Skin Sensitization Assessment for 2,575 Chemicals Evaluated Based on Extraction Testing of Consumer Products

**BACKGROUND**
For approximately 10 years, we have been evaluating various types of products to assess the potential for exposures during use (e.g., wear) to cause adverse skin reactions and, in particular, allergic contact dermatitis. Here, we summarize our assessment of skin sensitization risk for 2,575 chemicals leached from a wide range of products and draw conclusions about the extent of skin sensitization risk in such products.

Allergic contact dermatitis (also called skin sensitization) is an immune system response that can result from dermal exposure to natural and synthetic chemicals. Once sensitized to a chemical, even very small exposures can elicit a dermal reaction, a chronic susceptibility that may last for years if not a lifetime. Chemicals in skin-contacting consumer products, such as apparel, may leach during wear and provoke such reactions in sensitive individuals. Notable episodes of skin sensitization reactions from consumer products have occurred in the past few years and have been widely discussed via social media. As a result, such concerns have the attention of regulators and members of the general public. The goal of our research is to:

1. Identify chemicals with skin sensitization potential;
2. Assign each chemical an exposure threshold, also called a point of departure (POD), above which sensitization may occur; and
3. Provide product- or material-specific acceptable exposure limits (AELs) for the individual chemical components of those products and materials.

**DESIGN/METHODS**

**Chemical Extraction and Identification**
Chemicals were extracted from consumer products or raw materials incubated in a simulated sweat solution at 37 °C for 8 hours. Extractions and chemical identification were conducted by third-party analytical testing laboratories that used gas and liquid chromatography coupled to mass spectrometry to identify chemicals.

**Sensitization Hazard Assessment**
Chemicals were classified as skin sensitizers or non-sensitizers by a weight-of-evidence approach using experimental data, case reports, and computational predictions of sensitization hazard. For each chemical, public databases (e.g., European Chemicals Agency, National Toxicology Program, and Cosmetic Ingredient Review) were searched for experimental data. Examples of the experimental data used for hazard assessment include the results of the guinea pig maximization test, guinea pig Buehler assay, mouse local lymph node assay (LLNA), and human patch test studies. Computational toxicology programs used included ToxTree and/or Derek Nexus™. Based on the results of the review, the threshold for causing such effects was identified in units of μg chemical per cm² of skin contact area. The skin sensitization potency of each chemical was then categorized as strong (effect level ≤ 25 μg/cm²), moderate (between 25 and 250 μg/cm²), or weak (> 250 μg/cm²). A degree of confidence in the assessment was also assigned based on the quality of data available for evaluation. Finally, appropriate assessment (i.e., uncertainty) factors were used to translate the skin sensitization threshold to an AEL (also in μg/cm²).

**RESULTS**
A minority (37%) of chemicals evaluated were classified as skin sensitizers, while 63% were classified as non-sensitizers (Figure 1). Of skin sensitizers, only 7% were classified as strong sensitizers, which could constitute the greatest potential risk for consumers (Figure 2). High quality, specific experimental data were identified for 42% of the chemicals, resulting in a confidence rating of good, whereas limited data, requiring the use of surrogates and computational toxicology predictions, account for 58% of the chemicals. The distribution of thresholds/PODs for causing skin sensitization is shown in Figure 3 based on confidence rating. The two ranges clearly overlap. In addition, the median POD of the sensitizers with “good” confidence ratings was 787 μg/cm², whereas that for skin sensitizers with “limited” confidence ratings was 750 μg/cm², suggesting the level of data available for review did not significantly affect potency estimates.

**Table 1: Strong Skin Sensitizers Commonly Found in the Products Evaluated Above AELs**

<table>
<thead>
<tr>
<th>Chemical (Chemical Abstract Service No.)</th>
<th>AEL (μg/cm²)</th>
<th>Typical Source in Consumer Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Chloro-2-methyl-3(2H)-isothiazoline (26172-55-4)</td>
<td>0.02</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>Dipentaerythritol hexaacrylate (29570-58-9)</td>
<td>0.28</td>
<td>Adhesives or coatings</td>
</tr>
<tr>
<td>Dipentaerythritol pentaacrylate (60506-81-2)</td>
<td>0.28</td>
<td>Adhesives or coatings</td>
</tr>
<tr>
<td>2-Z(Ethoxycarbonyl) ethyl acrylate (7328-17-8)</td>
<td>0.87</td>
<td>Adhesives or coatings</td>
</tr>
<tr>
<td>5-Chloro-2,4-dinitrophenylamine (3013-86-3)</td>
<td>0.083</td>
<td>Pigment impurity</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**
- We conclude that the majority of the simulated sweat leachable chemicals evaluated do not pose significant skin sensitization risk.
- We identified only a few strong potency sensitizers as priority for monitoring. Lower potency sensitizers may still be a concern if the exposure concentration is sufficient.
- Skin health effects, such as sensitization, are a health concern of increasing concern to regulators and consumers. The work outlined in this poster demonstrates how such problems can be evaluated and how these risks can be managed.