November 16, 2020

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Subject: Comments re: DARTIC Prioritization of Methyl-, Propyl-, Butyl- and Isobutylparaben

The Personal Care Products Council (Council)[1] and the Consumer Healthcare Products Association (CHPA)[2] are pleased to submit the following Comments in response to prioritization of chemicals by the Developmental and Reproductive Toxicity Identification Committee (DARTIC) at their upcoming meeting. These comments address the four parabens that are on the prioritization list, namely methyl-, propyl-, butyl-, and isobutylparaben. As these ingredients serve an important preservative function, and have been extensively reviewed and approved by expert bodies both in and outside the United States, they should be considered low priority for DARTIC review.

Parabens are Important and Effective Preservatives

The parabens are esters of para-hydroxybenzoic acid and have been used extensively as antimicrobial preservatives for over 80 years.[3] The parabens function as preservatives in cosmetics, drugs, and food and are highly effective at preventing the growth of microorganisms including bacteria, yeast and molds. Individual parabens are often used in combination with other parabens or other preservatives to provide protection against a broad range of microorganisms.[4]

[1] Based in Washington, D.C., the Personal Care Products Council is the leading national trade association representing the global cosmetic and personal care products industry. Founded in 1894, PCPC's more than 600 member companies manufacture, distribute, and supply the vast majority of finished personal care products marketed in the United States. As the makers of a diverse range of products that millions of consumers rely on every day, from sunscreens, toothpaste, and shampoo to moisturizer, lipstick, and fragrance, member companies are global leaders committed to product safety, quality, and innovation. Visit www.personalcarecouncil.org

[2] The Consumer Healthcare Products Association (CHPA), founded in 1881, is the national trade association representing the leading manufacturers and marketers of over-the-counter (OTC) medicines, dietary supplements, and consumer medical devices. Every dollar spent by consumers on OTC medicines saves the U.S. healthcare system more than $7, contributing a total of $146 billion in savings each year. CHPA is committed to empowering consumer self-care by preserving and expanding choice and availability of consumer healthcare products.

[3] Cashman L and Warshaw E. (2005) Dermatitis Vol. 16(2):57-66.
[4] Charnock C, and Finsrud T. (2007) J Clin Pharm Ther. Vol. 32(6):567-72.

Parabens are effective at low use levels, possess a broad spectrum of antimicrobial activity, are relatively non-irritating, non-sensitizing[5], exhibit low toxicity, are stable over a wide pH range, and are sufficiently water soluble to be effective in the aqueous phase of formulations. These characteristics make them especially versatile and valuable as preservatives.

Parabens Have Been Reviewed Extensively and Approved Worldwide

Parabens have a long history of safe use, and have undergone review by agencies responsible for cosmetics, food and medicine in jurisdictions worldwide.

Cosmetics/Personal Care Products

- Cosmetic Ingredient Review (CIR)[6] – CIR has periodically reviewed parabens as used in cosmetics, with the first review published in 1984, and the most recent review published in 2020[7]. A risk assessment was conducted, and it was "determined that the commonly used limitation of 0.8% for Σparabens is conservative and safe for human health when parabens are used in combination in cosmetic products."

- Scientific Committee on Consumer Products (SCCP)/Scientific Committee on Consumer Safety (SCCS) in the European Union – Parabens have been the subject of several opinions by the SCCP/SCCS in recent years [2005 (SCCP/0874/05), 2006 (SCCP/1017/06), 2008 (SCCP/1183/08), 2010 (SCCS/1348/10), 2011 (SCCS/1446/11) and 2013 (SCCS/1514/13)][8]. Methylparaben is allowed for use at levels up to 0.4%, and propyl- and butylparaben are allowed for use at levels up to 0.14%. Of note is an October 2020 preliminary opinion on propylparaben which concludes that based on multiple recent studies "the NOAEL for reproductive and developmental effects in males and females with propylparaben is the top dose tested at 1000 mg/kg."[9]

- Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) - A review entitled "Parabens: Human health tier II assessment" was published by the Australian Government, Department of Health in 2016. This review of human health effects included thirteen paraben esters and their salts and concluded that the "available data do not indicate any risks associated with exposure to the chemicals in this group."" Specific to reproductive and developmental toxicity, the conclusion is "(t)he chemical does not show specific reproductive or developmental toxicity. Any reproductive and developmental effects were generally only observed secondary to maternal toxicity." [10]

- Health Canada is currently conducting a review of parabens (as cited in the OEHHA Prioritization document), which are allowed for use in cosmetics without restriction. Other jurisdictions approving parabens as cosmetic preservatives include Japan – approved up to 1% (total

[5] Paraben mix deemed '(non)allergen of the year': Fransway, AF et al. (2019) Dermatitis Vol. 30(1):3-31.
[6] CIR was established in 1976 by the Personal Care Products Council, with the support of the U.S. Food and Drug Administration and the Consumer Federation of America. The CIR's Expert Panel conducts comprehensive literature reviews in examining the safety of cosmetic ingredients.
[7] Cherian et al. (2020) Int J Toxicol. Vol. 39[1_suppl]:5S-97S; also cited in OEHHA's Prioritization Document.
[8] https://ec.europa.eu/health/scientific_committees/
[9] https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs_o_243.pdf
[10] https://www.nicnas.gov.au/__data/assets/pdf_file/0011/94547/Parabens_Human-health-tier-II-assessment.pdf

parabens) in finished products (HLW Notification 331, 2000, as amended 2005); China – approval level is 0.4% for a single ester and 0.8% for mixed esters, with the sum of propyl- and butyl- not to exceed 0.14% (China Safety &Technical Standards for Cosmetics, China Food and Drug Administration (CFDA), effective Dec. 1, 2016); and Brazil - approved limit is 0.4% for one ester, and 0.8% for mixtures of salts or esters (MERCOSUR/GMC/RES No. 07/11. MERCOSUR Technical Regulation regarding the list of substances allowed as preservatives for personal hygiene, cosmetic and perfume products).

Medicine

- In the U.S., parabens in drug products are listed in FDA's Inactive Ingredients Database at https://www.accessdata.fda.gov/scripts/cder/iig/index.cfm.

- The European Medicines Agency (EMA) published a favorable review of paraben use in oral products in 2015.[11]

Food

- The U.S. FDA has approved parabens for use as food additives, specifically as flavoring agents or adjuvants (methyl-, propyl- and butylparaben); and antimicrobial agents (methyl- and propylparaben) [CFR 172.515, 181.23, 184.1490, 184.1670]. Published data on levels in food, however, indicate minimal exposure to parabens from food. In an analysis of 267 food samples in the U.S. in 2013, the median value of the sum of five parabens was 0.92 ppb[12].

NTP Study Report is in Progress

The National Toxicology Program is currently conducting a Reproductive and Developmental Toxicity Assessment of Butyl Paraben (Continuous Breeding Study in Hsd: Sprague Dawley SD rats following Feed Exposure; current status listed as 'Report in Preparation'). This study is cited in the Prioritization Document. While we believe parabens should be low priority for review, we ask that any additional review wait until a report is available from NTP. The NTP website (https://doi.org/10.22427/NTP-DATA-NTP-DATA-RACB-BP) contains the following disclaimer: "Note: The study data are being disseminated prior to external peer review under applicable information quality guidelines and do not represent and should not be construed to represent any final NTP determination or policy."

Paraben Uses – Correction

In cosmetics, the order of frequency of use of the four parabens is methylparaben > propylparaben > butylparaben > isobutylparaben. We note a correction to the Prioritization Document regarding the number of cosmetic uses for butylparaben. The Priority Document states that butylparaben is used in more than 20,000 cosmetic products; the correct number is 3884.[13]

[11] https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-use-methyl-propylparaben-excipients-human-medicinal-products-oral-use_en.pdf
[12] Liao C, Liu F, Kannan, K. (2013) Environ Sci Technol. Vol. 47(8):3918-25.
[13] Cherian et al. (2020) Int J Toxicol. Vol. 39[1_suppl]:5S-97S

Conclusion

Given the extensive reviews and approvals for these important preservatives, a conclusion of 'low priority' is appropriate for the parabens.

Thank you again for the opportunity to submit these comments.

Sincerely,

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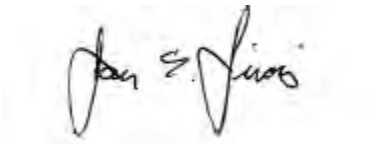

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