



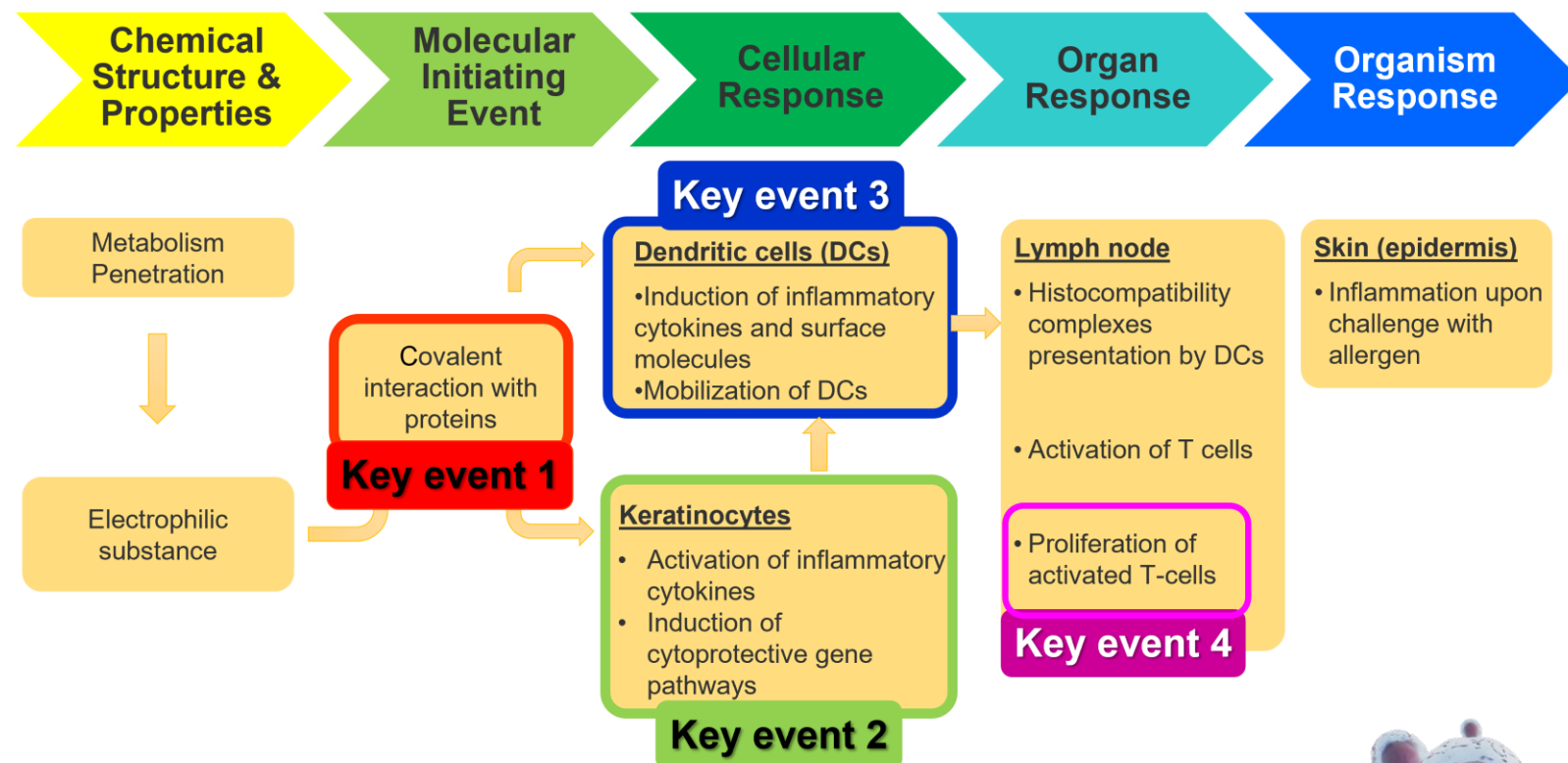
**Skin sensitization and photosensitization evaluation
through LC-MS/MS, HRMS and 3D reconstructed tissue
approaches : An integrative evaluation strategy
addressing the mixtures challenge**

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Skin sensitization and photosensitization evaluation through LC-MS/MS, HRMS and 3D reconstructed tissue approaches : An integrative evaluation strategy addressing the mixtures challenge

Adverse Outcome Pathway (AOP) :

- A conceptual construction defined by OECD
- Summarized in 4 Key Events (KE)

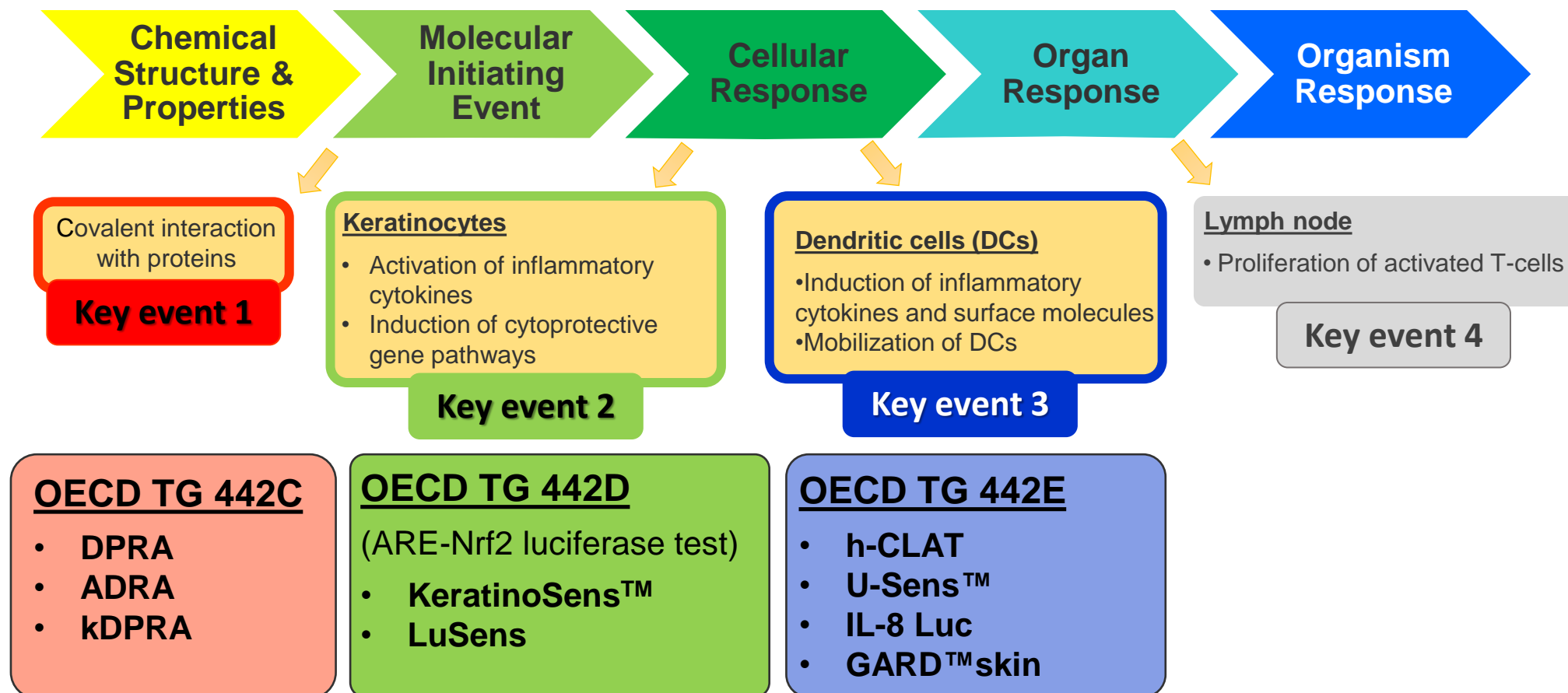


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The Adverse Outcome Pathway for Skin Sensitisation Initiated by Covalent Binding to Proteins

This document describes the state of knowledge of the adverse outcome pathway (AOP) for skin sensitisation initiated by covalent binding to proteins, assesses the weight-of-evidence supporting the AOP, identifies the key events, and identifies databases containing test results related to those key events. AOPs can be incorporated into chemical categories-based assessments or integrated approaches for testing and assessment.

"2 out of 3" ITS based on 3 OECD test guidelines, focused on the 3 first KEs



Standard Assay

Limits

Solutions

Covalent binding to proteins

OECD TG 442C

- Solvent must not absorb in UV
- Co-elution issues
- May be misleading in case of peptide dimerization
- Designed for molecule of known molecular weight

OECD TG 442C : DPRA by LC-MS/MS

- Wider solvent possibilities
- No co-elutions issues
- Peptide dimer detection
- Adapted to mixtures of unknown MW

ARE-Nrf2 luciferase test

OECD TG 442D

- Solubilization issues
- Solvent compatibility issues
- Sensitive to cytotoxicity

SensIL-18 (RhE IL-18)

- Reconstructed epidermises based assay
- Direct, topical application
- Less sensitive to cytotoxicity

Dendritic cells assay

OECD TG 442E

- Solubilization issues
- Solvent compatibility
- Sensitive to cytotoxicity

GARD™ skin

- High performance / broad applicability
- Optional quantitative potency assessment