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Amended Final Report of the Safety Assessment of Dibutyl Adipate as Used in Cosmetics[1]

Dibutyl Adipate, the diester of butyl alcohol and adipic acid, functions as a plasticizer, skin-conditioning agent, and solvent in cosmetic formulations. It is reportedly used at a concentration of 5% in nail polish and 8% in suntan gels, creams, and liquids. Dibutyl Adipate is soluble in organic solvents, but practically insoluble in water. Dibutyl Adipate does not absorb radiation in the ultraviolet (UV) region of the spectrum. Dibutyl Adipate is not toxic in acute oral or dermal animal toxicity tests. In a subchronic dermal toxicity study, 1.0 ml/kg day^{-1} caused a significant reduction in body weight gain in rabbits, but 0.5 ml/kg/day[1] was without effect. In a study with dogs, no adverse effects were observed when an emulsion containing 6.25% Dibutyl Adipate was applied to the entire body twice a week for 3 months. Dibutyl Adipate was tested for dermal irritation using rabbits and mice and a none to minimal irritation was observed. Dibutyl Adipate at a concentration of 25% was not a sensitizer in a guinea pig maximization study. Undiluted Dibutyl Adipate was minimally irritating to the eyes of rabbits and 0.1% was nonirritating. A significant increase in fetal gross abnormalities was observed in rats given intraperitoneal injections of Dibutyl Adipate at 1.75 ml/kg on 3 separate days during gestation, but no effect was seen in animals given 1.05 ml/kg. Dibutyl Adipate was not genotoxic in either bacterial or mammalian test systems. Clinical patch tests confirmed the absence of skin irritation found in animal tests. Clinical phototoxicity tests were negative. Dibutyl Adipate at 0.1% was not an ocular irritant in two male volunteers. In a clinical test of comedogenicity, Dibutyl Adipate produced no effect. The Cosmetic Ingredient Review (CIR) Expert Panel recognized that use of Dibutyl Adipate in suntan cosmetic products will result in repeated, frequent exposure in a leave-on product. The available data demonstrate no skin sensitization or cumulative skin irritation, no comedogenicity, and no genotoxicity. Combined with the data demonstrating little acute toxicity, no skin or ocular irritation, and no reproductive or developmental toxicity, these data form an adequate basis for reaching a conclusion that Dibutyl Adipate is safe as a cosmetic ingredient in the practices of use and concentrations as reflected in this safety assessment.

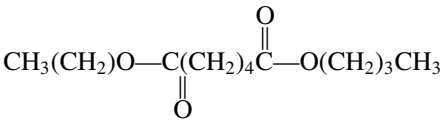
INTRODUCTION

Dibutyl Adipate is the diester of butyl alcohol and adipic acid. An earlier safety assessment (Andersen 1996) found the available data insufficient to support the safety of Dibutyl Adipate in cosmetic formulations. Additional data were made available that address the needs identified by the Cosmetic Ingredient Review (CIR) Expert Panel. These data, combined with those in the original report, updated as appropriate, form the basis for this amended safety assessment.

CHEMISTRY

Definition and Structure

As given in the *International Cosmetic Ingredient Dictionary and Handbook*, Dibutyl Adipate (CAS no. 105-99-7) is the diester of butyl alcohol and adipic acid that conforms to the following formula (Pepe et al. 2002):



Other names for Dibutyl Adipate include:

- Hexanedioic Acid, Dibutyl Ester (RTECS 1992);
- Adipic Acid Dibutyl Ester (RTECS 1992);
- Dibutyl Adipinate (RTECS 1992); and
- Dibutyl Hexandioate (RTECS 1992).

Trade names for Dibutyl Adipate include AEC Dibutyl Adipate, Cetiol B, Saboderm DBA, and Unitolate B (Pepe et al. 2002).

Chemical and Physical Properties

The physical and chemical properties are summarized in Table 1.

Dibutyl Adipate has a molecular weight of 258.36, a boiling point of 165°C, and a melting point of −32.4°C (Weast 1982). It has a density of 0.962 g/cm^3 (Aldrich Chemical Company 1992) and is soluble in alcohol and ethanol (Weast 1982). The flash point is greater than 230°F (Aldrich Chemical Company 1992).

In a data profile for Cetiol B®, Cognis Deutschland GmbH & Co. (2002a), Dibutyl Adipate is described as a clear, colorless, polar oil. It's high spreading value (1000 mm^3/10 min) is said to make this ingredient well-suited for use in cosmetic skin care preparations. The maximum acid value is 0.5, the saponification value is in the 420 to 440 range, the refractive index is between 1.4340 and 1.4370, and the density is 0.958 to 0.962 g/cm^3. The

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[1]Reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel.

TABLE 1
Chemical and physical properties of Dibutyl Adipate

Property	Description	Reference
Appearance	Clear, colorless oil	Cognis Deutschland GmbH & Co. 2002a
Molecular weight	258.36	Weast 1982
Density	0.962 g/cm^3	Aldrich Chemical Company 1992
	0.958–0.962 g/cm^3	Cognis Deutschland GmbH & Co. 2002a
Viscosity	5–7 Pascal (20°C)	Cognis Deutschland GmbH & Co. 2002a
Refractive index	1.4340–1.4370	Cognis Deutschland GmbH & Co. 2002a
Solubility	Soluble in alcohol and ethanol	Weast 1982
	Soluble in ethyl ether, chloroform, petrol ether, ethyl alcohol, and paraffin oil; practically insoluble in water	Cognis Deutschland GmbH & Co. 2002a
Flash point	>250°F	Aldrich Chemical Company 1992
Spreading value	~1000 mm^3/10 min	Cognis Deutschland GmbH & Co. 2002a
Acid value$_{max.}$	0.5	Cognis Deutschland GmbH & Co. 2002a
Hydroxyl value$_{max.}$	1.0	Cognis Deutschland GmbH & Co. 2002a
Iodine value$_{max.}$	1.0	Cognis Deutschland GmbH & Co. 2002a
Saponification value	420–440	Cognis Deutschland GmbH & Co. 2002a
Impurities		
Arsenic	<1 ppm	Cognis Deutschland GmbH & Co. 2002a
Heavy metals (as Pb)	<10 ppm	Cognis Deutschland GmbH & Co. 2002a
Sulfated ash	<0.1%	Cognis Deutschland GmbH & Co. 2002a
UV absorption	No absorption from 280–500 nm	Cognis Deutschland GmbH & Co. 2002b

maximum hydroxy and iodine values are both given as 1.0, and the viscosity (at 20°C) is between 5 and 7 mPascal.

The data profile also notes that Dibutyl Adipate is very soluble in ethyl ether, chloroform, petrol ether, ethyl alcohol, and paraffin oil. It is practically insoluble in water.

Impurities are generally not found due to the manufacturing process, but available data demonstrate that arsenic levels are below a detection limit of 1 ppm, heavy metals (as Pb) are below a detection limit of 10 ppm, and sulphated ash is below a detection limit of 0.1% (Cognis Deutschland GmbH & Co. 2002a).

Cognis Deutschland GmbH & Co. (2002b) stated that no absorption of ultraviolet (UV) radiation was detected in the 280 to 500 nm region.

Method of Manufacture

According to Cognis Deutschland GmbH & Co. (2002a), adipic acid and butyl alcohol are esterified at increased temperature (not specified). The water generated in the esterification is removed by distillation and Dibutyl Adipate is produced by further distillation.

USE

Cosmetic

The *International Cosmetic Ingredient Dictionary and Handbook* lists the functions of Dibutyl Adipate in cosmetic formulations as plasticizer; skin conditioning agent—emollient, and solvent (Pepe et al. 2002).

Product formulation data submitted to the Food and Drug Administration (FDA) in 1994 revealed use in one formulation in the "other fragrance preparations" product category (FDA 1994). In 2002, FDA received no reports of Dibutyl Adipate use, nor were any reports received of use of any of the trade name products (FDA 2002). Current concentration of use data provided by industry to CIR, however, indicate use at a maximum concentration of 5% in the nail polish and enamel product category and 8% in the suntan gels, creams, and liquids category (CTFA 2002).

Noncosmetic

The FDA has included a related chemical, diisobutyl adipate, in Part 181 of Title 21 of the Code of Federal Regulations (CFR)—Prior-sanctioned Food Ingredients, Subpart B—Specific Prior-Sanctioned Food Ingredients includes Sec. 181.27, Plasticizers. In this section, "substances classified as plasticizers, when migrating from food-packaging material shall include . . . diisobutyl adipate . . ." (21 CFR §181.27).

GENERAL BIOLOGY

Cytotoxicity

Dibutyl Adipate was tested for cytotoxicity in the metabolic inhibition test. A dilution series of Dibutyl Adipate was

suspended in HeLa cells. After 24 h, cell viability was determined by microscopy. Viability was also measured after 7 d by looking at the color change of the phenol red in the medium. Dibutyl Adipate had no acute toxicity to the cells, which the investigators attributed to its insolubility in water (Ekwall et al. 1982).

ANIMAL TOXICOLOGY

Acute Toxicity

Oral

The Mellon Institute of Industrial Research (1950) reported that the oral LD_{50} in rats was 11.26 g/kg for a 20% dispersion of Dibutyl Adipate in 1% Tergitol 7. At greater doses, the authors reported that rats became prostrate and narcotized within 4 h. Death occurred within 24 h, and the liver, kidneys, and gastrointestinal tract were congested at necropsy.

Smyth et al. (1951) reported that the oral LD_{50} of a 20% dispersion of Dibutyl Adipate in rats was 12.9 g/kg.

Cognis Deutschland GmbH & Co. (2002b) provided a summary of an acute oral toxicity study of Dibutyl Adipate in male Wistar rats. Undiluted (or diluted in olive oil—dilution factor not given) Dibutyl Adipate was given to five groups of 10 rats each. The reported oral LD_{50} dose was 1.52 g/kg.

Dermal

The dermal LD_{50} of Dibutyl Adipate (96%) for rabbits was 20 ml/kg (Smyth et al. 1951).

Inhalation

A group of six male albino rats were exposed to a flowing stream of air substantially saturated with Dibutyl Adipate for 8 h. No deaths occurred during exposure (Smyth et al. 1951).

Intraperitoneal

The intraperitoneal LD_{50} of Dibutyl Adipate (96%) for rats was 5.2441 ml/kg (Singh et al. 1973).

Subchronic Dermal Toxicity

In a study by the Mellon Institute of Industrial Research (1951), groups of 10 rabbits were given topical applications of 0.5 and 1.0 ml/kg/day of a 20% dispersion in Tergitol 7 of n-butyl adipate (should have been given as di-n-butyl adipate, aka Dibutyl Adipate) five times a week for 6 weeks. A control group of animals was untreated. The rabbits were weighed weekly and necropsy was performed either at the time of interim death or when the animals were killed at the termination of the study.

Five of the rabbits from the 1.0 ml/kg/day group and one rabbit from the 0.5 ml/kg/day group died from causes unrelated to treatment. A significant decrease in body weight gain was observed in the rabbits of the 1.0 ml/kg/day treatment group as compared to the control animals. Rabbits in the 0.5 ml/kg/day group also gained less weight, but the reduction was not significantly different from the control group. At necropsy, one of the rabbits from the 1.0 ml/kg/day group that survived the treatment period had slight cloudy hepatic swelling and slight cloudy swelling of the renal convoluted and loop tubules. One rabbit from the 0.5 ml/kg/day group had similar renal lesions.

In another study at this laboratory, four dogs were soaked with 2 ml/kg of an emulsion containing 6.25% Dibutyl Adipate in water (containing 0.625% of Emulsifier 75 H 14S) twice a week for a total of 28 applications during a 3-month testing period. The retained dosage was estimated as 1 ml/kg of the emulsion. A control group of two dogs was treated with the vehicle emulsifier. No statistically significant changes in body weight were observed during the study. Slight desquamation was found on the skin of three treated dogs and one of the control dogs, but there was no erythema (Mellon Institute of Industrial Research 1951).

Dermal Irritation

The Mellon Institute of Industrial Research (1950) placed 0.5-square-foot cloth bands impregnated with 1.0 g/sq. ft. of n-butyl adipate (should have been given as di-n-butyl adipate aka Dibutyl Adipate) around the clipped trunks of three rabbits. The bands were kept in contact with the skin for 3-day intervals for 3 weeks. Two of the rabbits had moderate erythema on their flanks after the first 3-day interval, but no signs of irritation were observed after 3 weeks of treatment.

In a similar study, the Mellon Institute of Industrial Research (1951) applied bands impregnated with 2.0, 4.0, and 8.0 g/ft^2 Dibutyl Adipate (see terminology explanation above) to the clipped trunks of groups of five rabbits. New bands were applied to the rabbits twice a week for a total of six applications during the 21-day testing period. No treatment-related progressive damage to the skin was observed.

This laboratory also applied 0.01 ml undiluted Dibutyl Adipate to the clipped skin of five albino rabbits eight times during a 4-h period. All of the rabbits had moderate erythema at 24 h.

In a 3-day repeated application test, this laboratory also treated three rabbits with 0.025 ml undiluted Dibutyl Adipate on intact and abraded sites of their abdomens. Applications were made three times a day at 3-h intervals. Erythema and/or capillary injection were observed in all three of the rabbits during the study. Three days following the last application, all of the rabbits had desquamation (Mellon Institute of Industrial Research 1951).

Smyth et al. (1951) applied undiluted Dibutyl Adipate (0.01 ml) to the clipped belly of albino rabbits (number of animals not stated), and the sites were evaluated after 24 h. Dibutyl Adipate was given a primary skin irritation score of 2 (maximum possible score: 8).

Cognis Deutschland GmbH & Co. (2002b) summarized two dermal studies. Dibutyl Adipate (10% in acetone) was applied once a day for 10 consecutive days to the right ears of five hairless mice (strain hr/hr). The left ears were the controls. No macroscopic adverse effects were observed in the treated ears. In the second study, Dibutyl Adipate was applied 2× per day to

the backs of hairless mice (number of animals not given) for 14 days. No dermal reactions were observed.

Ocular Irritation

Undiluted Dibutyl Adipate was instilled into the conjunctival sac of rabbits (number not specified) for 24 h. The primary irritation score was 1 (maximum possible score: 110) (Smyth et al. 1951).

Cognis Deutschland GmbH & Co. (2002b) summarized in vivo rabbit eye irritation studies. In one study, 0.1 ml of Dibutyl Adipate (0.1% in olive oil) was instilled into the eyes of two New Zealand rabbits, without rinsing. At 2, 6, and 24 h after application, no corneal, irital, or conjunctival reactions were observed. In another test, undiluted Dibutyl Adipate was instilled into the eyes of two New Zealand rabbits. After application, slight corneal irritation was observed. After a few days the reaction disappeared.

Phototoxicity

Cognis Deutschland GmbH & Co. (2002b) summarized an in vitro photohemolysis study conducted with Dibutyl Adipate. Human erythrocytes in culture were exposed to Dibutyl Adipate, followed by irradiation with ultraviolet (UV) light (1 J/cm^2 UVB plus 15 J/cm^2 UVA). Hemolysis is determined by measuring released hemoglobin. Because the material formed unstable emulsions, the assay was not exact, but hemolysis in the presence of UV radiation was slightly increased over non-irradiated samples. It was noted that Dibutyl Adipate does not absorb UV radiation in the UVB or UVA region.

Dermal Sensitization

Cognis Deutschland GmbH & Co. (2002b) summarized a maximization study in which 0.1 ml of 25% Dibutyl Adipate (vehicle not given) was given 10 times at 2-day intervals to five male Pirbright-White-W58 guinea pigs by intradermal injection. After 14 days, the animals were given a retreatment. A slight reddening was evident at the injection site in treated animals. This effect subsided within 2 days. No evidence of dermal sensitization was found.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

In a study by Singh et al. (1973), groups of five pregnant female Sprague-Dawley rats were given intraperitoneal injections of Dibutyl Adipate (96%) in doses of 0.1748, 0.5244, 1.0488, and 1.7480 ml/kg on days 5, 10, and 15 of gestation. Three other groups of pregnant females were injected with distilled water, normal saline, and cottonseed oil. The data obtained from these animals were pooled to determine a 95% confidence interval for an injected volume control. Another group of females was "blunt-needle-injected" (i.e., a needle was inserted but no substance was actually injected). On day 20 of gestation, the females were killed and the uterine horns, ovaries, and fetuses were examined.

The number of corpora lutea was comparable between the experimental and control groups. Resorptions occurred in all of the groups, and ranged from 2.9% to 9.4% in the test groups, 3.7% to 12.3% in the "pooled volume control," and was 6% in the "blunt-needle" group. Dead fetuses were found only in the experimental groups; one fetus from the 1.0488 ml/kg Dibutyl Adipate dose group and two fetuses from the 1.7480 ml/kg treatment group died.

In general, the body weights of the fetuses were lower than those of the control groups, but were not significantly different. No gross, skeletal, or visceral anomalies were found in the 0.1748 ml/kg Dibutyl Adipate group. Gross abnormalities were found in the higher dose groups, but the incidence was increased significantly only in the group receiving 1.7480 ml/kg (5.4%), when compared to both control values (0% for the "blunt-needle" group, and 0.7% to 3.1% for the "pooled volume control"). The types of abnormalities were not specified. However, this study investigated the effects of a number of other adipic acid esters, and the authors stated that the most common gross abnormalities observed among these esters were hemangiomas on various parts of the fetus, twisted hindlegs, and compact head and neck.

No visceral anomalies were found among the control groups, but one anomaly each was found in test groups treated with 0.5244 and 1.7480 ml/kg Dibutyl Adipate. Two skeletal malformations (6.7%) were found in the 1.7480 ml/kg Dibutyl Adipate group, and one (3%) occurred in the "blunt needle group." The 95% confidence interval for these types of anomalies in the "pooled volume control" ranged from 1.0% to 12.6% (Singh et al. 1973).

GENOTOXICITY

Dibutyl Adipate in DMSO was used in an Ames test (Henkel KgaA 1996). Strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 were treated with Dibutyl Adipate at 8, 40, 200, 1000, and 5000 μg/plate in one test and at 50, 125, 250, 500, and 1000 μg/plate in another, each with and without S-9 metabolic activation. Lethal effects were noted without metabolic activation at concentrations of $\geq$250 μg/plate. No mutations were induced by any concentration in any strain, with or without metabolic activation.

RCC Cytotest Cell Research GmbH (2002) performed an in vivo mouse micronucleus test. A single oral administration of 0, 500, 1000, and 2000 mg/kg of Dibutyl Adipate in olive oil was given (10 ml/kg body weight) to six male and six female NMRI mice. A second group of six male and six female mice was also given the high dose and a sixth group received a positive control, cyclophosphamide at 40 mg/kg. At 24 h after dosing, bone marrow cells were collected from the negative control, three dose level, and positive control groups. At 48 h after dosing, cells were collected from the second high dose group. At least 2000 polychromatic erythrocytes per animal were scored. No cytotoxic effects were observed, nor was there a statistically significant enhancement in the number of cells with micronuclei

at any dose or time after dosing. The positive control yielded the expected statistically significant increase in micronucleus frequency.

CLINICAL ASSESSMENT OF SAFETY

Patch Testing

Cognis Deutschland GmbH & Co. (2002b) provided a summary of clinical patch testing results. In a 24-h patch test, undiluted Dibutyl Adipate was tested using 10 volunteers (age, race, sex not given). No skin irritation was reported at 24 or 48 h. In another study, Dibutyl Adipate (20% in alcohol) was applied to the skin of 18 volunteers using large Finn chambers for 24 h. Only slight reactions (not further described) were seen in four subjects.

Phototoxicity

Gesellschaft für Therapie und Leistungforschung Cognis Deutschland GmbH & Co. (2002) summarized a test in which a 10% dilution of Dibutyl Adipate in liquid paraffin was applied to the back of each of 30 healthy volunteers in duplicate, under occlusive patches, for 24 h. The age range was 20 to 59 years, with a mean age of 36 $\pm$ 10 years. Skin types were I, II, and III (type I, always sunburns; type II, usually sunburns; type III, sometimes sunburns). At the time of patch removal, the area under one patch on each volunteer was exposed to 18 J/cm^2 of UVA radiation. Skin reactions were scored immediately, and at 24 and 48 h after irradiation. No skin reactions were observed.

Ocular Irritation

Cognis Deutschland GmbH & Co. (2002b) summarized a test in which 0.1% Dibutyl Adipate (in paraffin oil) was instilled in a single application into one eye of each of two male volunteers. Within 24 h, no conjunctival reactions were observed.

Comedogenicity

Cognis Deutschland GmbH & Co. (2002b) noted that Dibutyl Adipate was not comedogenic at concentrations of 10%, 20%, 50%, or 100% in volunteers. Isopropyl Myristate at 10% induced the expected positive response and the expected negative response at 2%.

SUMMARY

Dibutyl Adipate, the diester of butyl alcohol and adipic acid, functions as a plasticizer, skin conditioning agent, and solvent in cosmetic formulations. It is reportedly used at a concentration of 5% in nail polish and 8% in suntan gels, creams, and liquids. Dibutyl Adipate is soluble in organic solvents, but practically insoluble in water. Dibutyl Adipate does not absorb radiation in the UV region of the spectrum.

The oral LD_{50} values for a 20% dispersion of Dibutyl Adipate ranged from 11.26 to 12.9 g/kg in rats, and for undiluted Dibutyl Adipate was reported to be 15.2 g/kg. The dermal LD_{50} for undiluted Dibutyl Adipate was 20 ml/kg for rabbits.

In a subchronic dermal toxicity study, 1.0 ml/kg/day Dibutyl Adipate caused a significant reduction in body weight gain in rabbits. A dose of 0.5 ml/kg/d Dibutyl Adipate was without effect. In a study with dogs, no adverse effects were observed from an emulsion containing 6.25% Dibutyl Adipate when it was applied to the entire body twice a week for three months.

When undiluted Dibutyl Adipate was tested for dermal irritation using rabbits, it received a primary irritation score of 2, out of a maximum possible score of 8. Undiluted Dibutyl Adipate caused moderate erythema in rabbits following repeated exposure. However, material impregnated with Dibutyl Adipate was not irritating to the skin of rabbits. Application of Dibutyl Adipate at 10% in acetone produced no observable adverse effect when applied to rabbit ears. Dibutyl Adipate applied to the backs of hairless mice twice daily for 14 days produced no dermal reaction.

Dibutyl Adipate at a concentration of 25% was not a sensitizer in a guinea pig maximization study.

Undiluted Dibutyl Adipate was minimally irritating to the eyes of rabbits and 0.1% was not at all irritating.

A photohemolysis study was equivocal because of procedural problems.

In a developmental study in which pregnant mice were intraperitoneally injected with Dibutyl Adipate, a significant increase in fetal gross abnormalities was observed only with the largest dose tested.

In both an Ames test and in a mouse micronucleus test, Dibutyl Adipate was not genotoxic.

Clinical patch tests confirmed the absence of skin irritation found in animal tests. Clinical phototoxicity tests were unequivocal—no skin reactions were seen with Dibutyl Adipate alone or with UV radiation. Dibutyl Adipate at 0.1% was not an ocular irritant in two male volunteers. In a clinical test of comedogenicity, Dibutyl Adipate produced no effect.

DISCUSSION

The CIR Expert Panel previously had concluded that the available data were insufficient to support the safety of Dibutyl Adipate, citing a need for (1) types of cosmetic products Dibutyl Adipate is used in and the typical concentrations of use for each of these products; (2) impurities; (3) UV absorption data; and if absorbed in the UVA or UVB range, possibly photosensitization data; and (4) two genotoxicity assays (one using a mammalian system); if positive, possibly a dermal carcinogenicity assay by National Toxicology Program (NTP) standards.

Data addressing each of these needs has been provided. The Panel understands that Dibutyl Adipate may be used at a maximum concentration of 5% in nail polish and enamel products and 8% in suntan gels, creams, and liquids.

No impurities are present in Dibutyl Adipate that would suggest a toxicologic concern. Although the results were equivocal in an in vitro phototoxicity study, a clinical test demonstrated

that Dibutyl Adipate was not phototoxic. In an in vitro Ames test and an in vivo mouse bone marrow micronucleus assay, Dibutyl Adipate was not genotoxic.

Additional data demonstrated that Dibutyl Adipate was not a skin sensitizer.

The Panel recognized that use of Dibutyl Adipate in suntan cosmetic products will result in repeated, frequent exposure in a leave-on product. The newly available data demonstrate no skin sensitization or cumulative skin irritation, no comedogenicity, and no genotoxicity. Combined with the previous data in the safety assessment demonstrating little acute toxicity, no skin or ocular irritation, and no reproductive or developmental toxicity, these data form an adequate basis for reaching a conclusion regarding the safety of Dibutyl Adipate as currently used in cosmetics.

CONCLUSION

The CIR Expert Panel concluded that Dibutyl Adipate is safe as a cosmetic ingredient in the practices of use and concentrations as described in this safety assessment.

REFERENCES

Andersen, F. A. ed. 1996. Final report on the safety assessment of Dibutyl Adipate. *J Am. Coll. Toxicol.* 15(4):295–300.

Aldrich Chemical Company. 1992. *Catalog Handbook of Fine Chemicals*, 401. Milwaukee: Aldrich Chemical Co., Inc..

Cognis Deutschland GmbH & Co. 2002a. Data Profile: Cetiol® B. Unpublished data submitted by CTFA. 4 pages.[2]

Cognis Deutschland GmbH & Co. 2002b. Cetiol® B Toxicological Evaluation. Unpublished data submitted by CTFA. 8 pages.[2]

Cosmetic, Toiletry, and Fragrance Association (CTFA). 2002. Concentration of use of Dibutyl Adipate as a function of product type. Unpublished data submitted by CTFA. 1 page.[2]

Ekwall, B., C. Nordensten, and L. Albanus. 1982. Toxicity of 29 plasticizers to HeLa cells in the MIT-24 system. *Toxicology* 24:199–210.

Food and Drug Administration (FDA). 1994. Frequency of use of cosmetic ingredients. *FDA database*. Washington FDA.

FDA. 2002. Frequency of use of cosmetic ingredients by chemical and trade name. *FDA databases*. Washington, DC: FDA.

Gesellschaft für Therapie und Leistungforshung MBH. 1998. Single phototopatch test for phototoxicity. Unpublished data submitted by CTFA. 2 pages.

Henkel KgaA. 1996. *Salmonella*/mammalian-microsome mutagenicity test. Unpublished data submitted by CTFA. 6 pages.[2]

Mellon Institute of Industrial Research. 1951. Range finding tests and repeated inunction on n-Butyl Adipate. Submitted by FDA in response to an FOI request dated 01/11/93. 9 pages.[2]

Mellon Institute of Industrial Research. 1950. Range finding tests on n-Butyl Adipate. Submitted by FDA in response to an FOI request dated 01/11/93. 4 pages.[2]

Pepe, R. C., J. A. Wenninger, and G. N. McEwen, Jr., eds. 2002. *International Cosmetic Ingredient Dictionary and Handbook*. 9th ed., Vol. 2. Washington, DC: CTFA.

RCC Cytotest Cell Research GmbH. 2002. Micronucleus Assay in bone marrow cells of the mouse. Unpublished data submitted by CTFA. 23 pages.[2]

Registry of Toxic Effects of Chemical Substances (RTECS). 1992. Dibutyl Adipate Entry. *RTECS database*. Bethesda, MD: National Library of Medicine.

Singh, A. R., W. H. Lawrence, and J. Autian. 1973. Embryonic-fetal toxicity and teratogenic effects of adipic acid esters in rats. *J. Pharm. Sci.* 62:1596–1600.

Smyth, H. F., C. P. Carpenter, and C.S. Weil. 1951. Range-finding toxicity data: List IV. *AMA Arch. Ind. Hyg. Occup. Med.* 4:119–122.

Weast, R.C., ed. 1982. *CRC Handbook of Chemistry and Physics*, 63rd ed., C-81. Boca Raton, FL: CRC Press, Inc.

[2]Available for review upon request from: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036, USA.