

ANNEX

Inventory of Validated Non-Animal Testing Methods Applicable for Cosmetic Products and their Ingredients in all ICCR Regions

Date of Preparation: 31 August, 2026	Status: Finalized
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Table with Internationally Accepted Non-Animal Test Methods for Cosmetic Products/Ingredients Safety Testing, successfully worked upon by ICATM

The present document provides an update to the Annex of the ICCR Report on the Inventory of validated non-animal testing methods applicable for cosmetic products and their ingredients in all ICCR Regions (Document reference: Alternatives to animal testing/Report (text)/Final-2013-11-26), and provides an inventory of methods that are recognized by ICCR as validated non-animal testing methods applicable to cosmetics in ICCR member regions.

At the July 2019 ICCR-13 meeting in Montreal, Canada, the ICCR Steering Committee (SC) decided that the ICCR Chair of each respective ICCR cycle would coordinate an annual update of the table on the basis of work carried out by the International Cooperation on Alternative Test Methods (ICATM).

Taiwan Food and Drug Administration coordinated the annual update of the table in its role as ICCR-18 Chair, in collaboration with the National Health Research Institutes, who has been participating in ICATM activities.

Health Canada coordinated the annual update of this document in its role as ICCR-19 chair.

Ministry of Health, Labour and Welfare Japan coordinated the annual update of the table in its role as ICCR-20 Chair, in collaboration with the National Institute of Health Sciences.

Future updates to the table will be coordinated by each respective ICCR Chair.

The table below summarizes the status of adoption of OECD test guidelines (TGs) on *in vitro* methods from 2011 to July 2026. The reader is referred to the OECD website for additional information¹.

¹ OECD Test Guidelines for Chemicals: <https://www.oecd.org/en/topics/sub-issues/testing-of-chemicals/test-guidelines.html>

Human health	Test Method Description / OECD Testing Guideline (TG)
Skin corrosion	Transcutaneous Electrical Resistance (TER) test method, as included in OECD TG 430
Skin corrosion	Reconstructed human Epidermis (RhE) test methods, as included in OECD TG 431
Skin corrosion	<i>In vitro</i> membrane barrier test method for skin corrosion, as included in OECD TG 435
Skin irritation	Reconstructed human Epidermis (RhE) test methods, as included in OECD TG 439
Skin sensitisation	<i>In chemico</i> skin sensitisation assays addressing the Adverse Outcome Pathway (AOP) key event on covalent binding to proteins, as included in OECD TG 442C
Skin sensitisation	Key-event based Test Guideline 442D: <i>In vitro</i> skin sensitisation assays addressing the AOP key event on keratinocyte activation. In June 2025, Appendix IC was updated to add EpiSensA as an additional validated assay addressing this key event.
Skin sensitisation	<i>In vitro</i> skin sensitisation assays addressing the Key Event on activation of dendritic cells in the AOP for skin sensitisation, as included in OECD TG 442E
Skin sensitisation	Defined Approaches on Skin Sensitisation, as included in OECD Guideline 497. A Defined Approach (DA) consists of a selection of information sources (e.g in silico predictions, in chemico, in vitro data) used in a specific combination, and resulting data are interpreted using a fixed data interpretation procedure (DIP) (e.g. a mathematical, rule-based model). The DAs included in this Guideline use combinations of OECD validated in chemico and in vitro test data, in some cases along with in silico information, to come to a rules-based conclusion on potential dermal sensitisation hazard (Part I), on dermal sensitisation potency (Part II), and on a quantitative point-of-departure (Part III) .
Skin absorption	Skin absorption: <i>in vitro</i> method, as included in OECD TG 428
Phototoxicity	3T3 Neutral Red Uptake (NRU) phototoxicity test, as included in OECD TG 432

Human health	Test Method Description / OECD Testing Guideline (TG)
Phototoxicity	<i>In chemico</i> test method based on reactive oxygen species (ROS) and photostability, as included in OECD TG 495
Phototoxicity	<i>In vitro</i> phototoxicity - Reconstructed human Epidermis (RhE) phototoxicity test method, as included in OECD TG 498
Serious eye damage/eye irritation	Bovine corneal opacity and permeability test method for identifying i) chemicals inducing serious eye damage and ii) chemicals not requiring classification for eye irritation or serious eye damage, as included in OECD TG 437
Serious eye damage/eye irritation	Isolated chicken eye test method for identifying i) chemicals inducing serious eye damage and ii) chemicals not requiring classification for eye irritation or serious eye damage, as included in OECD TG 438
Serious eye damage/eye irritation	Fluorescein leakage test method for identifying ocular corrosives and severe irritants, as included in OECD TG 460
Serious eye damage/eye irritation	Short Time Exposure (STE) test method for the detection of chemicals causing serious eye damage and chemicals not requiring classification for serious eye damage or eye irritation, as included in OECD TG 491
Serious eye damage/eye irritation	Reconstructed human Cornea-like Epithelium (RhCE) test methods for the detection of chemicals not requiring classification and labelling for eye irritation or serious eye damage, as included in OECD TG 492
Serious eye damage/eye irritation	Serious eye damage/eye irritation, Reconstructed human Cornea-like Epithelium (RhCE) test method for eye hazard Identification own of chemicals (substances and mixtures) not requiring classification (No Cat), requiring classification for eye irritation (Cat 2) and requiring classification for serious eye damage (Cat 1) according to the UN GHS ocular hazard categories, as included in OECD TG 492B.
Serious eye damage/eye irritation	<i>In vitro</i> macromolecular test method for Identifying i) chemicals inducing serious eye damage and ii) chemicals not requiring classification for eye irritation or serious eye damage, as included in OECD TG 496. In June 2025, Appendix 3 was updated to include the

Human health	Test Method Description / OECD Testing Guideline (TG)
	OptiSafe Eye Irritation Test™ (OS) as an additional validated method.
Serious eye damage/eye irritation	Vitrigel-Eye irritancy test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage, as included in OECD TG 494
Serious eye damage/eye irritation	Defined Approaches for Serious Eye Damage and Eye Irritation, as included in OECD TG 467. A Defined Approach (DA) consists of a selection of information sources (e.g in silico predictions, in chemico, in vitro data) used in a specific combination, and resulting data are interpreted using a fixed data interpretation procedure (DIP) (e.g. a mathematical, rule-based model). In June 2025, TG 467 was updated to include a DA specifically designed for evaluating solid substances.
Carcinogenicity	<i>In vitro</i> Syrian Hamster Embryo (SHE) Cell Transformation Assay (CTA) as included in OECD GD No. 214 ²
Carcinogenicity	<i>In vitro</i> Bhas 42 Cell Transformation Assay (CTA) as included in OECD GD no 231 ²
Genotoxicity	Bacterial reverse mutation test as included in OECD TG 471
Genotoxicity	<i>In vitro</i> mammalian chromosome aberration assay as included in OECD TG 473
Genotoxicity	<i>In vitro</i> mammalian cell gene mutation test using <i>Hprt</i> and <i>xprt</i> genes as included in OECD TG 476
Genotoxicity	<i>In vitro</i> mammalian cell micronucleus assay as included in OECD TG 487
Genotoxicity	<i>In vitro</i> mammalian cell gene mutation tests using the <i>thymidine kinase</i> gene as included in OECD TG 490.
Genotoxicity	ToxTracker gene reporter assay for the identification of genotoxic hazard and genotoxic/non genotoxic mechanism of action as included in OECD TG 446A
Endocrine disruption	Performance-Based Test Guideline for Stably transfected transactivation <i>in vitro</i> assays to detect

² These test methods were initially proposed to be included in Test Guidelines. It was later decided to include them in Guidance Documents.

Human health	Test Method Description / OECD Testing Guideline (TG)
	Estrogen Receptor (ER) agonists and antagonists as included in OECD TG 455
Endocrine disruption	H295R steroidogenesis assay as included in OECD TG 456
Endocrine disruption	Stably transfected human androgen receptor transcriptional activation assay for detection of androgenic agonist and antagonist activity as included in OECD TG 458
Endocrine disruption	Performance-Based Test Guideline for human recombinant Estrogen Receptor (hrER) <i>in vitro</i> assays to detect chemicals with ER binding affinity as included in OECD TG 493. In July 2026, the Human Glucocorticoid Receptor Transactivation Assay for detecting glucocorticoid receptor agonist and antagonist activity was added as OECD TG 454A, expanding the suite of receptor-based <i>in vitro</i> assays.
Immunotoxicity	<i>In vitro</i> immunotoxicity, the IL-2 Luc assay and IL-2 Luc LTT assay as included in OECD TG 444A
Metabolism	Determination of Cytochrome P450 (CYP) Induction using Differentiated Human Hepatic Cells as included in OECD TG 445A

Note: It is up to the discretion of regulators from each ICCR jurisdiction to refer to the TGs in the table for regulatory purposes.

It should be noted that other OECD Documents could be useful for the cosmetic sector:

- (i) ***Guidance document on integrated approaches to testing and assessment (IATA) for serious eye damage and eye irritation, Series on Testing & Assessment No. 263.***
- (ii) ***Guidance document on the reporting of defined approaches and individual information sources to be used within integrated approaches to testing and assessment (IATA) for skin sensitisation, Series on Testing & Assessment No. 256.***
- (iii) ***Guidance document on developing and assessing adverse outcome pathways, Series on Testing & Assessment No. 184.***
- (iv) ***Guidance Document for Describing Non-Guideline In Vitro Test Methods, No. 211.***
- (v) ***Guidance document for the use of adverse outcome pathways in developing integrated approaches to testing and assessment (IATA), Series on Testing & Assessment No. 260.***
- (vi) ***Guidance Document on the Characterisation, Validation and Reporting of PBK Models for regulatory purposes Guidance document on the characterisation,***

- validation and reporting of Physiologically Based Kinetic (PBK) models for regulatory purposes, No. 331.*
- (vii) *Guidance for the regulatory assessment of (Quantitative) Structure Activity Relationship models, predictions, and results based on multiple predictions, Series on Testing & Assessment No. 386.*
 - (viii) *Case Study on use of an Integrated Approach to Testing and Assessment (IATA) and New Approach Methods to Inform a Theoretical Read-Across for Dermal Exposure to Propylparaben from Cosmetics, No. 320.*
 - (ix) *Case study on the use of integrated approaches for testing and assessment for systemic toxicity arising from cosmetic exposure to Caffeine, Series on Testing and Assessment, No. 321.*
 - (x) *Case study on use of an integrated approach for testing and assessment (IATA) for systemic toxicity of phenoxyethanol when included at 1% in a body lotion. Series on Testing and Assessment, No. 349.*
 - (xi) *Case Study on the Use of Integrated Approaches for Testing and Assessment for skin sensitisation: Demonstrating the Next Generation Risk Assessment Framework using Geraniol, No. 368.*
 - (xii) *Case Study on the Use of Integrated Approaches for Testing and Assessment for skin sensitisation of Diethanolamine: Application of a Next Generation Risk Assessment Framework, No. 374.*
 - (xiii) *OECD Omics Reporting Framework (OORF): Guidance on reporting elements for the regulatory use of omics data from laboratory-based toxicology studies, Series on Testing and Assessment No. 390.*
 - (xiv) *Guidance Document on Integrated Approaches to Testing and Assessment (IATA) for Phototoxicity Testing, Series on Testing and Assessment No. 397.*
 - (xv) *Guidance Document on Integrated Approaches to Testing and Assessment (IATA) for Serious Eye Damage and Eye Irritation, Third Edition, Series on Testing and Assessment.*