 91% and for the 3856 controls was 80%. Of the cases that responded, 92.3 (791) had basal-cell carcinoma, 4.8% (41) squamous-cell carcinoma and 2.9% (25) malignant melanoma. Nine per cent of the cases and 10.1% of the controls recalled use of preparations containing benzoyl peroxide, for average periods of 2.4 and 2.0 years, respectively. The odds ratio for use of benzoyl peroxide for all cases combined was 0.8 (95% CI, 0.5–1.3), and there was no association with the use of any single preparation containing benzoyl peroxide.

3. Studies of Cancer in Experimental Animals

Benzoyl peroxide was tested for carcinogenicity in mice and rats by oral administration in the diet and by subcutaneous administration, and in mice by skin application. In three studies by skin application in mice, benzoyl peroxide was tested for either initiating or promoting activity. All of the studies were inadequate for an evaluation of complete carcinogenicity; two studies indicated that benzoyl peroxide has promoting activity in mouse skin (IARC, 1985).

3.1 Skin application

Mouse: A group of 20 female SEN mice, four weeks of age, was treated twice weekly for 51 weeks with 0.2 mL of a 100 mg/mL solution of benzoyl peroxide in acetone applied to the skin shaved 48 h previously. A group of 15 mice receiving 0.2 mL acetone served as controls. At the termination of the experiment, there were no skin tumours among the control mice, compared with 8/20 in the benzoyl peroxide-treated mice ($p < 0.05$), of which 5/20 were squamous-cell carcinomas. The first tumour developed in week 24. Six of 20 mice showed epidermal hyperplasia (Kurokawa *et al*., 1984).

Groups of five male heterozygous TG.AC mice (carrying a v-Ha-*ras* gene) derived from the wild-type FVB/N strain were treated with 0, 1, 5 or 10 mg benzoyl peroxide in 0.2 mL acetone on the shaved dorsal skin twice a week for 20 weeks. Groups of five male FVB/N mice were similarly treated. No papillomas developed in the FVB/N mice. The incidences of papilloma-bearing mice in the four groups of TG:AC mice were 0/5, 0/5, 3/5 and 3/4, respectively (one papilloma-bearing mouse in the 10-mg group died before the end of the experiment) (Spalding *et al*., 1993).

3.2 Administration with known carcinogens

3.2.1 *Mouse*

Benzoyl peroxide was tested for promoting activity in groups of 20 and 15 female SEN mice receiving a single topical application of 20 nmol 7,12-dimethylbenz[*a*]anthracene (DMBA) followed by either 0.2 mL of a 100 mg/mL solution of benzoyl peroxide in acetone or acetone alone for 51 weeks. At the termination of the experiment, there were no skin tumours among the 15 control mice, compared with 20/20 in the benzoyl peroxide-treated mice ($p < 0.01$), of which 18/20 were squamous-cell carcinomas. The first tumour developed in week 8. All 20 treated mice showed epidermal hyperplasia (Kurokawa *et al*., 1984).

Groups of female SEN mice, five to seven weeks of age, were treated with a single topical application of 10 nmol DMBA on the shaved dorsal skin. Twice-weekly applications of 1 µg 12-*O*-tetradecanoylphorbol 13-acetate (TPA) were begun two weeks later and continued for 20 weeks. Beginning at week 21, one group of 21 papilloma-bearing mice continued to receive 1 µg TPA, while another group of 20 papilloma-bearing mice began twice-weekly treatments of 20 mg benzoyl peroxide. All solutions were applied in 0.2 mL acetone and treatments were ended at week 40. No new tumours appeared during weeks 21–40 in the benzoyl peroxide-treated group. At the end of the experiment, the proportion of mice with skin carcinomas was 70% in the benzoyl peroxide-treated group compared with 38% in the TPA-treated group and the cumulative number of carcinomas was 3.25-fold higher in the benzoyl peroxide-treated group. All skin tumours present at the end of the experiment were examined histologically. While no keratoacanthomas were identified in the TPA-treated group, 17 were found in the benzoyl peroxide-treated group. The authors concluded that benzoyl peroxide enhances the progression of benign to malignant tumours (O'Connell *et al*., 1986). However, in a similarly designed and

executed experiment, it was found that benzoyl peroxide did not enhance the progression of papillomas to squamous-cell carcinomas in SEN mice (Battalora *et al*., 1996).

Three groups of 16 male and 16 female *hr/hr* Oslo strain mice [age unspecified] were treated with a single topical application of 51.2 µg DMBA in 100 µL acetone. One group then received an application (rubbed into the skin [quantity not specified]) of Panoxyl, a gel containing 5% benzoyl peroxide used for the treatment of acne, twice each week for up to 60 or 61 weeks; a second group was similarly treated, but with gel not containing benzoyl peroxide and the third group was not treated further. A fourth group received Panoxyl treatment only. The total numbers of skin tumours in each group of mice were: DMBA alone, 22/32 (18 papillomas, 4 squamous-cell carcinomas); Panoxyl alone, 2/32 (2 squamous-cell carcinomas); DMBA + Panoxyl, 51/30 (49 papillomas, 3 squamous-cell carcinomas); DMBA + gel, 31/32 (31 papillomas). Both Panoxyl and the gel without benzoyl peroxide increased the multiplicity of papillomas induced by DMBA (Iversen, 1986).

The last experiment was repeated in part using *hr/hr* Oslo strain mice and extended by the use of SEN mice. The data were mainly presented as summary statistics. In contrast to the earlier results, the gel without benzoyl peroxide did not enhance DMBA carcinogenesis in *hr/hr* mice and Panoxyl did not enhance DMBA carcinogenesis in SEN mice. Groups of 32 *hr/hr* mice were also treated with ultraviolet radiation (UV) from new Phillips HP 3114 sunlamps, either alone twice a week or 5–30 min before treatment with Panoxyl or the gel without benzoyl peroxide. The numbers of mice with skin carcinomas (and the total numbers of skin tumours in each group of mice) were: UV alone, 26/32 (103 papillomas, 45 carcinomas); UV + Panoxyl, 22/32 (94 papillomas, 30 carcinomas); UV + gel, 23/32 (126 papillomas, 29 carcinomas). Thus, neither Panoxyl nor the gel without benzoyl peroxide had any significant effect upon the multiplicity of UV-induced skin tumours (Iversen, 1988).

One hundred and forty-eight Uscd (Hr) albino hairless mice [sex unspecified], three to four months of age, received 270 mJ/cm^2 UVB radiation to the posterior halves of their backs three times each week for eight weeks. The UVB source was an Hanovia air-cooled hot quartz contact lamp emitting 54 mJ/cm^2/s of UVB energy at a distance of 3.4 cm. Four weeks later the irradiated mice were divided into four groups that were treated in the irradiated area as follows: group 1 received 0.1 mL 0.1% croton oil in acetone five times per week for the duration of the study; group 2 received 0.1 mL acetone; group 3 received 0.1 mL benzoyl peroxide diluent; group 4 received 0.1 mL 5% benzoyl peroxide lotion [i.e., about 5 mg benzoyl peroxide]. At week 62, when the experiment was terminated, the tumour incidences in the irradiated areas of the skin were: group 1, 9/24; group 2, 1/20; group 3, 1/22; group 4, 2/26. Under the circumstances of the experiment, croton oil, but not benzoyl peroxide, enhanced the incidence of skin tumours induced by UVB radiation (Epstein, 1988).

A comparative initiation/promotion skin application study was conducted with B6C3F$_1$, CD-1 and SEN mice. In the portions of the study that are relevant to benzoyl peroxide, groups of 30 male and 30 female mice of each strain were treated on the shaved

skin as follows: A, acetone, the vehicle for all the substances (0.1 mL) alone, once per week; B, 2.5 µg DMBA, once, followed one week later with 0.1 mL acetone once per week for 51 weeks; C, 25 µg DMBA, once, followed one week later with 0.1 mL acetone once per week for 51 weeks; D, 20 mg benzoyl peroxide, followed one week later with 20 mg benzoyl peroxide in 0.2 mL acetone once per week for 51 weeks; E, as group B, followed one week later with 20 mg benzoyl peroxide in 0.2 mL acetone once per week for 51 weeks; F, as group C, followed one week later with 20 mg benzoyl peroxide in 0.2 mL acetone once per week for 51 weeks; G, 100 µg *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine (MNNG), once, followed one week later with 0.1 mL acetone once per week for 51 weeks; H, 500 µg MNNG, once, followed one week later with 0.1 mL acetone once per week for 51 weeks; I, as group D; J, as group G, followed one week later with 20 mg benzoyl peroxide in 0.2 mL acetone once per week for 51 weeks; and K, as group H, followed one week later with 20 mg benzoyl peroxide in 0.2 mL acetone once per week for 51 weeks. For each strain, survival of male and female mice in most groups was similar, but it was significantly reduced ($p < 0.01$) in male CD-1 and SEN mice of group H. Body weight gain also was similar in most groups, but was significantly reduced in female B6C3F_1 mice of group K ($p < 0.01$). The skin tumour responses are shown in Table 1. In neither sex of any strain did benzoyl peroxide act as a complete skin carcinogen, but it was active as a promoter in both sexes of SEN mice, following initiation with DMBA (at both dose levels) or MNNG (at both dose levels). The CD-1 strain and, in particular, the B6C3F_1 strain, were clearly less sensitive than the SEN strain (United States National Toxicology Program, 1996).

3.2.2 *Hamster*

Male Syrian hamsters [age unspecified] were randomized into five groups of 20 and treated as follows: group 1 received 1 mL acetone applied to the shaved dorsal area three times each week; group 2 received 10 mg/kg bw DMBA in sesame oil once by gavage; group 3 received 160 mg benzoyl peroxide in 1 mL acetone applied to the shaved dorsal skin three times per week; group 4 was treated with DMBA as group 2, followed one week later by 80 mg benzoyl peroxide in 1 mL acetone applied to the shaved dorsal skin three times per week; group 5 was treated with DMBA as group 2, followed one week later by treatment as group 3. After 16 months, all surviving hamsters were killed. The 25% survival in the groups was: group 1, 442 days; group 2, 376 days; group 3, 427 days; group 4, 342 days; group 5, 407 days. Histological assessment of the treated areas of skin indicated that the numbers of melanotic foci per hamster (arithmetic means and 95% CI) were: group 2, 6.3 (3.6–9.0); group 4, 17.4 (13.2–21.6); group 5, 26.9 (22.5–31.2); the corresponding numbers of melanotic tumours per hamster were: group 2, 0.6 (0.2–1.0); group 4, 2.2 (1.3–3.1); group 5, 2.9 (2.0–3.7). Benzoyl peroxide treatment enhanced the frequency of melanotic skin tumours in Syrian hamsters treated with DMBA (Schweizer *et al*., 1987).

Table 1. Skin tumour responses to treatment with carcinogens and/or benzyl peroxide in mice

Sex, group (treatment)	$B6C3F_1$	CD-1	SEN
Male A (acetone)	0/30	0/30	0/30
Male B (DMBA 2.5 µg)	0/30	0/30	0/29
Male C (DMBA 25 µg)	0/30	0/30	0/31
Male D (benzoyl peroxide/benzoyl peroxide)	0/30	0/30	0/30
Male E (DMBA 2.5 µg/benzoyl peroxide)	1/30	1/30	20/30
Male F (DMBA 25 µg/benzoyl peroxide)	1/30	6/30	22/30
Male G (MNNG 100 µg)	0/30	1/30	2/30
Male H (MNNG 500 µg)	1/30	7/30	19/30
Male I (benzoyl peroxide /benzoyl peroxide)	0/30	0/30	0/30
Male J (MNNG 100 µg/benzoyl peroxide)	0/30	1/30	9/30
Male K (MNNG 500 µg/benzoyl peroxide)	3/30	11/30	25/30
Female A (acetone)	0/30	0/30	0/29
Female B (DMBA 2.5 µg)	0/30	0/30	0/31
Female C (DMBA 25 µg)	0/30	0/30	0/29
Female D (benzoyl peroxide/benzoyl peroxide)	0/30	0/30	0/30
Female E (DMBA 2.5 µg/benzoyl peroxide)	4/30	1/30	22/30
Female F (DMBA 25 µg/benzoyl peroxide)	2/30	5/30	20/30
Female G (MNNG 100 µg)	0/30	0/30	0/30
Female H (MNNG 500 µg)	0/30	6/30	8/30
Female I (benzoyl peroxide/benzoyl peroxide)	0/30	0/30	1/30
Female J (MNNG 100 µg/benzoyl peroxide)	1/30	3/30	9/30
Female K (MNNG 500 µg/benzoyl peroxide)	3/30	13/30	16/30

From United States National Toxicology Program (1996)
DMBA, 7,12-dimethylbenz[*a*]anthracene; MNNG, *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine
All doses of benzoyl peroxide were 20 mg.

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Incubation of benzoyl peroxide with keratinocytes and the spin trap 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) results in the generation of an electron paramagnetic resonance spectrum characteristic of an alkyl radical adduct (Kensler *et al*., 1988). Indeed, it has been known for a long time that benzoyl peroxide decomposes to benzoyloxyl and phenyl radicals in the presence of metals and heat. Electron paramagnetic resonance

spectroscopy and spin trapping in physiological media support the formation of benzoyloxyl and phenyl radicals, but not hydroxyl radicals (Hazlewood & Davies, 1996). The involvement of benzoyloxyl radicals in covalent binding to macromolecules is supported by the similar binding of both ring-^{14}C- and carbonyl-^{14}C-labelled benzoyl peroxide to protein. Binding to DNA was not observed in this study. Binding of labelled benzoic acid did not occur with either protein or DNA (Swauger *et al*., 1990). The production of free radicals continues at non-toxic concentrations of benzoyl peroxide in both freshly isolated and cultured human keratinocytes (Iannone *et al*., 1993).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

A single exposure to 10^{-10} mol/L benzoyl peroxide stimulated DNA synthesis in primary liver cells from four-day-old rats cultured in low-calcium medium. This effect was fully suppressed by simultaneous addition of α-tocopherol, selenous acid or superoxide dismutase (Romano *et al*., 1986). However, benzoyl peroxide was not mitogenic to human bronchial epithelial cells (Saladino *et al*., 1985).

Treatment of inbred SEN mouse skin with 20 mg benzoyl peroxide led to the transient induction of transforming growth factor β1 mRNA (Patamalai *et al*., 1994) and interleukin-1 (Lee *et al*., 1993). The number of mast cells also increased during benzoyl peroxide treatment, in a 30 μm-wide strip below the epidermis (de Rey *et al*., 1994).

A role for free radicals generated from benzoyl peroxide in tumour promotion is suggested by the general inhibitory (> 90%) effect of antioxidants, such as butylated hydroxytoluene, butylated hydroxyanisole, *para*-hydroxyanisole, disulfiram, α-tocopherol and ascorbic acid, the inhibitory effect of free radical scavengers, such as glutathione and *N*-acyl dihydroxylamines, and the enhancing effect of diethyl maleate, which reduces glutathione levels (Slaga, 1995).

4.3 Reproductive and developmental effects

The available data were inadequate to evaluate the teratogenic potential of benzoyl peroxide (IARC, 1985).

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 2 for references)

Benzoyl peroxide was not mutagenic to bacteria, did not induce chromosomal aberrations in Chinese hamster lung cells and did not induce dominant lethal effects in mice. It has subsequently been shown to induce DNA single-strand breaks and DNA–protein

Table 2. Genetic and related effects of benzoyl peroxide

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	2500	Ishidate *et al*. (1980)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	2500	Ishidate *et al*. (1980)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	2500	Ishidate *et al*. (1980)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	2500	Ishidate *et al*. (1980)
SAS, *Salmonella typhimurium* TA92, reverse mutation	–	–	2500	Ishidate *et al*. (1980)
SAS, *Salmonella typhimurium* TA94, reverse mutation	–	–	2500	Ishidate *et al*. (1980)
CIC, Chromosomal aberrations, Chinese hamster lung CHL cells *in vitro*	–	NT	200	Ishidate *et al*. (1980)
AIA, Aneuploidy, Chinese hamster lung CHL cells *in vitro*	–	NT	200	Ishidate *et al*. (1980)
DIH, DNA single-strand breaks and DNA–protein cross-links, human bronchial epithelial cells *in vitro*	+	NT	242	Saladino *et al*. (1985)
DLM, Dominant lethal test, mice	–		62 ip × 1	Epstein *et al*. (1972)
ICR, Inhibition of gap-junctional intercellular communication, primary mouse keratinocytes *in vitro*	+	NT	40	Jansen *et al*. (1996)
ICR, Inhibition of gap-junctional intercellular communication, initiated primary mouse keratinocytes *in vitro*	+	NT	10	Jansen & Jongen (1996)
Increase in intercellular communication, Syrian hamster embryo cells *in vitro*	+	NT	242	Mikalsen & Sanner (1994)

[a] +, positive; –, negative; NT, not tested
[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL; in-vivo tests, mg/kg bw/day; ip, intraperitoneal

cross-links in cultured human bronchial epithelial cells. Benzoyl peroxide (10 μM, 1–2 h) produced a maximum three-fold increase in levels of 8-hydroxy-2′-deoxyguanosine in the DNA of cultured mouse keratinocytes, whereas the stable metabolic product, benzoic acid, did not produce this adduct (King *et al*., 1996). Results have been reported that are consistent with both the addition of benzoyloxyl and phenyl radicals to the C5–C6 double bond of pyrimidines and, to a lesser extent, hydrogen abstraction from sugar rings of RNA and DNA. The benzoyloxyl radical appears to be responsible for the majority of DNA strand breaks and high yields of altered bases through the formation of base adducts (Hazlewood & Davies, 1996).

Benzoyl peroxide generally inhibits gap-junctional intercellular communication in cultured cells. In contrast, an increase in gap-junctional intercellular communication was observed in a Syrian hamster embryo cell line. Changes in the expression of gap-junctional proteins (connexins) concomitant with inhibition of gap-junctional intercellular communication have been observed. In SEN mice treated with 83 μmol benzoyl peroxide, keratinocytes expressed the gap-junctional connexin 26 gene (not normally expressed in adult mouse skin), transiently increased the expression of connexin 43 and reduced the expression of connexin 31.1 (Budunova *et al*., 1995, 1996). In primary mouse keratinocyte cultures, benzoyl peroxide strongly decreased the amount of E-cadherin protein (Jansen *et al*., 1996).

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Exposure to benzoyl peroxide may occur in its manufacture and use as an initiator in polymer production, food bleaching and rubber curing. Consumer exposure occurs from acne medications and dental products containing benzoyl peroxide.

5.2 Human carcinogenicity data

Two case–control studies have evaluated exposure to benzoyl peroxide among cases of malignant melanoma. One of these studies (the smallest) (among chemists) suggested a greater frequency of exposure among cases than controls. A third large population-based case–control study, designed specifically to evaluate the possible risk of benzoyl peroxide used as an acne medication among young persons, included largely cases of basal-cell carcinoma of the skin. There was no association with use of benzoyl peroxide in this study.

5.3 Animal carcinogenicity data

Benzoyl peroxide was tested in two studies by skin application in strains of mice susceptible to the development of skin papillomas and in several skin-painting studies in mice and in one study in hamsters in combination with known carcinogens. In one study by skin application in mice, it induced benign and malignant skin tumours and, in the

other study, benign skin tumours. Benzoyl peroxide was active as a skin tumour promoter in several strains of mice.

5.4 Other relevant data

Benzoyl peroxide forms radicals that are involved in its covalent binding to macromolecules. Its biological effects are inhibited by antioxidants.

Its genotoxic properties have received little attention. DNA damage has been observed in treated mammalian cells, but it is not mutagenic in bacteria and does not cause chromosomal damage in cultured mammalian cells or dominant lethal effects in mice.

5.5 Evaluation

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

There is *limited evidence* in experimental animals for the carcinogenicity of benzoyl peroxide.

Overall evaluation

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

6. References

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