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Summary

Cosmetics must undergo a human safety assessment which is described in the Product Information File. This is focused on an *in vitro* testing strategy in accordance with the Cosmetics Products Regulation (EC) No 1223/2009.

SAFETY ASSESSMENT

Cosmetic Product Testing Services

The SCCS provides guidance on testing that may need to be performed (SCCS/1564/15) for all substances intended to be incorporated in a cosmetic product. Charles River scientists have been involved in the shaping of many of these tests; e.g., advising on the skin penetration guidance (SCCS/1358/10), and supporting the validation of new assays, e.g. HCE ocular irritation. They've also advised clients and Cosmetics Europe.

We can test individual ingredients, mixtures or final products using a broad range of *in silico*, *in chemico* or *in vitro* methods that meet both testing and compliance requirements. This range of model systems results in multiple toxicity endpoints.

Dermal/Percutaneous Absorption

- Radiolabeled and non-radiolabeled tests with human skin in static or flow cells (OECD 428; SCCS/1358/10)

Metabolism

- Hepatic metabolism using hepatocytes and microsomes
- Dermal metabolism during absorption or in tissue fractions

Acute Toxicity

- 3T3 neutral red uptake test (OECD 129) for acute oral toxicity

Skin Corrosion and Skin Irritation

- *In vitro* in 3D tissue models for skin corrosion (OECD 431) and skin irritation (OECD 439)
- *In chemico* skin corrosion testing with Corrositex™ (OECD 435)

Serious Eye Damage and Eye Irritation

- Bovine corneal opacity and permeability test (OECD 437) for eye damage
- Reconstructed human cornea-like epithelium test (OECD 492) for ocular irritation

Skin Sensitization*

- Utilizes a battery of tests
- *In silico* skin sensitization assessment by Lhasa DEREK
- *In chemico* Direct Peptide Reactivity Assay (OECD 442C)
- *In vitro* ARE-Nrf2 luciferase test method (OECD 442D)
- *In vitro* Myeloid U937 skin sensitization test or *in vitro* (OECD 442E)

*This is supported by weight-of-evidence approaches including non-validated tests (e.g., SenzaGen Genomic Allergen Rapid Detection test).

Mutagenicity/Genotoxicity

- *In silico* mutagenicity assessment using Lhasa DEREK and Lhasa SARAH or MultiCase™
- Bacterial reverse mutation (Ames) test (OECD 471)
- *In vitro* micronucleus test (OECD 487)
- *In vitro* chromosome aberration assay (OECD 473)
- *In vitro* mammalian gene mutation test using the HPRT gene (OECD 476) or TK gene (OECD 490)

Photo-Induced Toxicity

- 3T3 neutral red uptake phototoxicity test (3T3 NRU PT) (OECD 432)
- Phototoxicity assessment in 3D differentiated human keratinocytes (PhotoEpiderm™)
- Ultraviolet-visible spectral analysis (OECD 101)

Endocrine Disruption

- Estrogen receptor binding using rat uterine cytosol (OPPTS/OCSPP 890.1250)
- Estrogen receptor transcriptional activation (OPPS/OCSPP 890.1300 and OECD 455)
- Androgen receptor binding using rat prostate cytosol (OPPTS/OCSPP 890.1150)
- Androgen receptor transactivation using the AR-EcoScreen™
- Steroidogenesis using human cell line H295R (OPPTS/OCSPP 890.1550 and OECD 456)
- Aromatase human recombinant (OPPTS/OCSPP 890.1200)

Regulatory Framework

In Europe, cosmetic ingredients like colorants, preservatives and UV filters require a safety assessment to be submitted to the Scientific Committee on Consumer Safety (SCCS) for evaluation. For cosmetic products, according to the Cosmetics Product Regulation (EC) No 1223/2009, a full safety assessment needs to be performed and included in a Product Information File kept at the cosmetic product company. This file also includes a description of the product, the product safety report, information about the manufacturing methods, and proof of effects claimed.

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