

Scientific Literature Review Notice to Proceed – March 17, 2023

Ethyl Tafluprostamide and Isopropyl Cloprostenate

Cosmetic Ingredient Review (CIR) Procedures call for the development of a review of the available scientific literature for each cosmetic ingredient (and wherever appropriate, closely related ingredients) on the basis of the annual priority list. The Scientific Literature Review (SLR) shall consist of a bibliography of relevant scientific literature, study reports that have been submitted by interested parties, and a description of each literature reference or submitted study report.

According to 2023 FDA VCRP data, Isopropyl Cloprostenate is used in 3 total formulations of the product category “other eye makeup preparations.”¹ There are no reported uses for Ethyl Tafluprostamide. A concentration of use survey is currently underway for these two ingredients.

Although use information has been reported for Isopropyl Cloprostenate, an intensive search of the published information on this ingredient, as well as Ethyl Tafluprostamide, resulted in insufficient information to justify preparation of a formal SLR. CIR, therefore, is issuing this SLR Notice to Proceed (NTP) to alert interested parties that a safety assessment is being prepared and significant data needs remain.

Both Ethyl Tafluprostamide and Isopropyl Cloprostenate are synthetic prostaglandin analogs that are reported to function as hair conditioning agents in cosmetics.² Ethyl Tafluprostamide is also reported to function as a nail conditioning agent. The minimal data found in the published literature include a case report indicating periorbital hollowing and skin discoloration following the use of a product containing Isopropyl Cloprostenate,³ a report indicating periocular discoloration following use of a serum containing Isopropyl Cloprostenate,⁴ an acute toxicity assay evaluating hematological parameters in rats following intraperitoneal injection of Isopropyl Cloprostenate,⁵ and a study performed in male mice specifically evaluating the effects of Isopropyl Cloprostenate on reproductive organs (general toxicological evaluations were not performed).⁶ Also found was a Scientific Committee on Consumer Safety (SCCS) opinion on prostaglandin and prostaglandin-analogs used in cosmetic products.⁷ This document contains minimal chemical/physical properties and impurities data on Ethyl Tafluprostamide and Isopropyl Cloprostenate, predictive values for the dermal absorption and genotoxic potential of Isopropyl Cloprostenate, as well as a summarized human eye irritation study in which subjects used an eyelash formulation containing 10% Isopropyl Cloprostenate, a summarized clinical trial evaluating various ophthalmological parameters following exposure to Isopropyl Cloprostenate, and summarized studies regarding ophthalmological parameters evaluated following exposure to Isopropyl Cloprostenate in animal models. Based on the limited data, the SCCS was not able to conclude on the safety of Ethyl Tafluprostamide and Isopropyl Cloprostenate.

All interested persons are provided 60 days from the above date (i.e., **May 16, 2023**) to submit comments and/or published or unpublished data.* A draft report will be prepared, and reviewed by the Expert Panel for Cosmetic Ingredient Safety at a future meeting, which **may be as soon as June 12-13, 2023**. If data are provided in response to this SLR NTP, those data will be incorporated into that draft report.

Given that this notice is being issued because of a general absence of information, CIR is seeking information in a wide range of areas, including:

- Chemistry information, including composition and structure, method of manufacture, and impurity data;
- Toxicokinetics data relevant to routes of exposure expected with cosmetic use;
- General toxicity data;
- Developmental and reproductive toxicity data;
- Genotoxicity data;
- Carcinogenicity data;
- Dermal irritation and sensitization data;
- Ocular toxicity/irritation data

- Inhalation toxicity data; and
- Any other relevant safety information that may be available

Please forward relevant data and comments to Dr. Bart Heldreth, Executive Director. This notice was prepared, and the search indicated above was performed, by Priya Cherian, M.S., Senior Scientific Analyst/Writer.

*Because all unpublished data submitted to CIR will be evaluated in public meetings and may be included in the final published safety assessment, CIR may not accept any confidential or proprietary data or information that cannot be made public. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient.

REFERENCES

1. US Food and Drug Administration (FDA) Center for Food Safety & Applied Nutrition (CFSAN). 2023. Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. (Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2023; received February 2, 2023). College Park, MD.
2. Nikitakis J, Kowcz A. wINCI: *International Cosmetic Ingredient Dictionary and Handbook*. <http://webdictionary.personalcarecouncil.org/jsp/Home.jsp>. Washington, DC: Personal Care Products Council. Last Updated: 2023. Accessed: February 28, 2023.
3. Jamison A, Okafor L, Ullrich K, Schiedler V, Malhotra R. Do prostaglandin analogue lash lengtheners cause eyelid fat and volume loss? *Aesthet Surg J*. 2022;42(11):1241-1249.
4. Horváth NO, Letulé V, Ruzicka T, Herzinger T, Goldscheider I, von Braunmühl T. Periocular discoloration after using a prostaglandin analog for eyelash enhancement: evaluation with reflectance confocal microscopy. *J Cosmet Dermatol*. 2017;16(1):18-20.
5. Udeanu D, Mihele D, Cocu F, Caraene G, Vulturescu V, Iova D. Study on the influence of the treatment with some newly synthesized antiglaucoma prostamides on the hematological parameters on rats. 2008;56:669-674.
6. Sava A, Motoc AG, Stan CI. Electron microscopic aspects of the effects of certain prostaglandin analogs on mouse testes. *Rom J Morphol Embryol*. 2015;56(2 Suppl):771-775.
7. Scientific Committee on Consumer Safety (SCCS). Opinion on prostaglandins and prostaglandin-analogs used in cosmetic products. https://health.ec.europa.eu/system/files/2022-02/sccs_o_258.pdf. Last Updated: 2022. Accessed: March 1, 2023.