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Safety Assessment of Poloxamers 101, 105, 108, 122, 123, 124, 181, 182, 183, 184, 185, 188, 212, 215, 217, 231, 234, 235, 237, 238, 282, 284, 288, 331, 333, 334, 335, 338, 401, 402, 403, and 407, Poloxamer 105 Benzoate, and Poloxamer 182 Dibenzoate as Used in Cosmetics[1]

Poloxamers are polyoxyethlyene, polyoxypropylene block polymers. The impurities of commercial grade Poloxamer 188, as an example, include low-molecular-weight substances (aldehydes and both formic and acetic acids), as well as 1,4-dioxane and residual ethylene oxide and propylene oxide. Most Poloxamers function in cosmetics as surfactants, emulsifying agents, cleansing agents, and/or solubilizing agents, and are used in 141 cosmetic products at concentrations from 0.005% to 20%. Poloxamers injected intravenously in animals are rapidly excreted in the urine, with some accumulation in lung, liver, brain, and kidney tissue. In humans, the plasma concentration of Poloxamer 188 (given intravenously) reached a maximum at 1 h, then reached a steady state. Poloxamers generally were ineffective in wound healing, but were effective in reducing postsurgical adhesions in several test systems. Poloxamers can cause hypercholesterolemia and hypertriglyceridemia in animals, but overall, they are relatively nontoxic to animals, with LD_{50} values reported from 5 to 34.6 g/kg. Short-term intravenous doses up to 4 g/kg of Poloxamer 108 produced no change in body weights, but did result in diffuse hepatocellular vacuolization, renal tubular dilation in kidneys, and dose-dependent vacuolization of epithelial cells in the proximal convoluted tubules. A short-term inhalation toxicity study of Poloxamer 101 at 97 mg/m^3 identified slight alveolitis after 2 weeks of exposure, which subsided in the 2-week postexposure observation period. A short-term dermal toxicity study of Poloxamer 184 in rabbits at doses up to 1000 mg/kg produced slight erythema and slight intradermal inflammatory response on histological examination, but no dose-dependent body weight, hematology, blood chemistry, or organ weight changes. A 6-month feeding study in rats and dogs of Poloxamer 188 at exposures up to 5% in the diet produced no adverse effects. Likewise, Poloxamer 331 (tested up to 0.5 g/kg day^{-1}), Poloxamer 235 (tested up to 1.0 g/kg day^{-1}), and Poloxamer 338 (at 0.2 or 1.0 g/kg day^{-1}) produced no adverse effects in dogs. Poloxamer 338 (at 5.0 g/kg day^{-1}) produced slight transient diarrhea in dogs. Poloxamer 188 at levels up to 7.5% in diet given to rats in a 2-year feeding study produced diarrhea at 5% and 7.5% levels, a small decrease in growth at the 7.5% level, but no change in survival. Doses up to 0.5 mg/kg day^{-1} for 2 years using rats produced yellow discoloration of the serum, high serum alkaline phosphatase activity, and elevated serum glutamicpyruvic transaminase and glutamic-oxalacetic transaminase activities. Poloxamers are minimal ocular irritants, but are not dermal irritants or sensitizers in animals. Data on reproductive and developmental toxicity of Poloxamers were not found. An Ames test did not identify any mutagenic activity of Poloxamer 407, with or without metabolic activation. Several studies have suggested anticarcinogenic effects of Poloxamers. Poloxamers appear to increase the sensitivity to anticancer drugs of multidrug-resistant cancer cells. In clinical testing, Poloxamer 188 increased the hydration of feces when used in combination with a bulk laxative treatment. Compared to controls, one study of angioplasty patients receiving Poloxamer 188 found a reduced myocardial infarct size and a reduced incidence of reinfarction, with no evidence of toxicity, but two other studies found no effect. Poloxamer 188 given to patients suffering from sickle cell disease had decreased pain and decreased hospitilization, compared to controls. Clinical tests of dermal irritation and sensitization were uniformly negative. The Cosmetic Ingredient Review (CIR) Expert Panel stressed that the cosmetic industry should continue to use the necessary purification procedures to keep the levels below established limits for ethylene oxide, propylene oxide, and 1,4-dioxane. The Panel did note the absence of reproductive and developmental toxicity data, but, based on molecular weight and solubility, there should be little skin penetration and any penetration of the skin should be slow. Also, the available data demonstrate that Poloxamers that are introduced into the body via routes other than dermal exposure have a rapid clearance from the body, suggesting that there would be no risk of reproductive and/or developmental toxicity. Overall, the available data do not suggest any concern about carcinogenesis. Although there are gaps in knowledge about product use, the overall information available on the types of products in which these ingredients are used, and at what concentration, indicates a pattern of use. Based on these safety test data and the information that the manufacturing process can be controlled to limit unwanted impurities, the Panel concluded that these Poloxamers are safe as used.

INTRODUCTION

The generic CAS No. 9003-11-6 applies to all Poloxamers. Poloxamer 105 Benzoate and Poloxamer 182 Dibenzoate have no CAS numbers. These polymers are synthetic block copolymers of ethylene oxide and propylene oxide. In medical and research applications, they commonly are referred to as Pluronic® block polymers, a Poloxamer trade name. Available

[1]Reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel. Subhashni D. Singh-Joy, former scientific analyst, and Valerie C. McLain, CIR scientific analyst, prepared this report. Address correspondence to Ms. Valerie C. McLain, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036, USA.