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Query: Records containing the term 46

1
NAME: BENZYL ALCOHOL

RN: 100-51-6

HUMAN HEALTH EFFECTS:

HUMAN TOXICITY EXCERPTS:

/HUMAN EXPOSURE STUDIES/ Results /were reported/ of a cosmetic intolerance assay that patch tested 5202 patients with possible allergic contact dermatitis (537 of the patients had a history of "intolerance," allergy, or irritation to cosmetics). Patch test conditions were not specified. A reaction was noted in 48 (0.92%incidence) to benzyl alcohol. Reactions were noted in 2 of the 155 patients with cosmetic allergy.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/HUMAN EXPOSURE STUDIES/ Four positive patch tests to 6.5% benzyl alcohol /were reported/ among 242 patients with histories of contact allergy of varying origin. An index of simultaneous reactivity in which the number of reactions to other perfume ingredients was divided by the number of positive reactions to benzyl alcohol had a value of 0.50 (one individual responded to eugenol and another to isoeugenol).[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/HUMAN EXPOSURE STUDIES/ Patch test results /were complied/ from 12 dermatologists over a 6-year period. Patches had been applied to the upper back for 48 hours of contact, and sites were evaluated at 48 and 72 hours. Three cutaneous reactions to 5% benzyl alcohol in petrolatum were noted among 713 cosmetic dermatitis patients.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/HUMAN EXPOSURE STUDIES/ The Research Institute for Fragrance Materials, Inc. (RIFM) report on benzyl alcohol cited an unpublished Kligman Maximization study that tested 10% benzyl alcohol in petrolatum using 25 male volunteers (skin types: 10 were Caucasian and 15 were Black). Benzyl alcohol (and three other test materials) was applied under occlusive patches to the forearm of panelists. A total of five 48-hour exposures occurred during induction and each was preceded by a 24-hour occlusive pretreatment of the sites with 5% aqueous sodium lauryl sulfate (SLS). Following a 10-day nontreatment period, panelists were challenged on the scapular back with a 48 hour patch. Challenge sites were pretreated for 1 hour with 10%SLS. Challenge sites were examined at 48 and 72 hours. No reactions were observed.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/HUMAN EXPOSURE STUDIES/ A repeat-insult patch test (RIPT) was conducted using a nonexclusive group of 110 panelists. Two mascara formulations each containing 0.65% benzyl alcohol were tested. During a 3-week induction period nine occlusive 24-hour patches (containing 0.15 g of test material) were applied to the same site on either the upper arm or back. Sites were evaluated 24 hours after patch removal (i.e., prior to application of subsequent patch). Following a 12- to 20-day nontreatment period, a challenge patch was applied to both the original site and a previously unexposed site. Challenge sites were evaluated at 24 and 48 hours after patch removal. No reactions were noted during induction or at challenge to either formulation.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract"

target=new>PubMed Abstract

/HUMAN EXPOSURE STUDIES/ Benzyl alcohol (3%) was applied in a polypropylene chamber to the same site on the back of nine healthy female panelists for 4 consecutive days. The duration of exposure was not specified. Sites were visually evaluated on the fifth day. Benzyl alcohol was an irritant according to the Frosch-Kligman scoring system.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/HUMAN EXPOSURE STUDIES/ ... During 4 periods of 6 months, from 1 January 2003 to 31 December 2004, 26 fragrances were patch tested additionally to the standard series in a total of 21,325 patients; the number of patients tested with each of the fragrances ranged from 1658 to 4238. ... The following frequencies of sensitization (rates in %, standardized for sex and age) were observed: tree moss (2.4%), HMPCC (2.3), oak moss (2.0), hydroxycitronellal (1.3), isoeugenol (1.1), cinnamic aldehyde (1.0), farnesol (0.9), cinnamic alcohol (0.6), citral (0.6), citronellol (0.5), geraniol (0.4), eugenol (0.4), coumarin (0.4), lilial (0.3), amyl-cinnamic alcohol (0.3), benzyl cinnamate (0.3), benzyl alcohol (0.3), linalool (0.2), methylheptin carbonate (0.2), amyl-cinnamic aldehyde (0.1), hexyl-cinnamic aldehyde (0.1), limonene (0.1), benzyl salicylate (0.1), gamma-methylionon (0.1), benzyl benzoate (0.0), anisyl alcohol (0.0). ...[Schnuch A et al; Contact Dermatitis 57 (1): 1-10 (2007)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/17577350?dopt=Abstract" target=new>PubMed Abstract

/HUMAN EXPOSURE STUDIES/ A blinded, controlled study in healthy volunteers who were treated with 3 mL of saline with or without benzyl alcohol (9 mg/mL) found that the benzyl alcohol group had bronchitis with erythema, tracheobronchial mucosal edema, metaplasia, denudation of cilia, and mucosal lymphocytic infiltration on bronchoscopy.[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1232] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Benzyl alcohol and especially benzoic acid and sodium benzoate are among various compounds (such as some food additives) recognized in the published literature to induce nonimmunologic contact reactions in certain populations. These agents "produce the reaction without any previous sensitization in most or almost all exposed persons." The hypersensitivity has been indicated by flexural dermatitis, rhinitis, and/or asthma. However, cutaneous changes such as urticaria, angioneurotic edema, and contact urticaria were the more common manifestations. The terms nonimmunologic contact urticaria or nonimmunologic immediate contact reactions were used to describe the occurrence.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/SIGNS AND SYMPTOMS/ Nebulizers of bacteriostatic saline containing benzyl alcohol as a preservative can cause bronchitis in healthy adults.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/SIGNS AND SYMPTOMS/ In 1981 and 1982 several neonatal deaths were ascribed to benzyl alcohol present as a preservative in isotonic saline (9 mg/mL) that had been used to flush catheters. The syndrome consisted of metabolic acidosis, central neural depression, respiratory distress progressing to gasping respiration, hypotension, renal failure, and sometimes seizures and intracranial hemorrhages. In alerting pediatricians of the findings, the FDA reported an estimated daily intake of 99 to 404 mg/kg, which was 20 to 90 times the 4.5-mg/kg dose considered safe for healthy adults. Although the infants involved had "serious underlying disease," biochemical evidence of benzyl alcohol toxicity was found. Blood and urine specimens contained high concentrations of benzyl alcohol, benzoic acid, and hippuric acid.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/SIGNS AND SYMPTOMS/ Benzyl alcohol poisoning can cause the gasping syndrome in neonates. The infants had a typical course of gradual neurologic deterioration, severe metabolic acidosis, the striking onset of gasping respirations, thrombocytopenia, hepatic and renal failure, hypotension, cardiovascular collapse and death. In every infant,

unmetabolized benzyl alcohol was identified in the urine.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.293 (2001). Available from, as of July 9 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ A "gasping" syndrome, which included hypotension, bradycardia, gasping respiration, hypotonia, progressive metabolic acidosis, seizures, cardiovascular collapse, and death, was first described in low-birth-weight neonates in intensive care units. All the infants had received either bacteriostatic water or sodium chloride solution containing 0.9% benzyl alcohol to flush intravenous catheters or in parenteral medications reconstituted with bacteriostatic water or saline. The syndrome occurred in infants who had received greater than 99 mg/kg of benzyl alcohol (range, 99-234 mg/kg).[Goldfrank, L.R., Goldfrank's Toxicologic Emergencies 8th Ed. 2006., McGraw-Hill, New York, N.Y., p. 831] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Epidural or intrathecal injection of 7.5 mg or more benzyl alcohol as a diluent has been followed by paraparesis and flaccid paraplegia. Residual symptoms may be present 26 months after the initial injury.[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1231] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Benzyl alcohol is believe to have a role in the increased frequency of cerebral intraventricular hemorrhages and mortality reported in very-low-birth-weight (VLBW) infants (weight < 1000 g) who received flush solutions preserved with benzyl alcohol. An increased incidence of developmental delay and cerebral palsy is also noted in the same VLBW patient population, suggesting a secondary damaging effect of benzyl alcohol.[Goldfrank, L.R., Goldfrank's Toxicologic Emergencies 8th Ed. 2006., McGraw-Hill, New York, N.Y., p. 831] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Paraparesis and flaccid paraplegia after epidural or intrathecal administration of more than 7.5 mg of benzyl alcohol as a diluent are suggestive of benzyl alcohol toxicity.[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1231] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Benzyl alcohol toxicity is a clinical diagnosis and may be confirmed by serum or urine benzyl alcohol, benzoic acid, and hippuric acid levels. The temporal relation between parenteral benzyl alcohol exposure and progressive anion gap metabolic acidosis, respiratory distress, altered central or peripheral nervous system function, seizures, and hemolysis is highly suggestive of the diagnosis. Progressive anion gap metabolic acidosis precedes the onset of the symptoms, which occur around the second to fourth day of exposure and include hypoactivity, hypotonia, depression of sensorium, respiratory distress, apnea, progressive bradycardia, seizures, progressive unresponsiveness, and coma. Marked skin breakdown may be evident. Hypotension and renal failure herald cardiovascular collapse and death.[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1231] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Hypersensitively reactions may occur after parenteral or dermal exposure to benzyl alcohol. Acute reactions include urticaria, erythema, palpable edema, fatigue, nausea, diffuse angioedema, maculopapular rash, and fever. A delayed hypersensitivity reaction characterized by erythema, edema, and vesiculation may appear in 2 to 3 days after an immediate reaction to a single benzyl alcohol challenge in the same patient.[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1232] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Benzyl alcohol is an aromatic organic alcohol that is a preservative, a solvent, and a local anesthetic. It rarely causes allergic contact dermatitis and is patch-tested as a 5% concentration in petrolatum.[Marks, J.G. Jr., DeLeo V.A., Contact and Occupational Dermatology. St. Louis, MO: Mosby Year Book 1992., p. 128] **PEER REVIEWED**

/CASE REPORTS/ Two patients with contact dermatitis were found to be sensitized by benzyl alcohol: 1 percent in petrolatum.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.265 (2001). Available from, as of July 9 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/CASE REPORTS/ A 53-year-old African-American man with relapsed

non-Hodgkin's lymphoma developed seizures and respiratory arrest 2 hr after an infusion of high-dose etoposide in preparation for an autologous bone marrow transplant. Laboratory tests revealed both rapid hemolysis and severe metabolic acidosis. The patient died the following day. Based on toxicities observed, /it was suspected/ that /the/ patient possessed an ethnic polymorphism of the enzyme alcohol dehydrogenase. Further research is required to determine the relationship between the benzyl alcohol metabolic rate and toxicity and genetic polymorphisms of alcohol dehydrogenase in African-Americans.[Smith AL et al; Pharmacotherapy 21 (6): 764-6 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11401189?dopt=Abstract" target=new>PubMed Abstract

/CASE REPORTS/ A patient with allergic contact dermatitis caused by benzyl alcohol in a hearing aid impression material and in topical medications is described. In addition, the patient had topical and probably systemic corticosteroid allergy. Benzyl alcohol allergy is reviewed. allergic contact dermatitis is the most commonly reported allergic reaction to benzyl alcohol. There is also 1 report of contact urticaria. ... Reported allergic reactions to injected benzyl alcohol include generalized urticarial reactions, 1 generalized maculopapular reaction and 1 delayed localized reaction.[Shaw DW; Am J Contact Dermat 10 (4): 228-32 (1999)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/10594301?dopt=Abstract" target=new>PubMed Abstract

/CASE REPORTS/ A fatal case of metabolic acidosis was reported in a 5 year old girl who had received 2.4 mg/kg/hr diazepam preserved with benzyl alcohol for 36 hours to control status epilepticus. Elevated benzoic acid levels were identified in serum and urine samples. The estimated daily dosage of benzyl alcohol was 180 mg/kg.[Goldfrank, L.R., Goldfrank's Toxicologic Emergencies 8th Ed. 2006., McGraw-Hill, New York, N.Y., p. 831] **PEER REVIEWED**

/CASE REPORTS/ ... Intraocular use of sodium chloride solution preserved with 2% benzyl alcohol during cataract surgery and peripheral iridectomy caused severe striated keratopathy, progressing to chronic edema of cornea, with vesicles, bullae, and dirty pigmented appearance of endothelium. ... Iris was also affected.[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 143] **PEER REVIEWED**

/CASE REPORTS/ Benzyl alcohol, which is used as a preservative in intravascular flush solutions, caused neurological deterioration and deaths in very low birth weight infants. Preterm infants who received large volumes of fluids containing 0.9% benzyl alcohol via catheter developed "gasping baby syndrome." Estimated intakes of 99 to 405 mg benzyl alcohol/kg body weight for 2 to 28 days caused effects including severe metabolic acidosis, gasping, neurological deterioration, blood abnormalities, skin breakdown, liver and kidney failure, lowered blood pressure, heart failure, and death. No effects were seen for intakes of 27 to 99 mg/kg body weight over similar periods, although there is one report of 32 to 105 mg/kg body weight for 7 days causing breathing difficulty.[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 500] **PEER REVIEWED**

/CASE REPORTS/ Sixteen neonatal deaths thought to be caused by the benzyl alcohol preservative used in some intravascular solutions have been reported to the Food and Drug Administration (FDA) by 2 medical centers ... . The deaths occurred in pre-term neonates weighing 2500 gm who had central intravascular catheters flushed periodically each day with bacteriostatic normal saline containing 9 mg/mL benzyl alcohol. Ten deaths occurred in 1 institution over a 6-month period and 6 deaths occurred in the other institution over a 16-month period. Investigators in the 2 hospitals have reported that similar deaths have not occurred since flush solutions without preservatives have been substituted for those with the benzyl alcohol. Onset of toxic illness in the infants occurred between several days and a few weeks of age with a characteristic clinical picture that included metabolic acidosis progressing to respiratory distress and gasping respirations. Many infants also had central-nervous-system dysfunction, including convulsions and intracranial hemorrhage; hypotension leading to cardiovascular collapse was a late finding usually presaging death. Gas chromatographic analysis demonstrated benzyl alcohol or its metabolites in blood and urine samples from infants in 1 hospital. Retrospective analysis of urine samples from 5 infants in the other hospital for organic acid profile by gas-liquid chromatography showed urine benzoate levels of 4.4-16.1 mg/mg creatinine and hippurate levels of 7.4-33.3 mg/mg creatinine (normal values = 0-trace); serum benzoic acid levels were 8.4-28.7 mEq/L (normal = 0). Review of the medical records of the affected infants resulted in estimates of daily intake of benzyl alcohol ranging from 99 to 405 mg/kg/day. Based on these reports, the FDA

has recommended that intravascular flush solutions containing benzyl alcohol not be used for newborns and that diluents with this preservative not be used as medications for these infants.[CDC/MMWR; Neonatal Deaths Associated With Use Of Benzyl Alcohol -- United States. Morbidity and Mortality Weekly Repost 31(22);290-1 (June 11, 1982). Available from, as of July 23, 2008: http://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm] **PEER REVIEWED**

/ALTERNATIVE and IN VITRO TESTS/ Suspensions of human erythrocytes were incubated with benzyl alcohol, benzoic acid, and sodium benzoate. Each material was tested at 10-5, 10-4, and 10-3 mol/L. Erythrocytefree samples were also incubated with the test materials and used as controls. Following incubation, suspensions and samples were exposed to varying amounts of ultraviolet A (UVA) light from one of three sources. Hemolysis was measured as a function of absorbance of 550 nm light. None of the three substances produced significant photohemolysis.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/ALTERNATIVE and IN VITRO TESTS/ ... To identify phototoxic effects, 43 fragrances were evaluated in vitro with a photohemolysis test using suspensions of human erythrocytes exposed to radiation sources rich in ultraviolet (UV) A or B in the presence of the test compounds. Hemolysis was measured by reading the absorbance values, and photohemolysis was calculated as a percentage of total hemolysis. ... Moderate UVA-induced hemolysis (5-11%) was found with benzyl alcohol ... The phototoxic effects depended on the concentration of the compounds and the UV doses administered. ...[Placzek M et al; Acta Derm Venereol 87 (4): 312-6 (2007)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/17598033?dopt=Abstract" target=new>PubMed Abstract

/ALTERNATIVE and IN VITRO TESTS/ Cultured retinal pigment epithelial (RPE) cells from a human cell line (ARPE-19) and from rabbits were exposed to the balanced salt solution (control) or benzyl alcohol (BA) (0.0225, 0.225, 0.9, 3 or 9 mg/mL) for 5, 30, 60, or 120 min. ... The proportions of dead cells were quantitatively measured by the trypan blue exclusion assay, and those of functional cells were assessed by a mitochondrial dehydrogenase assay. The mechanism of cytotoxicity was determined by the acridine orange/ethidium bromide staining and DNA laddering technique. Furthermore, ultrastructural changes were observed by transmission electron microscopy. The results showed that RPE cell damage was dose- and time-dependent. BA 0.225 mg/mL, the clinically relevant concentration in TA following intravitreal injection, caused ultrastructural damage and impaired human RPE cell function at 2 hr; but BA 0.0225mg/mL did not. BA 9.0 mg/mL, the concentration in commercial TA suspensions, was toxic within 5 min on each assay for both human and rabbit RPE cells. The major mechanism of cell death was necrosis.[Chang YS et al; Exp Eye Res 86 (6): 942-50 (2008)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/18420195?dopt=Abstract" target=new>PubMed Abstract

/OTHER TOXICITY INFORMATION/ Reports are available contraindicating the use of neuromuscular blocking agents containing benzyl alcohol. Use of these agents was not advised in neonates or in the epidural space[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/OTHER TOXICITY INFORMATION/ /Benzyl alcohol/ is used as a bacteriostatic agent and is commonly added to pharmaceuticals (eg, etoposide, aminodarone, diazepam, bacteriostatic water, and sodium chloride) intended for intravenous administration. The amount of benzyl alcohol in pharmaceuticals may be 0.9% to 2.0%, and significant amount of benzyl alcohol may be inadvertently administered to a patient during continuous (repeated) drug infusion or when bacteriostatic water or sodium chloride is used to flush IV lines. Benzyl alcohol toxicity has been reported in both pediatric and adult patients.[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1230] **PEER REVIEWED**

/OTHER TOXICITY INFORMATION/ No direct ocular injury from external contact has been reported in human beings, but one death and one case of serious illness with delirium and visual disturbances were supposed to have been caused by absorption of benzyl alcohol from an impure preparation of benzyl benzoate which was employed in massaging the skin.[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 144] **PEER REVIEWED**

SKIN, EYE AND RESPIRATORY IRRITATIONS:
It is slightly irritating to the skin ... .[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983., p. 111] **PEER REVIEWED**

Vapor: Irritating to eyes, nose and throat. Liquid: Irritating to skin & eyes.[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.] **PEER REVIEWED**

DRUG WARNINGS:
Common side effects of /Benzyl Alcohol Lotion, 5%/ include irritations of the skin, scalp, and eyes, and numbness at the site of application. As with all medications, it is important to use benzyl alcohol, 5%, as labeled to maximize benefits and minimize risks. The product should be applied only to the scalp or the hair attached to the scalp. It is not approved for use in children younger than six months. Use in premature infants could lead to serious respiratory, heart- or brain-related adverse events such as seizure, coma, or death.[FDA; FDA Approves Benzyl Alcohol Lotion for the Treatment of Head Lice, FDA News (April 9, 2009) Available from, as of April 20, 2009: http://www.fda.gov/bbs/topics/NEWS/2009/NEW01993.html] **PEER REVIEWED**

It also seems prudent to avoid the use of products containing benzyl alcohol to pregnant patients within whom the benzyl alcohol molecule, given its small size, presumably crosses the placental barrier into immature fetal tissues as readily as it crosses the blood-brain barrier.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.294 (2001). Available from, as of July 9 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

Premature neonates may receive multiple drugs in the neonatal intensive care unit, some of which may contain benzyl alcohol. As there may be no safe lower dose of benzyl alcohol in these patients, it would seem prudent to avoid the use of multiple dose vials containing benzyl alcohol whenever alternatives exist.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.294 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

Benzyl alcohol is believe to have a role in the increased frequency of cerebral intraventricular hemorrhages and mortality reported in very-low-birth-weight (VLBW) infants (weight < 1000 g) who received flush solutions preserved with benzyl alcohol. An increased incidence of developmental delay and cerebral palsy is also noted in the same VLBW patient population, suggesting a secondary damaging effect of benzyl alcohol.[Goldfrank, L.R., Goldfrank's Toxicologic Emergencies 8th Ed. 2006., McGraw-Hill, New York, N.Y., p. 831] **PEER REVIEWED**

Benzyl alcohol, which is used as a preservative in intravascular flush solutions, caused neurological deterioration and deaths in very low birth weight infants. Preterm infants who received large volumes of fluids containing 0.9% benzyl alcohol via catheter developed "gasping baby syndrome." Estimated intakes of 99 to 405 mg benzyl alcohol/kg body weight for 2 to 28 days caused effects including severe metabolic acidosis, gasping, neurological deterioration, blood abnormalities, skin breakdown, liver and kidney failure, lowered blood pressure, heart failure, and death. No effects were seen for intakes of 27 to 99 mg/kg body weight over similar periods, although there is one report of 32 to 105 mg/kg body weight for 7 days causing breathing difficulty.[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 500] **PEER REVIEWED**

Benzyl alcohol is normally oxidized rapidly to benzoic acid, conjugated with glycine in the liver, and excreted as hippuric acid. However, this metabolic pathway may not be well developed in premature infants. The benzyl alcohol may therefore have been metabolized to benzoic acid, which could not be conjugated by the immature liver but accumulated, causing metabolic acidosis ... .[CDC/MMWR; Neonatal Deaths Associated With Use Of Benzyl Alcohol -- United States. Morbidity and Mortality Weekly Repost 31(22);290-1 (June 11, 1982). Available from, as of July 23, 2008: http://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm] **PEER REVIEWED**

POPULATIONS AT SPECIAL RISK:
Premature neonates are at high risk of /benzyl alcohol/ toxicity.[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1231] **PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 404,916 workers (236,470 of these were female) were potentially exposed to benzyl alcohol in the US(1). Occupational exposure to benzyl alcohol may occur through inhalation and dermal contact with this compound at workplaces where benzyl alcohol is produced or used. Monitoring and use data indicate that the general population may be exposed to benzyl alcohol via dermal contact with consumer products containing benzyl alcohol and to a lesser extent via inhalation of ambient air, ingestion of food and drinking water(SRC).[(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981-1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available at http://www.cdc.gov/noes/ as of July 9, 2008.] **PEER REVIEWED**

ANIMAL TOXICITY STUDIES:

NON-HUMAN TOXICITY EXCERPTS:

/LABORATORY ANIMALS: Acute Exposure/ A polyvinyl chloride (PVC) cup containing 10% w/v benzyl alcohol was fastened (using surgical tape) to the dorsal side of three male nude mice for 24 hours of contact. Following exposure, mice were immediately killed and specimens of the exposed areas and of an adjacent untreated area were taken for microscopic examination. The skin sections were fixed in formalin, dehydrated, and embedded in paraffin. Sections were stained with hematoxylin and eosin and scored using the Ingram & Grasso system. A typical section from benzyl alcohol-treated areas had severe compact hyperkeratosis, acanthosis, spongiosis, intracellular edema, and some areas of ulceration of the epidermis. The collagen bundles in the dermis appeared slightly fragmented and slight cell infiltration of the area was noted. The final score for benzyl alcohol was 22, the modal score for at least three animals. Scores greater than 21 were considered "unacceptably severe damage." The investigators acknowledged that male nude mice were not an ideal model for human skin; however, the study was done to establish the relative dermal tolerance of various penetration enhancers.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ In a cumulative irritation study, three male albino guinea pigs received a daily open application of 10% benzyl alcohol in squalane (0.3 mL) on the back for 3 successive days. Sites were evaluated for erythema and edema 24 hours after each application and scored on a scale of 0 to 4. Benzyl alcohol in squalane received a cumulative score of 0.4, falling in the < /=2.0 range of "none to weak irritant".[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ In a primary irritation study 10% benzyl alcohol in squalane was applied (0.3 mL) in a 24-hour occlusive patch to the back of eight male albino rabbits. The sites had been clipped free of hair and were abraded in four rabbits. Sites were evaluated according to the Draize scoring system at the time of patch removal and 72 hours later. No irritation was observed; there was a score of zero on a scale of 0 to 8.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Undiluted benzyl alcohol /was administered/ intravenously (via the tail vein) to groups of 10 mice (5 of each sex). Three different mice strains were used with the following dose ranges. CD2F1 mice received 0.05 to 0.2 mL/kg, B6D2F1 mice received 0.05 to 0.4 mL/kg, and C57BL/6N mice received 0.025 to 0.1 mL/kg. All mice weighed between 14 and 18 g. The highest dose given did not exceed the LD50. Body weight was determined prior to the start of dosing, and 1 week thereafter. Animals were observed for 14 days and postmortem examinations were performed on day 15. Blood samples were withdrawn from the abdominal aorta and analyzed for hemolysis and precipitation potential. Convulsions, dyspnea, and reduced mobility were noted at the first 24-hour observation in mice treated with all but the lowest dose of benzyl alcohol. Decreased body weight gain or slight decrease in body weight was noted in B6D2F1 and C57BL/6N mice treated with all but the lowest dose. Postmortem alteration included hyperemia and edema in most animals that had died during the observation period (number not reported). Occasional hemorrhagic foci were observed in the spleen of C57BL/6N mice from all dose groups that had survived benzyl alcohol treatment. The blood from benzyl alcohol- treated

mice had a potential for hemolysis and precipitation. Undiluted benzyl alcohol was ranked the most toxic of the five vehicles tested, which included dimethyl sulfoxide, polyethylene glycol 400, dimethylformamide, and absolute ethanol.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Rats could inhale air saturated with benzyl alcohol vapor for a maximum of 2 hours. Inhalation at a concentration of 1000 ppm for 8 hours caused death of three of six animals within 14 days of exposure.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Three groups of six Sherman rats were exposed for 4 hours to a 2000-ppm concentration of benzyl alcohol vapor in normal atmosphere. Nine rats died within 14 days of exposure. The investigators considered the compound to be a moderate hazard.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Acute intravenous toxicity of benzyl alcohol was determined in CD2F1 (0.05-0.2 mL/kg bw), B6D2F1 (0.05-0.4 mL/kg) and C57BL/6 mice. The lowest dose was a safe dose and the highest one was the dose causing mortality in no more than half the animals of each group. Clinical signs were convulsion, dyspnea and reduced mortility in all strains for 24 hours. The slight decrease in body weight in the first week following treatment returned to normal in the second week.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.303 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Benzyl alcohol was found to be not sensitizing in the guinea pig Draize Test, guinea pig maximization test, but was shown to be sensitizing in the guinea pig by the Freund's Complete Adjuvant Test and the Open Epicutaneous Test. /From table/.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.264-265 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Benzyl alcohol was not irritating to rabbit skin in a 4 hour exposure experiment but was moderately irritating following 24 hours exposure. It was a moderate to severe eye irritant.[European Medicines Agency (EMEA), The European Agency for the Evaluation of Medicinal Products, Veterinary Medicines Evaluation Unit, Committee for Veterinary Medicinal Products; Benzyl Alcohol, Summary Report (1997). Available from, as of July 8, 2008: http://www.emea.europa.eu/pdfs/vet/mrls/Benzylalcohol.pdf] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ ...To test the toxicity of intravitreal injections of benzyl alcohol ... nine New Zealand rabbits were injected with either a control or ... benzyl alcohol calculated to give final injected concentrations of 0.0073%, 0.022%, 0.073%, 0.222%, and 0.733% benzyl alcohol. The 0.022% concentration corresponds to the concentration of benzyl alcohol in human eyes when 0.1 mL of /a / commercial /product/... is used. Baseline examination of the rabbits was performed along with postinjection examinations on days 1, 3, 7, and 14. The eyes were enucleated and examined by light and electron microscopic examinations. ... Eyes injected with benzyl alcohol concentrations of 0.073%, 0.222%, and 0.733% displayed changes in the outer retina including loss of, and shortening of, outer segments and photoreceptors.[Morrison VL et al; Retina 26 (3): 339-44 (2006); Comment in: Retina 26 (9): 1100 (2006)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/16508436?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ ...To assess retinal toxicity of the vehicle of triamcinolone, benzyl alcohol (BA), when injected into the vitreous cavity of rabbits.... 24 pigmented rabbits /were/ assigned into two groups: group 1 (experimental, n = 12) received intravitreal 0.1 ml of BA, and group 2 (control, n = 12) received intravitreal 0.1 mL of balanced

salt solution (BSS); all injections were done in the right eyes. Clinical examinations [slit lamp biomicroscopy, indirect ophthalmoloscopy, and three intraocular pressure (IOP) measurements] were done on both eyes before injection, at 1 and 3 hr post injection, together with electroretinograms (ERGs) at 3 days, 1, 2, 4, and 6 weeks following injections. Three rabbits from each group were euthanased at 1, 2, 4, or 6 weeks and eyes were sent for light and electron microscopic examination for quantitative morphometric measurements. ... The mean amplitudes of the a and b waves of the BA-injected eyes were 6.42 +/- 9.02 uv and 11.18 +/- 15.18 uv at 3 days, respectively, which were significantly reduced compared with the BSS-injected eyes (30.87 +/- 8.22 uv and 57.90 +/- 13.38 uv, respectively; P < 0.01 t-test) and the non-injected contralateral eyes (36.20 +/- 7.85 uv and 64.10 +/- 9.36 uv, respectively; P < 0.01 t-test). These ERG responses continued to be significantly reduced in the BA-injected eyes (P < 0.01 t-test) throughout the study period. The mean ganglion cell count was significantly reduced (P < 0.005 t-test) in the BA-injected eyes (8.42 +/- 2.4) compared with the BSS- and non-injected eyes (16.42 +/- 3.9 and 16.5 +/- 4.2, respectively). The mean thicknesses of the inner nuclear layer (INL) and outer nuclear layer (ONL) were significantly reduced (P < 0.005 t-test) in the BA-injected eyes (3.78 +/- 0.96 um and 11.77 +/- 1.29 um, respectively) compared with the BSS- (6.1 +/- 0.92 um and 21.82 +/- 0.95 um, respectively) and non-injected eyes (7.05 +/- 1.9 um and 22.49 +/- 1.01 um, respectively). Electron microscopy showed moderate to severe intracellular changes in the ganglion cell layer, INL, ONL, and photoreceptor layer at 6 weeks in BA-injected eyes, with no significant changes in BSS-injected eye. There was no significant rise in the IOP or clinical evidence of increased lens density during the study period in any of the eyes. /It was concluded that/ triamcinolone acetonide's vehicle, BA, produced severe ERG and structural damage to the retina when injected intravitreally.[Macky TA et al; Graefes Arch Clin Exp Ophthalmol 245 (6): 817-24 (2007)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/17111149?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Undiluted benzyl alcohol was moderately irritating when applied to the depilated skin of guinea pigs for 24 hr. It was moderately irritating when applied to rabbit skin. Benzyl alcohol was severely irritating to the eyes of rabbits.[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 498] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ No fatalities or symptoms were found in rats exposed for 6 hr to a calculated concentration of 61 ppm nor were symptoms produced by exposures obtained by bubbling air through the liquid heated to 100 and 150 deg C. ... Doses of 0.2 mL/kg or more, administered to dogs by stomach tube induced emesis and defecation. This was apparently due to irritation of the gastric mucosa ... Diuresis was more pronounced in the rabbit than in the dog, after administration of benzyl alcohol by various routes. The injection of 5 to 10% benzyl alcohol in oil of sweet almond in the region of the auditory meatus of cats caused temporary degeneration of the small facial nerves.[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982., p. 4639] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Mice suffered respiratory stimulation, respiratory and muscular paralysis, convulsions, and ... /CNS depression/ following sc injection. ... Observed a decrease in arterial blood pressure of rabbits, cats, and dogs following iv injection of benzyl alcohol, but failed to find such decrease in the case of dogs following oral administration of 0.1-1.0 mL/kg of bw. ... Iv injection of 94% ... into dogs caused dyspnea, diarrhea, ataxia, mydriasis, nystagmus, urination, respiratory arrest, collapse, and cardiac arrest. In some instances deaths were delayed; in these cases, death was due to pulmonary hemorrhage and edema.[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982., p. 4639] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ When aqueous humor was replaced in one /rabbit/ eye with pure sterile 0.9% sodium chloride solution and in the other eye was replaced with the same solution plus 2% benzyl alcohol, no toxic effect was produced by the plain saline solution, but the eyes with benzyl alcohol solution rapidly developed evidence of injury of endothelium, with much bluish swelling of the cornea. Also, the irises in the eye with benzyl alcohol solution became hyperemic and had poorly reactive pupils. The corneal edema in rabbits disappeared more rapidly than in the human patients, clearing partially in one week and completely in two weeks.[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 143] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Benzyl alcohol (1 mL/kg iv) had no effect on respiration, ECG, or blood pressure on anesthetized monkeys and dogs. Lethal iv dose of 0.9% benzyl alcohol in anesthetized dogs was 0.83-1.06 g/kg.[Kimura ET et al; Toxicol Appl Pharmacol 18 (1): 60-8 (1971)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/5542834?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Administration of 9% benzyl alcohol produced transient respiratory arrest in adult dogs and death in immature dogs, and 7% and 4.5% benzyl alcohol produced clonic seizures in puppies.[Deland FH; Toxicol Appl Pharmacol 25 (2): 153-6 (1973)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/4740372?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Benzyl alcohol displayed antiarrhythmic-antifibrillatory effects when injected iv (0.2-0.4 mL/kg of a 4% solution) into dogs and rats with spontaneous and drug induced arrhythmias. IV injections of high doses caused intravascular hemolysis.[Eichbaum FW, Yasaka WJ; Basic Res Cardiol 71 (4): 355-70 (1976)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/971216?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ The length of the estrus cycle was reduced when 0.52-2.1 d (1-4 mg/kg bw) benzyl alcohol was injected into the uterus of each of 48 cows.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.300 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Microscopic examination revealed local nerve degeneration when 5 % benzyl alcohol was injected into the side of a cat's face. At 10 % local anesthesia was produced.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.300 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Groups of 20 F344/N rats and B6C3F1 mice (10 of each sex) received 50, 100, 200, 400, or 800 mg/kg benzyl alcohol, 5 days a week for 13 weeks. Experimental conditions were the same as in the 16-day study. The death of five rats was attributed to rupture caused by the gavage procedure. Gavage related deaths were considered to result from the trauma of the gavage procedure combined with the neurotoxic/anesthetic effect of the compound. Aside from these, four male rats and one female of the 800-mg/kg group, as well as one female of the 400-mg/kg group and one male of the 200-mg/kg group died on study. The 800-mg/kg group had signs of neurotoxicity, including staggering, labored breathing, and lethargy after dosing. Blood around the nose and mouth was noted in 5 of 10 males of this group after week 8. Compared to vehicle controls, final mean body weights were 7% and 5% smaller, respectively, in male and female rats of the highest dose group. At histopathologic evaluation, lesions observed in rats of the highest dose group included necrosis of the dentate gyrus of the hippocampus in 7 of 7 males and 9 of 9 females; skeletal muscle necrosis in 5 of 10 males, thymic congestion, hemorrhage, and atrophy in 8 of 10 males, and nephrosis in 6 of 9 males. Renal lesions were similar to those noted in age-related spontaneous renal disease. Nine of 10 deaths (mice) were attributed to the gavage procedure. Final mean body weights of females of the 400- and 800-mg/kg groups were 5% and 8% lower, respectively, than the vehicle control. Staggering was noted during the first and second weeks of dosing in mice of the high-dose group. No compound-related histopathologic alterations were observed. A Sendai virus infection was suspected.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Technical grade benzyl alcohol (99% pure) in corn oil at doses of 125, 250, 500, 1000, or 2000 mg/kg was administered to groups of 10 F344/N rats and B6C3F1 mice (5 of each sex). Animals were dosed 5 days a week for 16 days (total of 12 doses). Feed and water were provided ad libitum. On days 8 and 9, both rats and mice of the 125-mg/kg group received doses that were 10-fold too high. All rats that received 2000 mg/kg and two of five males and three of five females that received 1000 mg/kg benzyl alcohol died before the end of the study. Rats of the two highest dose groups had blood around the nose and mouth, subcutaneous hemorrhages, and blood in the urinary and

gastrointestinal tracts. Final body weight of male rats of the 1000 mg/kg group was 18% less than that of vehicle controls. Lethargy was observed in rats of the two highest dose groups; rough coats were noted in males of the 500- and 1000-mg/kg groups and in females of the 250- and 500-mg/kg groups. No compound-related histopathologic changes were noted. All mice that received 2000 mg/kg and one of five males and two of five females that received 1000 mg/kg benzyl alcohol died before the end of the study. Lethargy and rough coats were noted in males that received > /= 500 mg/kg and in females that received > /= 1000 mg/kg. Blood in the urinary bladder was noted at necropsy in mice of the two highest dose groups. No compound related histopathologic changes were noted.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Benzyl alcohol was administered by gavage daily and for 8 days to mice at doses of 325, 645, 1300, and 2595 mg/kg/day. Decreased muscle coordination, a "hunched" appearance, depression, and fur changes were reported in mice given 645 mg/kg, but not in those receiving 325 mg/kg or below. At 1300 mg/kg, animals additionally suffered breathing difficulties, discharge from the eyes, and various CNS effects, and death occurred on day 1 in all mice given 2595 mg/kg.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.274 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Fischer 344 rats were given oral doses of 50, 100, 200, 400, and 800 mg/kg for 13 weeks. The high dose produced clinical signs indicative of neurotoxicity including staggering, respiratory difficulty, and lethargy. Reduction in weight gain was noted in males at 800 mg/kg and females at equal to or greater than 200 mg/kg. The high dose animals also showed hemorrhages around the mouth and nose, and histological lesions in the brain, thymus, skeletal muscle, and kidney.[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 498] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ B6C3FI mice were given oral doses of 50, 100, 200, 400, and 800 mg/kg for 13 weeks. The high dose appeared to produce clinical signs of neurotoxicity. Reduction in weight gain was noted in males at equal to or greater than 400 mg/kg and females at equal to or greater than 200 mg/kg. No treatment related histopathological effects were noted.[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 498] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Benzyl alcohol applied daily to guinea pigs with experimental trichophytosis on surface of scarred infected skin produced paralysis in hind limbs after several days.[Wollmann H et al; Pharmazie 22 (8): 455 (1967)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/5601620?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ The blood sugar of fasting animals was increased somewhat by prolonged admin of benzyl alcohol.[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982., p. 4640] **PEER REVIEWED**

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ A nonoxidative hair dye containing 2.0% benzyl alcohol and 0.016% benzoic acid was painted onto the skin /of groups 8120 Eppley Swiss mice (60/sex) at a dose of 0.05 mL/application, three times weekly for 20 months. Sites were shaved of hair 24 hours before each application and a new bottle of dye was used each week. Two groups of control animals were shaved but not treated. Nine months into the study, 10 mice/sex/group were killed. Body weights and survival differed little between treatment and control groups. Varying degrees of chronic dermal inflammation were noted in all groups, including the controls. A significant (p < .01) increase in malignant lymphomas was noted in treated females (23/60). However, the researchers noted that one concurrent control group had a very low incidence (7/60 or 12%) for that tumor type. The rate was 22% for the other control group and had averaged 33% for three control groups in previous studies. Thus, the findings were not considered treatment related. The incidence of pulmonary adenomas and hepatic hemangiomas, which are common to this mouse strain, were similar between treated and control groups. No unusual neoplasms were observed.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract"

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/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Groups of 100 F344/N rats (50 each sex) were dosed with 200 or 400 mg/kg benzyl alcohol in corn oil, 5 days per week for 103 weeks. Groups of 100 B6C3F1 mice were dosed with 100 or 200 mg/kg benzyl alcohol following the same schedule. During week 80, mice were mistakenly dosed for four days with 375 (low-dose group) and 750 mg/kg (high-dose group) of alpha -methylbenzyl alcohol. No adverse effects were apparent. Mean body weights were comparable among dosed and vehicle control rats throughout the study. A number of accidental deaths was due to gavage procedures in female rats of both dose groups (17 deaths, low-dose; 13 deaths, high-dose) and in males of the 400 mg/kg group (14 deaths). Survival of female rats of the low- and high-dose groups was significantly lower than that of vehicle controls after weeks 71 and 50, respectively. At the end of the study, 17 female rats survived from each of the dose groups, compared to 35 female vehicle-controls; 27 low-dose males and 24 high-dose males survived, compared to 28 male vehicle controls. Clinical signs characteristic of sialodacryoadenitis (cervical swelling, pink eyes, red exudate around eyes) were observed in dosed and vehicle-control rats. The diagnosis was confirmed by serum analysis. Epithelial hyperplasia of the nonglandular stomach was noted in four high-dose males. A squamous cell papilloma was noted in 1 of 19 low-dose and 1 of 50 high-dose males. (It was not stated why only 19 low-dose male rats were examined.) No other compound-related clinical signs were observed. Mean body weight was comparable among dosed and vehicle control mice throughout the study. Survival of female vehicle controls was significantly lower than that of the high-dose group after week 74 (female: vehicle control, 26/50; low dose, 32/50; high dose, 36/50). Corpora amylacea (foci of mineralization in the thalamus) was observed at an increased incidence in highdose mice (male: vehicle control, 15/49; low dose, 21/48; high dose, 22/50; female: 14/50; 15/48; 25/50), but was noted to be a common and spontaneously occurring lesion[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ ... Conclusions: Under the conditions of these 2 yr gavage studies, there was no evidence of carcinogenic activity of benzyl alcohol for male or female F344/N rats dosed with 200 or 400 mg/kg. Survival in both dose groups of female rats was 50% that of vehicle controls, primarily due to an incr number of gavage related deaths. There was no evidence of carcinogenic activity of benzyl alcohol for male or female B6C3F1 mice dosed with 100 or 200 mg/kg for 2 years.[Toxicology & Carcinogenesis Studies of Benzyl Alcohol in F344/N Rats and B6C3F1 Mice (Gavage Studies). Technical Report Series No. 343 (1989) NIH Publication No. 89-2599 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ In a study which assayed the teratogenic activity of ethinyloestradiol sulfonate in Wistar rats, a vehicle control group that was treated with benzyl alcohol/peanut oil was maintained. On GDs 10, 13, 6 to 10, or 10 to 14, rats (number not stated) received intraperitoneal (ip) injections of either the test material or an unspeci. ed amount of vehicle. Fetuses were removed on day 21 and examined. No teratogenic effect was noted.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ A group of 50 pregnant SPF CD-1 albino mice was dosed with 550 mg benzyl alcohol/kg/day on GDs 6 to 15 by gavage. The benzyl alcohol was dissolved in corn oil; a vehicle-control group was maintained. Maternal status (survival, body weight changes), gestation index (length of gestation), reproductive index, postnatal survival, average litter weight, and average pup weight were comparable between treated and control animals.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ In screening a new developmental toxicity assay, 50 pregnant CD-1 mice were gavaged on GDs 6 to 13 with benzyl alcohol at a rate of 750 mg/kg/day. The dose selected was the LD(10) value determined in preliminary dose-finding studies. Mice were allowed to deliver. Litter size, birth weight, and neonatal growth and survival to postnatal day 3 were measured. Nineteen (38%) of the dams of the benzyl alcohol group died prior to delivery; the corresponding vehicle control group (which received water) had no maternal

death. (Mice that died were not necropsied.) Maternal weight was significantly less changed in the benzyl alcohol group (6.2 +/= 3.6 g) as compared to controls (7.9 +/= 2.3 g). Viability in the benzyl alcohol group was 21 of 22 litters (controls had 29/29 viability) with an average of 10.0 liveborns per litter. Birth weight (1.6 g/pup) and 3-day weight gain (0.5 g/pup) for pups of the Benzyl Alcohol treatment group were signi. cantly less (p < .05) than the corresponding values in controls (1.7 and 0.7 g/pup, respectively). The reduced birth weight was classified as "some evidence of developmental toxicity." The researchers noted the 10% false-negative rate for toluene, a "presumptive teratogen."[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ A group of 50 specific pathogen- free (SPF) CD-1 mice received 750 mg/kg/day benzyl alcohol (in distilled water) by gavage on GDs 7 to 14. (Earlier toxicity studies had determined the maximum tolerated dose was between 645 and 1300 mg/kg/day, and the 750-mg/kg/day dose was selected for the reproduction study.) The concurrent vehicle control had 50 mice. Mice were individually caged and feed and water were available ad libitum. Clinical observations were made daily. Maternal body weights were recorded prior to dosing, on day 18, and on postnatal day 3; the weight on day 7 determined the dose volume administered over the entire treatment period. Mice were allowed to deliver their litters and nurse the pups for 3 days. There were 18 compound-related deaths during the dosing period, and one on GD 15. Mice that died were discarded without necropsy. No procedure-related deaths (i.e., gavage error) were recorded. Body tremors, hunching, subdued behavior, prostration, ataxia, swelling, and/or cyanosis of the abdomen and piloerection were noted in mice that died during the study as well as those that produced litters. No significant differences in reproductive and gestation indices, or in mean gestation length were noted between treated and control mice. A significantly lower day 18 mean body weight and a marginally reduced maternal weight on postpartum day 3 were noted in dosed dams. Decreased mean litter mean pup weight was noted on postpartum days 1 (p < .01) and 3 (p < .001). On postpartum days 1 to 3, a decreased mean litter weight change (p < .05) and decreased mean litter mean pup weight (p < .001) were noted. No significant differences were noted between treated and control pups in group litter viability. The investigators considered benzyl alcohol a suspect reproductive hazard and was 58 mg/kg/day.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Fifty female mice were given benzyl alcohol at 550 mg/kg bw per day by gavage on days 6-15 of gestation; a further 50 mice received the corn oil vehicle. All dams were allowed to deliver naturally, and pups and dams were observed until day 3 post partum, when the experiment was terminated. Body weight, clinical observations, and mortality were recorded daily throughout treatment and up to day 3 post partum. Mortality was not significantly increased in animals given benzyl alcohol over that in the control group. One treated mouse showing languid behavior, labored breathing, and a rough coat died, but no other deaths or clinical signs were reported. Maternal body weight and body-weight gain during treatment and up to day 3 post partum were virtually identical for treated and control animals. All other parameters examined, including gestation index, average number of live pups per litter, and postnatal survival and pup body weight on days 0 and 3 post partum, were not significantly different from the control values. The authors concluded that, at the predicted LD10, benzyl alcohol had no significant effects on the development of CD-1 mice. NOAEL = 550 mg/kg bw per day[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.27 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Benzyl alcohol was evaluated for developmental toxicity in a proposed new short term in vivo animal bioassay. In this assay, pregnant mice were dosed with the test agent in mid-pregnancy and allowed to go to term. Observations were then made on litter size as well as the birth weight, neonatal growth, and survival of pups as indicators of developmental toxicity. Fifty pregnant CD-1 mice were given 750 mg/kg/day benzyl alcohol in water by gavage on days 6-13 of gestation and were allowed to deliver. A decrease in the birth weight and weight gain in the pups was observed, but was not toxic to the mothers and had no effect on pup viability.[Hardin BD et al; Teratog Carcinog Mutagen 7: 29-48 (1987)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/2884741?dopt=Abstract"

target=new>PubMed Abstract

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ In a study in rats, lumbosacral dorsal root action potential amplitudes were measured after exposure to 0.9% or 1.5% benzyl alcohol in either 0.9% sodium chloride solution or distilled water. Rats exposed to all benzyl alcohol solutions for less than 1 minute had inhibited dorsal root actions potentials. This was attributed to the local anesthetic effects of benzyl alcohol. Nerve function was 50-90% restored after rinsing the nerves with 0.9% sodium chloride solutions. Chronic intrathecal exposure to benzyl alcohol 0.9% over 7 days showed scattered areas of demyelinization and early remyelinization. The 1.5% benzyl alchol solution-exposed dorsal nerve roots showed greater changes with widespread areas of demyelinization and fatty degeneration of nerve fibers.[Goldfrank, L.R., Goldfrank's Toxicologic Emergencies 8th Ed. 2006., McGraw-Hill, New York, N.Y., p. 832] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ ... 0.01 or 0.02 mL of benzyl alcohol /injected/ into yolk sac of the chick from before incubation up to the 7th day. Meningoceles and skeletal defects were produced.[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986., p. 71] **PEER REVIEWED**

/ALTERNATIVE and IN VITRO TESTS/ Hemolysis of red blood cells washed with normal saline containing benzyl alcohol was studied. It was confirmed that benzyl alcohol was responsible for hemolysis, when the volume of saline exceeds the volume of blood.[McOrmond P et al; Drug Intell Clin Pharm 14 (Jul-Aug): 549 (1980)] **PEER REVIEWED**

/ALTERNATIVE and IN VITRO TESTS/ Local anesthetics and alcohols inhibited mitochondrial electron transport at several points along the chain. N-butanol and benzyl alcohol inhibited each of segments of rat liver and beef heart mitochondrial electron transport chain assayed; these include cytochrome c oxidase, durohydroquinone oxidase, succinate oxidase and dehydrogenase, NADH oxidase, succinate-cytochrome c oxidoreductase, and others.[Chazotte B, Vanderkooi G; Biochim Biophys Acta 636 (2): 153-61 (1981)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/6269599?dopt=Abstract" target=new>PubMed Abstract

/GENOTOXICITY/ Benzyl alcohol was negative in the Ames test with and without metabolic activation, sex-linked recessive lethal (flies), and replicative DNA synthesis (male rats) assays. Results of a mouse lymphoma forward mutation assay in the absence of S9 activation /were considered/ to be "questionable," whereas a positive response /was reported/ at concentrations associated with toxicity. Both studies were negative with S9 activation. Benzyl alcohol, with S9 activation, was positive in the chromosome aberration test in Chinese hamster ovary (CHO) cells. Equivocal results were noted in the sister chromatid exchange (SCE) assay.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/GENOTOXICITY/ The A31-1-13 clone of BALB/c-3T3 cells was used to evaluated the transforming potential of numerous chemicals including benzyl alcohol. Each transformation assay contained a standard clonal survival assay, a co-culture clonal survival assay, and a transformation assay. ... ... Benzyl Alcohol can be oxidized by air and may have been altered during the treatment period. ... Benzyl Alcohol was noncytotoxic to BALB/c-3T3 cells and ... the statistical sensitivities for trial 1 and 2 were 2 and 38/110, respectively. Benzyl Alcohol was evaluated as active in this assay with actual and estimated rank t-statistics both 1.95. ... Benzyl alcohol was grouped as a noncytotoxic, nonmutagenic, noncarcinogenic chemical.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.277-278 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ A Drosophila melanogaster SRL assay with benzylalcohol 5000 ppm (feed) and 8000 ppm (injection) was negative.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.21 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ A Replicative DNA Synthesis assay using male B6C3F1 male mice given a single dose of 0, 400 or 800 mg/kg bw benzyl alcohol by gavage was negative at all doses tested.[Organization for Economic

Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.21 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ A Replicative DNA Synthesis assay using male Fischer 344 rats given a single dose of 0, 300, or 600 mg/kg bw benzyl alcohol by gavage was negative at all doses tested.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.21 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ A Mouse Micronucleus assay using 50, 100, 200 mg/kg benzyl alcohol by ip injection was negative at all doses tested.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.21 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ /In a/ recombination assay with Bacillus subtilus H17 and M45, /benzyl alcohol/ was positive.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.19 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ In a cytogenic assay using CHO cells /benzyl alcohol/ was negative without metabolic activation and positive with metabolic activation.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.19 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ Benzyl alcohol was not mutagenic /in the/ Escherichia coli reverse mutation assay ... with and without metabolic activation.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.19 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

/GENOTOXICITY/ ... /Benzyl alcohol was/ evaluated for genotoxicity in the wing somatic mutation and recombination test (SMART) of Drosophila melanogaster. Third-instar larvae trans-heterozygous for two genetic markers mwh and flr, were treated at different concentrations (0.1, 0.5, 1, 10, 25 and 50 mM) of the test compounds. Wings of the emerging adult flies were scored for the presence of spots of mutant cells, which can result from either somatic mutation or mitotic recombination. Also lethal doses of benzyl derivatives used as flavor ingredients were determined in the experiments. For the evaluation of genotoxic effects, the frequencies of spots per wing in the treated series were compared to the control group, which is distilled water.[Demir E et al; Food Chem Toxicol 46 (3): 1034-41 (2008)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/18068884?dopt=Abstract" target=new>PubMed Abstract

/GENOTOXICITY/ Benzyl alcohol was found to be negative when tested for mutagenicity in the Salmonella/microsome preincubation assay using the standard protocol approved by the National Toxicology Program (NTP). Benzyl alcohol was tested at doses of 0.1, 0.333, 1.0, 3.333, 5.0, and 6.666 mg/plate in as many as 5 Salmonella typhimurium strains (TA1535, TA1537, TA97, TA98, and TA100) in the presence and absence of rat or hamster liver S-9. The highest ineffective dose tested without toxicity in any S. typhimurium strains was 5.0 mg/plate. Slight inhibition of the background bacterial lawn occurred in cultures at 6.666 mg/plate but no significant change was seen in the results.[Mortelmans K et al; Environ Mutagen 8: 1-119 (1986)] **PEER REVIEWED**

/OTHER TOXICITY INFORMATION/ Compared to control rats, benzyl alcohol noncompetitively inhibited activity of hepatic alcohol dehydrogenase (L-ADH) of rats maintained for a short term on 5% ethanol.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/OTHER TOXICITY INFORMATION/ Messiha reported that short-term intake of 2%

benzyl alcohol in the drinking water resulted in an inhibition of hepatic alcohol dehydrogenase and mitochondrial aldehyde dehydrogenase isoenzyme activities in female rats. The effects were not noted in male rats.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/OTHER TOXICITY INFORMATION/ Studies reported benzyl alcohol to increase activity of membrane-bound Ca2+C-dependent enzymes such as adenylate cyclase and thiol proteinase. Conversely, benzyl alcohol inhibited activities of various glycosyltransferases of the rat liver Golgi membrane. The activities of erythrocyte-bound p-nitrophenylphosphatase and acetylcholinesterase were increased at some concentrations of benzyl alcohol and inhibited by others. The effect on cell membranes was considered the mechanism by which benzyl alcohol inhibited lymphocyte-mediated cytolysis in vitro. Benzyl alcohol induced time-, dose-, and temperaturedependent hemolysis of erythrocytes.[Benzyl Alcohol. Cosmetic Ingredient Review; International Journal of Toxicology; 20(suppl 3):23-50 (2001)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/11766131?dopt=Abstract" target=new>PubMed Abstract

/OTHER TOXICITY INFORMATION/ Benzyl alcohol is a membrane "fluidizer" that affects lipid bilayer structure. It has been demonstrated to act on membranes of erythrocytes and hepatocytes.[Benzyl Alcohol. Cosmetic Ingredient Review; Journal of American College of Toxicology; 15(6):527-42 (1996)] **PEER REVIEWED**

/OTHER TOXICITY INFORMATION/ Benzyl alcohol displays a pronounced antiarrhythmic-anti- fibrillatory effect, when injected iv into dogs and rats with spontaneous or drug-induced arrhythmias. Mechanisms which might be responsible for the antiarrhythmic effect: lengthening of the effective refractory period, local and general anesthetic effects, changes of osmolality. The iv injection of benzylalcohol in high doses, produces intravascular hemolysis.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.300 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

NATIONAL TOXICOLOGY PROGRAM STUDIES:

... Toxicology and carcinogenesis studies of technical grade benzyl alcohol (99% pure) ... were conducted by admin chemical by gavage in corn oil vehicle to groups of F344/N rats and B6C3F1 mice for ... 2 yr. /Based on mortality, reduction in relative body weight gain, and the histopathologic lesions, doses selected for the 2 year studies in rats were 0, 200, and 400 mg/kg. Doses selected for 2 year studies in mice were 0, 100, and 200 mg/kg, based on mortality and depression in relative body weight gain./ ... Fifty animals of each species and sex were administered benzyl alcohol in corn oil by gavage 5 days per week for 103 weeks. Administration of benzyl alcohol did not affect survival in male rats (final survival rates: vehicle control, 28/50; low dose, 27/50; high dose, 24/50) but reduced survival of dosed female rats by half (36/50; 18/50; 17/50). Many of the early deaths were considered related to the gavage procedure. Survival in mice was not affected by benzyl alcohol administration (male: 34/50; 33/50; 35/50; female: 26/50; 32/50; 36/50). No effect of benzyl alcohol on body weight gain in rats or mice was observed. In the third month of the studies, clinical signs of sialodacryoadenitis virus infection were observed in rats. A positive serologic reaction for rat coronavirus was observed in sentinel animals at 6 months and again at 18 months. No apparent compound-related nonneoplastic responses were observed. Dose-related negative trends in the incidences of anterior pituitary gland neoplasms were seen in female rats (vehicle control, 29/50; low dose, 17/47; high dose, 9/49) and of harderian gland adenomas in male mice (8/50; 3/50; 2/50). Adenomas of the adrenal cortex occurred at an increased incidence in high dose male mice (0/48; 0/44; 3/48), but this slight increase was not considered to be related to chemical exposure.[DHHS/NTP; Toxicology & Carcinogenesis Studies of Benzyl Alcohol in F344/N Rats and B6C3F1 Mice (Gavage Studies). Technical Report Series No. 343 (1989) NIH Publication No. 89-2599. Available from, as of July 9, 2008: http://ntp-server.niehs.nih.gov/] **PEER REVIEWED**

Toxicology and carcinogenesis studies of technical-grade benzyl alcohol (99% pure), a textile dye additive, solvent, and food flavoring agent, were conducted by administering the chemical by gavage in corn oil vehicle to groups of F344/N rats and B6C3F1 mice of each sex for 16 days, or 13 weeks. In 16-day studies, all five male and five female rats and mice dosed with 2,000 mg/kg benzyl alcohol died. Two of five male and 3/5 female rats and 1/5 male and 2/5 female mice dosed with 1,000 mg/kg died. Rats and mice of each sex in the two highest dose groups were lethargic

after dosing. Other toxic responses to benzyl alcohol in these dose groups included blood around the mouth and nose, subcutaneous hemorrhages, and blood in the urinary and gastrointestinal tracts of rats and blood in the urinary bladder of mice. Animals administered lower doses of benzyl alcohol (125, 250, or 500 mg/kg) had no compound-related histologic lesions. Doses selected for the 13-week studies were 0, 50, 100, 200, 400, and 800 mg/kg for rats and mice. Eight of 10 male rats dosed with 800 mg/kg died during weeks 7 and 8; four of these deaths were described as gavage related. Rats dosed with 800 mg/kg exhibited clinical signs indicative of neurotoxicity including staggering, respiratory difficulty, and lethargy. Hemorrhages occurred around the mouth and nose, and there were histologic lesions in the brain, thymus, skeletal muscle, and kidney. In mice, deaths were scattered among all dose levels, but none occurred in vehicle controls. Four male and six female mice died after being dosed; all deaths but one were described as gavage related. Staggering after dosing also occurred during the first 2 weeks of the studies in mice dosed with 800 mg/kg. Some of the deaths in the rats and mice may have been caused by a combination of the gavage procedure and chemical toxicity, since there was evidence that benzyl alcohol induced neurotoxic effects. There were reductions in relative weight gain in male rats dosed with 800 mg/kg benzyl alcohol, in female rats dosed with 200 mg/kg or more, in male mice dosed with 400 or 800 mg/kg, and in female mice dosed with 200 mg/kg or more. No notable changes in body weight gain or compound-related histopathologic lesions were observed in rats or mice from the lower dose groups. Based on mortality, reduction in relative body weight gain, and the histopathologic lesions, doses selected for 2-year studies in rats were 0, 200, and 400 mg/kg. Doses selected for 2-year studies in mice were 0, 100, and 200 mg/kg, based on mortality and depression in relative body weight gain.[DHHS/NTP; Toxicology & Carcinogenesis Studies of Benzyl Alcohol in F344/N Rats and B6C3F1 Mice (Gavage Studies). Technical Report Series No. 343 (1989) NIH Publication No. 89-2599. Available from, as of July 9, 2008: http://ntp-server.niehs.nih.gov/] **PEER REVIEWED**

Genetic Toxicology: Benzyl alcohol was not mutagenic when tested by the preincubational protocol in the presence or absence of exogenous metabolic activation in Salmonella typhimurium strains TA98, TA100, TA1535, or TA1537. In the mouse L5178Y/TK+/- lymphoma assay, benzyl alcohol induced an increase in trifluorothymidine (Tft)-resistant cells in the absence, but not in the presence, of S9; the effect was associated with toxicity. In cytogenetic assays with Chinese hamster ovary (CHO) cells, treatment with benzyl alcohol produced an increase in sister chromatid exchanges (SCEs) which was judged to be equivocal both with and without S9; a significant increase in chromosomal aberrations was observed after exposure to benzyl alcohol in the presence, but not the absence, of S9.[DHHS/NTP; Toxicology & Carcinogenesis Studies of Benzyl Alcohol in F344/N Rats and B6C3F1 Mice (Gavage Studies). Technical Report Series No. 343 (1989) NIH Publication No. 89-2599. Available from, as of July 9, 2008: http://ntp-server.niehs.nih.gov/] **PEER REVIEWED**

NON-HUMAN TOXICITY VALUES:

LD50 Mouse sc 950mg/kg bw[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.259 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Rat sc 1700mg/kg bw[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.258 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Guinea pig ip > 400-800mg/kg bw[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.258 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Rat ip > 400-800mg/kg bw[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.258 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Rat oral 1230-3120 mg/kg bw[European Medicines Agency (EMEA), The European Agency for the Evaluation of Medicinal Products, Veterinary Medicines Evaluation Unit, Committee for Veterinary Medicinal Products; Benzyl Alcohol, Summary Report (1997). Available from, as of July 8, 2008: http://www.emea.europa.eu/pdfs/vet/mrls/Benzylalcohol.pdf] **PEER REVIEWED**

LD50 Mouse iv < 0.5 mL/kg /94% benzyl alcohol/[Kimura ET et al; Toxicol Appl Pharmacol 18 (1): 60-8 (1971)] **PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/pubmed/5542834?dopt=Abstract" target=new>PubMed Abstract

LC100 Rat inhalation 200-300 ppm/8 hr[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 284] **PEER REVIEWED**

LC50 Rat inhalation 74.178 mg/L/4hr[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.14 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Mouse oral 1580 mg/kg[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 498] **PEER REVIEWED**

LD50 Rabbit oral 1940 mg/kg[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 498] **PEER REVIEWED**

LD50 Rabbit dermal 2000 mg/kg[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.13 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Guinea pig dermal < 5 mL/kg[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 498] **PEER REVIEWED**

LC50 Rat inhalation 1000 ppm/8 hr[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 498] **PEER REVIEWED**

LD50 Rat iv 53mg/kg bw[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.259 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Rat iv 314mg/kg bw[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.259 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Mouse iv 324 mg/kg[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 399] **PEER REVIEWED**

LD50 Mouse oral 1360 mg/kg[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 399] **PEER REVIEWED**

LD50 Rat iv 53 mg/kg[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 399] **PEER REVIEWED**

LD50 Mouse CD-1, Male ip 1000mg/kg bw after 4 hours[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.258 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LD50 Rat ip 400 mg/kg[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 399] **PEER REVIEWED**

ECOTOXICITY VALUES:

EC50 Haematococcus pluvialis (Algae) 2600mg/L/24hr, effect: inhibition of photosynthesis[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.249 (2001). Available from, as of July 9 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

EC50 Chlorella pyrenoidosa (Algae) 95 mg/L/3hr, Effect: inhibition of photosynthesis[Organization for Economic Cooperation and Development;

Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.248 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LC50 Petrumyzon marinus > =5mg/L/24hr, static bioassay[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.245 (2001). Available from, as of July 9 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LC50 Leuciscus idus 646mg/L/48hr, static bioassay[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.245 (2001). Available from, as of July 9 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

LC50 Pimephales promelas (fathead minnows) 770 mg/l/48 hr, static bioassay in Lake Superior water at 18-22 deg C.[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 283] **PEER REVIEWED**

LC50 Pimephales promelas (fathead minnows) 480 mg/l/72 hr, static bioassay in Lake Superior water at 18-22 deg C[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 283] **PEER REVIEWED**

LC50 Pimephales promelas (fathead minnows) 460 mg/l/96 hr, static bioassay in Lake Superior water at 18-22 deg C[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 283] **PEER REVIEWED**

LC50 Lepomis macrochirus (bluegill sunfish) 10 ppm/96 hr, static bioassay in fresh water at 23 deg C, mild aeration after 24 hr[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 283] **PEER REVIEWED**

LC50 Menidia beryllina (tidewater silverside fish) 15 ppm/96 hr, static bioassay in synthetic seawater at 23 deg C, mild aeration after 24 hr[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 283] **PEER REVIEWED**

EC50; Species: Tetrahymena pyriformis (Ciliate, GL-C strain); Conditions: freshwater, static; Concentration: 853470 ug/L for 48 hr (95% confidence interval: 686420-1057020 ug/L); Effect: decreased population, population changes, general /formulated product/[Schultz TW et al; In: GW Suter II and MA Lewis (Eds.), Aquatic Toxicology and Environmental Fate, 11th Volume, ASTM STP 1007 :410-23 (1989) Available from, as of June 23, 2008: http://cfpub.epa.gov/ecotox/quick_query.htm] **PEER REVIEWED**

ONGOING TEST STATUS:

The following link will take the user to the National Toxicology Program (NTP) Test Agent Search Results page, which tabulates all of the "Standard Toxicology & Carcinogenesis Studies", "Developmental Studies", and "Genetic Toxicity Studies" performed with this chemical. Clicking on the "Testing Status" link will take the user to the status (i.e., in review, in progress, in preparation, on test, completed, etc.) and results of all the studies that the NTP has done on this chemical.[Available from: http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=100-51-6]

DRUG WARNINGS:

Common side effects of /Benzyl Alcohol Lotion, 5%/ include irritations of the skin, scalp, and eyes, and numbness at the site of application. As with all medications, it is important to use benzyl alcohol, 5%, as labeled to maximize benefits and minimize risks. The product should be applied only to the scalp or the hair attached to the scalp. It is not approved for use in children younger than six months. Use in premature infants could lead to serious respiratory, heart- or brain-related adverse events such as seizure, coma, or death.[FDA; FDA Approves Benzyl Alcohol Lotion for the Treatment of Head Lice, FDA News (April 9, 2009) Available from, as of April 20, 2009: http://www.fda.gov/bbs/topics/NEWS/2009/NEW01993.html] **PEER REVIEWED**

It also seems prudent to avoid the use of products containing benzyl alcohol to pregnant patients within whom the benzyl alcohol molecule, given its small size, presumably crosses the placental barrier into immature fetal tissues as readily as it crosses the blood-brain barrier.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2,

100-51-6 p.294 (2001). Available from, as of July 9 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

Premature neonates may receive multiple drugs in the neonatal intensive care unit, some of which may contain benzyl alcohol. As there may be no safe lower dose of benzyl alcohol in these patients, it would seem prudent to avoid the use of multiple dose vials containing benzyl alcohol whenever alternatives exist.[Organization for Economic Cooperation and Development; Screening Information Data Set for Benzoates, CAS #s 65-85-0, 532-32-1, 582-25-2, 100-51-6 p.294 (2001). Available from, as of July 9, 2008: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html] **PEER REVIEWED**

Benzyl alcohol is believe to have a role in the increased frequency of cerebral intraventricular hemorrhages and mortality reported in very-low-birth-weight (VLBW) infants (weight < 1000 g) who received flush solutions preserved with benzyl alcohol. An increased incidence of developmental delay and cerebral palsy is also noted in the same VLBW patient population, suggesting a secondary damaging effect of benzyl alcohol.[Goldfrank, L.R., Goldfrank's Toxicologic Emergencies 8th Ed. 2006., McGraw-Hill, New York, N.Y., p. 831] **PEER REVIEWED**

Benzyl alcohol, which is used as a preservative in intravascular flush solutions, caused neurological deterioration and deaths in very low birth weight infants. Preterm infants who received large volumes of fluids containing 0.9% benzyl alcohol via catheter developed "gasping baby syndrome." Estimated intakes of 99 to 405 mg benzyl alcohol/kg body weight for 2 to 28 days caused effects including severe metabolic acidosis, gasping, neurological deterioration, blood abnormalities, skin breakdown, liver and kidney failure, lowered blood pressure, heart failure, and death. No effects were seen for intakes of 27 to 99 mg/kg body weight over similar periods, although there is one report of 32 to 105 mg/kg body weight for 7 days causing breathing difficulty.[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V6 500] **PEER REVIEWED**

Benzyl alcohol is normally oxidized rapidly to benzoic acid, conjugated with glycine in the liver, and excreted as hippuric acid. However, this metabolic pathway may not be well developed in premature infants. The benzyl alcohol may therefore have been metabolized to benzoic acid, which could not be conjugated by the immature liver but accumulated, causing metabolic acidosis ... .[CDC/MMWR; Neonatal Deaths Associated With Use Of Benzyl Alcohol -- United States. Morbidity and Mortality Weekly Repost 31(22);290-1 (June 11, 1982). Available from, as of July 23, 2008: http://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm] **PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 404,916 workers (236,470 of these were female) were potentially exposed to benzyl alcohol in the US(1). Occupational exposure to benzyl alcohol may occur through inhalation and dermal contact with this compound at workplaces where benzyl alcohol is produced or used. Monitoring and use data indicate that the general population may be exposed to benzyl alcohol via dermal contact with consumer products containing benzyl alcohol and to a lesser extent via inhalation of ambient air, ingestion of food and drinking water(SRC).[(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981-1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available at http://www.cdc.gov/noes/ as of July 9, 2008.] **PEER REVIEWED**

SKIN, EYE AND RESPIRATORY IRRITATIONS:

It is slightly irritating to the skin ... .[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983., p. 111] **PEER REVIEWED**

Vapor: Irritating to eyes, nose and throat. Liquid: Irritating to skin & eyes.[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.] **PEER REVIEWED**