GENOTOX

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Jinqiu Zhu, PhD, DABT, ERT, DCST, CIR Toxicologist
Date: February 17, 2026
Subject: Notes on Non-OECD Genotoxicity Testing

At recent meetings and in follow-up communications, concerns were raised by the Panel regarding the interpretability and regulatory relevance of certain genotoxicity assays historically included in CIR safety assessments.

It has been noted that Organisation for Economic Co-operation and Development (OECD) Test Guidelines (TGs) have abandoned several assays for genotoxicity testing due to their limited use, low specificity, less reliability and reproducibility, and the availability of core and newer methods with superior performance for the same endpoints. These discontinued assays include the in vitro sister chromatid exchange (SCE) test, the in vitro unscheduled DNA synthesis (UDS) test, the Rec assay in *Bacillus subtilis*, and the mouse spot test.[1] In addition, while the UDS test with mammalian liver cells in vivo (TG 486) has been retained, the OECD has explicitly highlighted its limitations, noting that "*When evaluating the mutagenic potential of a test chemical, more weight should be given to the measurement of permanent DNA changes (i.e. mutations) than to DNA damage events that are reversible…the UDS test should not be considered as a surrogate for a gene mutation test and it may be less reliable than other primary DNA damage tests.*" More broadly, OECD TGs generally recommend genetic toxicology test batteries that *"include tests to detect gene mutations and structural as well as numerical chromosomal damage (aneuploidy) in both in vitro and in vivo tests; however, more recently, in some jurisdictions the emphasis has been on using only in vitro, and no, or fewer, well-chosen, in vivo tests."* [1]

In light of this, it is recommended that CIR adopt a standard disclaimer for use in reports whenever these assays are mentioned. ***Should such a disclaimer be stated in the genotoxicity section of CIR reports wherein the endpoint summaries of such studies are included, or dealt with elsewhere in the reports?*** A possible wording could be: "Certain genotoxicity assays (e.g., SCE, UDS, Rec assay in *B. subtilis*) are considered obsolete for genotoxicity testing according to OECD guidance. Results from these assays are of limited interpretability and should only be considered as supportive information within the overall weight-of-evidence." This would ensure consistency across review process and clarify to stakeholders that results from these assays are not weighted as primary evidence in hazard identification or risk assessments.

By applying a weight-of-evidence approach, the Panel integrates findings from gene mutation, structural chromosomal aberration, and aneuploidy assays, with interpretations tailored to the dataset available for each ingredient under review. This integrated evaluation ensures that conclusions are both scientifically robust and appropriately reliable, while also providing a framework for the incorporation of methodological advances such as New Approach Methods (NAMs) that offer human-relevant, predictive alternatives to animal testing. For example, the OECD is currently advancing the ToxTracker reporter assay as a draft TG under public consultation,[2] and the 3D reconstructed skin micronucleus (RSMN) assay has recently been added to the OECD Work Plan for the TG Program (Project 4.139).[3]

The Panel is requested to discuss whether to adopt a boilerplate disclaimer for the outdated assays, or to develop such a statement as part of an internal SOP. In addition, further consideration should be given to the appropriate role of NAMs in CIR safety evaluations moving forward.

References:

1. Organisation for Economic Co-operation and Development (OECD). 2016Overview of the Set of OECD Genetic Toxicology Test Guidelines and Updates Performed in 2014-2015
Series on Testing & Assessment no. 238.

2. Organisation for Economic Co-operation and Development, (OECD). 2025. OECD Guideline for the Testing of Chemicals Draft Toxtracker Gene Reporter Assay for Genotoxic Hazard Identification. https://www.oecd.org/en/events/public-consultations/2025/07/draft-new-test-guideline-on-the-toxtracker-gene-reporter-assay-for-genotoxic-hazard-identification.html .

3. Doak SH, Andreoli C, Burgum MJ, et al. Current status and future challenges of genotoxicity OECD Test Guidelines for nanomaterials: a workshop report. *Mutagenesis*. 2023;38(4):183–191.