cyprotex
AN EVOTEC COMPANY

Skin Sensitization Services

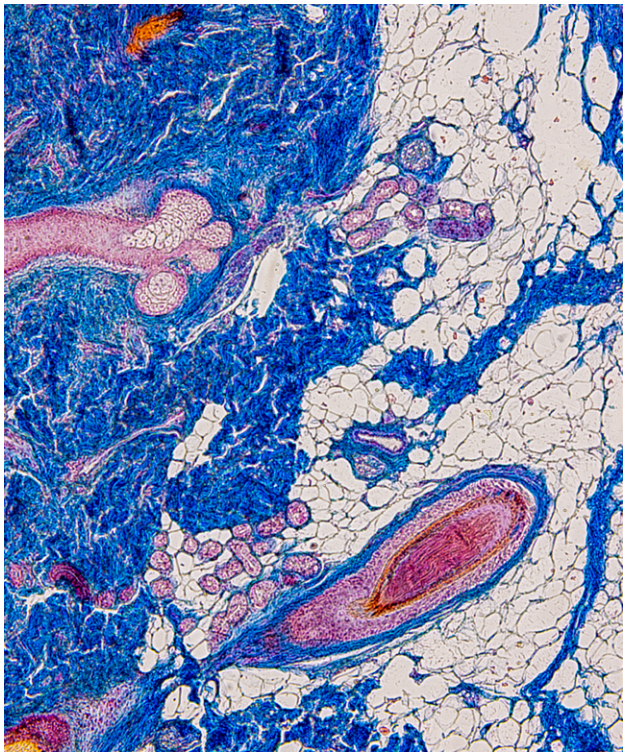
Allergic Contact Dermatitis (ACD) is a common inflammatory skin condition resulting from an immune-mediated reaction to an allergen that encounters the skin. During initial exposure, the immune system becomes sensitized to the allergen, and upon subsequent exposures, a localized allergic response characteristic of ACD develops. The molecular events underlying the skin sensitization adverse outcome pathway (AOP) are well characterized. This has enabled the development of validated *in chemico* and *in vitro* assays to assess the sensitization potential of chemical substances.

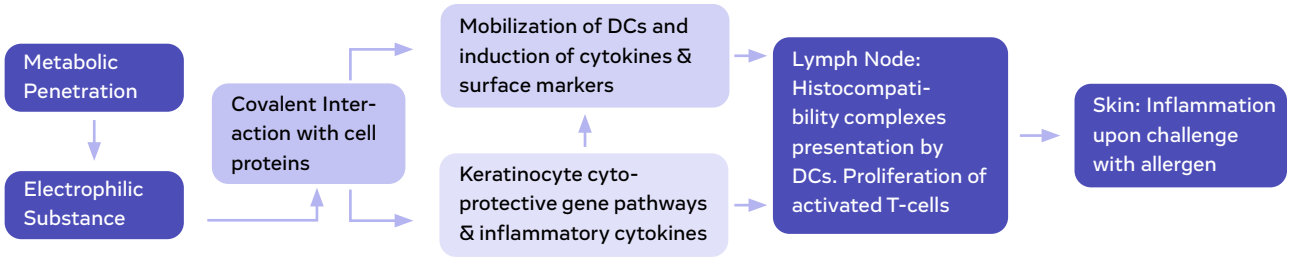
At Cyprotex, we offer the suite of assays in accordance with the OECD test guideline 442 series, designed to identify skin sensitizers by targeting key events in the AOP, including the molecular initiating event (protein binding), keratinocyte activation, and dendritic cell (immune) activation.

- **OECD TG 442C Direct Peptide Reactivity Assay (DPRA).** Investigate the molecular initiation event of skin sensitization (haptenation). Quantify the reactivity of test chemicals towards lysine and cysteine containing synthetic peptides through peptide depletion via HPLC detection.

- **OECD TG 442D KeratinoSens™.** Sensitizing compounds are electrophiles and can cause the formation of reactive oxygen species. Measure the activation of antioxidant response element (ARE)-regulated genes using a luciferase reporter keratinocyte cell line.

- **OECD TG 442E U-SENS™.** Determine the activation of dendritic cells to test chemical treatment. Sensitizing chemicals activate the human acute monocytic leukemia cell line U937 leading to an upregulation of CD86, a co-stimulatory molecule involved in T-cell activation.





Key Event 1 Protein Binding	Covalent binding of chemical to skin proteins **(haptenation)**	**OECD TG 442C** Direct Peptide Reactivity Assay
Key Event 2 Keratinocyte Activation	Release of pro-inflammatory cytokines and **cyto-protective** pathways in keratinocytes	**OECD TG 442D** KeratinoSens™ Assay
Key Event 3 Dendritic Cell Activation	Maturation and mobilization of **dendritic cells (DC)** in the skin	**OECD TG 442E** U-SENS™ Assay

Your Partner in Skin Sensitization Assessment

- **Regulatory Compliance.** The OECD guidelines are internationally recognized and accepted by regulatory bodies in OECD member countries (REACH - EU, TSCA – US etc.).
- **Alternative to Animal Testing.** These *in vitro* and *in chemico* assays form part of the integrated approach to testing and assessment (IATA), aiming to replace traditional animal-based tests like the Local Lymph Node Assay (LLNA). Their development supports the 3Rs principle—replacement, reduction, and refinement of animal use in testing.
- **Economic Benefits.** *In vitro* and *in chemico* assays can be more cost-effective and faster than their *in vivo* counterparts, supporting industries that need to screen high volumes of substances rapidly, such as cosmetics, pharmaceuticals, and industrial chemicals.
- **Scientific Relevance.** Each of the OECD 442 assays targets a specific key event in the skin sensitization AOP, such as haptenation (DPRA), keratinocyte activation (KeratinoSens™), or dendritic cell activation (U-SENS™). When used together as part of an integrated approach, they provide robust, mechanistically informed data on sensitization potential.
- **Confidence in Results.** Gain confidence in the reliability of your chemical assessments with the high accuracy of the full suite of OECD 442 skin sensitization assays, supporting informed and effective downstream decision-making.

Table 1: The sensitivity, specificity and accuracy of the OECD 442 suite of skin sensitization assays.

Assay Prediction Metric	DPRA	KeratinoSens™	U-SENS™
Sensitivity (%)	80	78	91
Specificity (%)	77	76	65
Accuracy (%)	80	77	86

All the OECD TG 442 suite of assays offered at Cyprotex have been fully validated for technical proficiency in accordance with the designed compound proficiency sets as outlined in OECD TG 442C (DPRA), OECD TG 442D (KeratinoSens™) and OECD TG 442E (U-SENS™).