



Safety Statement

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Product Name: AC PolyJackharides

Code: 20963

INCI Name: Water & Artocarpus Heterophyllus Fruit Extract

AC PolyJackharides is manufactured by first processing (mechanical grinding/milling) *Artocarpus heterophyllus* (jackfruit), followed by extraction and filtration.

AC PolyJackharides was tested using *in vitro* dermal and ocular irritation models, including phototoxicity irritation (EpiDerm™ EPI-200-SIT). This product was found to be non-irritating in all models, including non-phototoxic for the *in vitro* dermal model.

A *Salmonella typhimurium* reverse mutation standard plate incorporation study was conducted to evaluate whether AC PolyJackharides would cause mutagenic changes in the average number of revertants for histidine-dependent *Salmonella typhimurium* strains in the presence and absence of S9 metabolic activation. This study was conducted to satisfy, in part, the Genotoxicity requirement of the International Organization for Standardization: Biological Evaluation of Medical Devices, Part 3: Tests for Genotoxicity, Carcinogenicity and Reproductive Toxicity. AC PolyJackharides was considered to be nonmutagenic to the *Salmonella typhimurium* tester strains under the conditions of this assay.

AC PolyJackharides was also tested via the OECD TG 442C Direct Peptide Reactivity and OECD TG 442D In Vitro Skin Sensitization Assays in accordance with the EURL ECVAM and UN GHS guidelines. This product was determined to be a non-skin sensitizer in both *in chemico* and *in vitro* models.

A Freshwater Alga Growth Inhibition test via OECD 201 was subsequently performed to determine the potential toxicity of AC PolyJackharides. In this assay, *Pseudokirchneriella subcapitata* are exposed to the test substance for 72 hours and growth and growth inhibition through cell count against control is performed. The response is evaluated as a function of the exposure concentration in comparison with the average growth of replicate, unexposed control cultures. After 72 hours, the percent inhibition for AC PolyJackharides was determined to be 106.75 mg/L EC₁₀ and 218.30 mg/L EC₂₀. The results of this assay indicate that the product is not classified and therefore not harmful to aquatic organisms.

AC PolyJackharides was also assessed for ready biodegradability in an aerobic aqueous medium via the OECD 301 B Ready Biodegradability: CO₂ Evolution (Modified Sturm Test). AC PolyJackharides achieved 91.8% biodegradation after 28 days of testing, indicating that the product meets method requirements for the Ready Biodegradable classifications.

The full reports for each safety study analyzing AC PolyJackharides are attached for reference.

Due to the restriction placed on animal testing of cosmetic raw materials, and Active Concepts, LLC's internal non-animal testing policy, this product was not tested for NOAEL. However, there is substantial amounts of published data for *Artocarpus heterophyllus* that provides useful information to calculate approximate NOAEL and demonstrate the non-cytotoxic effects of AC PolyJackharides. Investigation of the following data for *Artocarpus heterophyllus* along with US Food and Drug Administration guidelines¹ has allowed us to estimate AC PolyJackharides exposure based off dosage in topical form, with an approximate NOAEL of 32.5 mg/kg/day.

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For example, at an average 2% use level in 1 oz (or 28 g) finished product per day on a person averaging a 65 kg body weight, a daily exposure of 8.62 mg/kg is expected ($28 \text{ g} \times 2\% = 0.56 \text{ g}$ or 560 mg; 560 mg / 65 kg). Although there is not one established standard to convert LD₅₀ to NOAEL, a conservative conversion factor such as the ISO 10993-17 standard as well as published LD₅₀ data can be used to estimate NOAEL for AC PolyJackharides.^{1,2} The published LD₅₀ value for *Artocarpus heterophyllus* is 5,000 mg/kg.³ Therefore, it is expected that AC PolyJackharides has an estimated aforementioned NOAEL of 32.5 mg/kg/day, based on the following calculation: $[(LD_{50} \times BW)/10,000]$, so $[(5,000 \text{ mg/kg} \times 65 \text{ kg})/10,000]$.

When AC PolyJackharides is used at approximately 2% in a finished formula sample, we do not expect exposure to exceed 8.62 mg/kg daily, which is well under the NOAEL estimate of 32.5 mg/kg/day.

Additionally, *Artocarpus heterophyllus* is commonly used in the food and nutraceutical industries.⁴ Since *Artocarpus heterophyllus* is intentionally used in food, the extract of *Artocarpus heterophyllus* may be classified as Generally Recognized as Safe (GRAS) according to the FDA's Federal Food, Drug and Cosmetic Act.⁵

The act states:

Any substance that is intentionally added to food is a food additive, that is subject to premarket review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excluded from the definition of a food additive.⁵

Several, published data sets exist to support the safety of AC PolyJackharides. Additionally, the molecular weight of this product (approximately 31,867 Da) is larger than what is required to penetrate skin. Therefore, hazards that may otherwise occur via this route are not an issue. It is presented in an aqueous carrier, all but eliminating its risk for inhalation. Toxicological, irritation, and sensitization assays have all been performed with favorable results for each. This knowledge combined with the tested and published toxicity assays allows us to support the safety of AC PolyJackharides in cosmetic applications.

It is logically concluded that AC PolyJackharides is safe in cosmetic applications at use levels of 1.00 – 10.00%. No further testing is required at this time.

1. U.S. Food and Drug Administration (FDA) – Assessing Safety When Toxicity Data are Limited. <https://pdfs.semanticscholar.org/presentation/a8c3/4a1ed34f929156bbc3d8db6693b6f22c8f9b.pdf>
2. APIC 2014, Guidance on Aspects of Cleaning Validation in Active Pharmaceutical Ingredient Plants. <https://apic.cefic.org/pub/APICCleaningValidationGuide-updateSeptember2016-final.pdf>
3. Prakash, Om & Kumar, Rajesh & Chandra, D. & Kumar, A. & Kumar, P.. (2015). Effect of *Artocarpus heterophyllus* Lam. (Jackfruit) on Indomethacin-Induced ulcer model in albino rats. *Der Pharmacia Lettre*. 7. 81-85.
4. Hettiaratchi UP, Ekanayake S, Welihinda J. Nutritional assessment of a jackfruit (*Artocarpus heterophyllus*) meal. *Ceylon Med J*. 2011 Jun;56(2):54-8. doi: 10.4038/cmj.v56i2.3109. PMID: 21789865.
5. Federal Food, Drug and Cosmetic Act. U.S Food and Drug Administration. www.fda.gov.

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