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Technical Guidelines for Integrated Approaches to Testing and Assessment (IATA) of Skin Sensitization

皮肤致敏性整合测试与评估策略应用技术指南

National Institutes for Food and Drug Control

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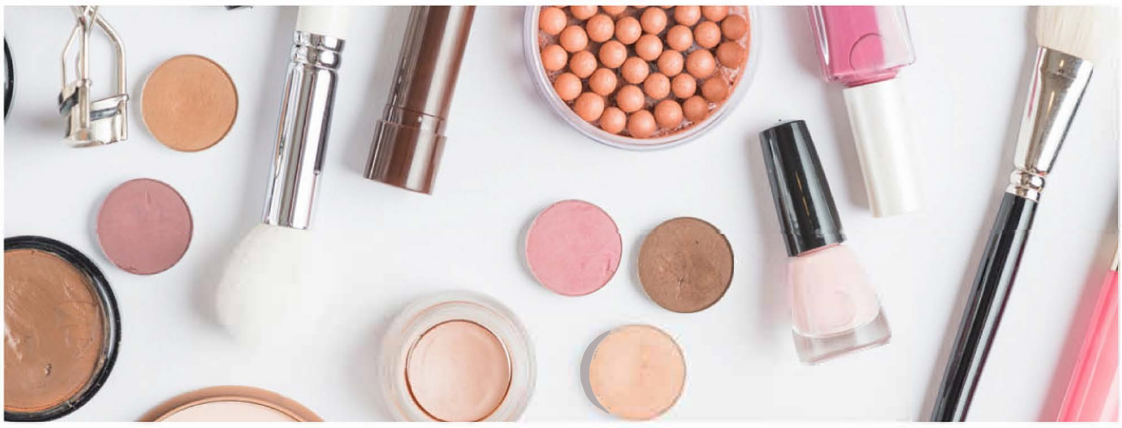

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Attachment 4

Technical Guidelines for Integrated Approaches to Testing and Assessment (IATA) of Skin Sensitization

——"2 out of 3 Tests" Strategy

National Institutes for Food and Drug Control

Contents

I. Overview

Skin sensitization (allergic contact dermatitis) is an immunogenic skin reaction of the skin to a substance. The skin sensitization test is a commonly used method to evaluate the sensitization of cosmetic ingredients. With the development of animal welfare and scientific technology, the integrated approaches to testing and assessment for skin sensitization, which is based on a combination of various toxicological evaluation tools, such as *in vitro* tests and non-testing toxicity prediction methods, has been gradually applied internationally to the evaluation of the potential sensitization risks of cosmetic ingredients.

Currently, it is widely recognized in science that skin sensitization starts with covalent binding of proteins which then undergoes a series of biological responses including cells, tissues and organs, ultimately leading to the adverse outcome of allergic contact dermatitis. The integrated approaches to testing and assessment for skin sensitization is based on the adverse outcome pathway (AOP) of skin sensitization and a series of alternative toxicological tests developed for key events (KEs) in the AOP. It integrates the data related to the ingredient to be assessed for a weight-of-evidence analysis to complete the evaluation of potential skin sensitization risks of cosmetic ingredients.

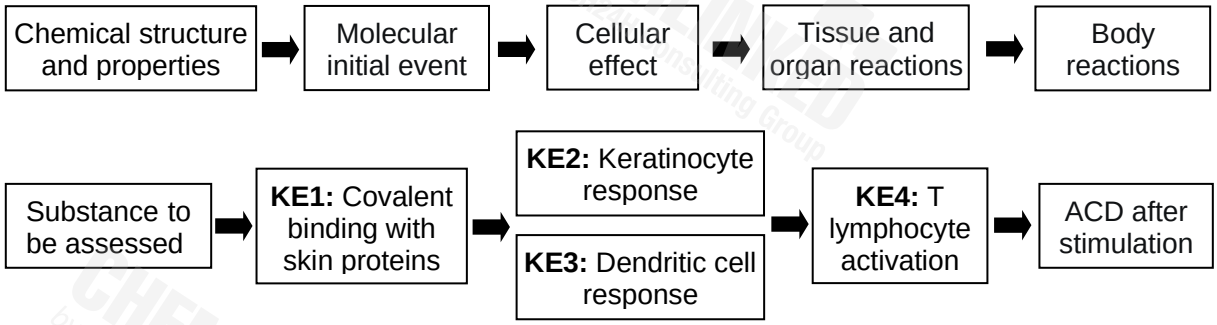

Figure 1 Schematic Diagram of Skin Sensitization AOP

In skin sensitization AOP, KE1 refers to the molecular initial event, KE2 and KE3 refer to the immune responses of keratinocytes and dendritic cells, respectively, and KE4 refers to the immune response of tissues and organs (proliferation of T lymphocytes).

II. Application Scope

This *Guidelines* is applicable to the evaluation of skin sensitization of cosmetic ingredients. The toxicological test methods for testings of KE1~KE3 based on the skin sensitization AOP constitute a "2 out of 3 tests" strategy whose application scope shall meet the requirements of the applicability of all test methods involved in the strategy.

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附件 4

皮肤致敏性整合测试与评估策略应用技术指南

——“3 选 2 试验”策略

中国食品药品检定研究院

目 录

一、概述

皮肤变态反应（过敏性接触性皮炎 Skin sensitization, allergic contact dermatitis），是皮肤对一种物质产生的免疫源性皮肤反应。皮肤变态反应试验是评价化妆品原料致敏性的常用方法，随着动物福利及科学技术的发展，国际上也逐步开展采用体外试验、非测试的毒性预测方法等多种毒理学评价工具组合的皮肤致敏性整合测试与评估策略，用于评价化妆品原料的潜在致敏风险。

目前科学上普遍认可皮肤过敏是以蛋白质共价结合为起始事件，经过细胞、组织器官等一系列生物学应答，最终导致过敏性接触性皮炎这一有害结局。皮肤致敏性整合测试与评估策略基于皮肤致敏有害结局路径（Adverse Outcome Pathway，AOP）以及针对其中各关键事件（Key Events，KEs）研发的系列替代毒理学试验，整合待评估原料相关数据进行证据权重分析，对化妆品原料潜在的皮肤致敏性风险进行评价。

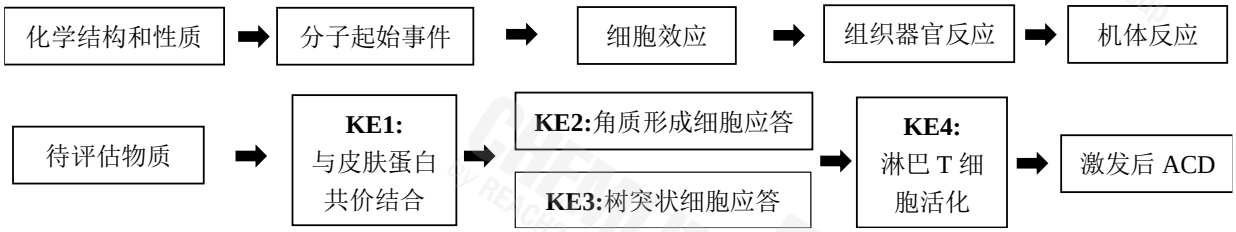

图1 皮肤致敏AOP示意图

在皮肤致敏性AOP中，关键事件KE1为分子起始事件，关键事件KE2和KE3分别为角质形成细胞免疫应答和树突状细胞免疫应答，关键事件KE4为组织器官免疫应答反应（淋巴T细胞增殖）。

二、适用范围

本应用指南适用于化妆品原料皮肤致敏性评价。采用皮肤致敏性AOP检测关键事件KE1～KE3的毒理学试验方法组成“3选2试验”策略，其适用范围应符合所选所有试验方法适用性的要求。

三、基本原则

结合化妆品原料的特点，基于皮肤致敏AOP的机制，形成固定的逐步获取和评估检测数据的顺序测试策略，根据所获得的检测结果决定是否需要开展后续检测，可对化妆品原料皮肤致敏性进行危害识别。在策略中应说明覆盖了AOP中哪些关键事件、试验方法的选择顺序、对已知不确定性的考虑（如所选试验方法局限性、阳性结果判定的阈值边界范围等）内容。

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