30th September 2022

Call for evidence on the skin sensitization in consumer mixtures

Being a cross-sector association with member companies operating in different industries and stages in the supply chain, JBCE welcomes the opportunity to contribute to the call for evidence on the skin sensitization in consumer mixtures[1].

1. Introduction

Chemical substances enrich human life by being properly used with clear understandings. JBCE strongly supports the concepts and objectives of EU REACH and CLP to contribute to human health and the environment. JBCE also believes that risk management approaches should properly address the use of chemical substances. Although the following might not be a direct information for Call for Evidence, JBCE would like to share our views and insights on skin sensitizing chemicals substances, their use in mixtures and the regulation thereof.

2. Details

(i) Substances and mixtures

As a principle, chemicals and/or mixtures which react with thiol groups (-SH) of cysteine and/or amino groups (-NH_2) of lysine in proteins could show skin sensitization. For example, reactive monomers used for various polymers (e.g. acrylates, acrylamides, epoxides, isocyanates, aldehydes, etc.), reductant and color dye formation agents (hydroquinone, phenylenediamine), metal (e.g. nickel, copper,)[2]. Many functions cannot be achieved without the chemical reactivity of these groups, both for consumer and professional applications. These chemicals are broadly used as raw materials and products in both consumer and professional applications; functional resins, glues, adhesives, fragrances, dyes for inks, ion exchange materials, antiseptic reagents, antioxidants, dispersants and surfactants, UV stabilizers, accessories. Chemicals with these functional substituents are key raw materials for products such as polymers, resins, adhesives, fragrances, dyes, preservatives, antioxidants, oils, moisturizers, surfactants, UV stabilizers, accessories, etc. These products contribute to enrich human life.

In general, chemical substances are rarely used alone. Instead, most are used in mixtures. Industrial stakeholders who design, develop, and manufacture chemical products that contain substances do and indeed should investigate the chemical hazards of their products. However, actual hazard assessment of mixtures is not the simple addition of the hazards of its components. Even though a particular ingredient of a mixture might exhibit hazards such as skin irritation (H314), skin corrosion (H315), and skin sensitization (H317) by itself, mixtures containing that ingredient do not always exhibit the same hazard. The GHS classification of mixtures calculated from their ingredients does not always agree with the results of actual evaluation or tests on the mixture. Thus, hazard classification and assessment as mixtures just based on ingredients is sometimes incorrect. Since hazard classifications derived merely from the ingredients of a formulation can overestimate

[1] Call for evidence on skin sensitization in consumer mixtures

[2] The Journal of Toxicological Science, 2019, Volume 44, Issue 12, Pages 821-832.

the actual hazard significantly, it can be important to test the actual mixture for those hazards. In order to evaluate the skin sensitisation of mixtures, ADRA (Amino acid Derivative Reactivity Assay), an alternative test method for skin sensitisation tests, has been developed and adopted in the test guidelines[3] of the Organisation for Economic Co-operation and Development (OECD). Evaluation and confirmation by multiple tests are advisable[4].

We are concerned that an approach to mixtures based solely on the hazards of the individual ingredients, rather than actual risk posed by the mixture will deprive EU industry and citizens of safe and beneficial products.

(ii) Communication, exposures, and risk assessment

For professional and industrial use, exposure and contacting opportunities to skin sensitizing chemicals have been reduced by not only product design but also appropriate communication (labels, technical data sheets), proper equipment (full-controlled exhausting system, local exhausting system), and personal protective equipment (PPE) and clothing. Regarding communications, industrial stakeholders use product labels and safety data sheet (SDS) to inform users. SDSs explain appropriate usage environments, protective equipment (face protection, mask, gloves, protective clothing, etc). The user can handle a chemical product appropriately based on the information on the label and/or SDS.

Even though some of foods also exhibit sensitization (soybeans, peanuts, milk, wheat, eggs), we do not consider depriving all EU citizens of these foods. Instead, we make sure that information is available. The degree of sensitization varies by person. Consider the impact of handling a small amount of a highly hazardous substance with proper equipment versus, and large amounts of a less hazardous substance with inappropriate equipment and conditions. The latter would be more dangerous and higher risk for people. We believe that appropriate communication by labels, explanation sheets, and education will be more important for ensuring human health even in consumer applications.

(iii) Balancing function and minimum concentration

Reactive, and potentially sensitizing, substances are used in products to perform some key function. When we consider the concentration of such substances, it is important to consider the mechanism how skin sensitization occurs and starts. Skin sensitization is an allergic reaction caused by exposure of the skin to a chemical substance. Skin sensitization is caused by the immune system remembering chemicals as external substances. As the chemical exposed to human again, human body could show excessive reactions like erythema (redness), and edema (swelling) as symptoms. Since this is mediated by the immune system, there is a complex process from exposure of the skin to a sensitizing agent to the appearance of symptoms. OECD defines the following four key steps: i) binding of protein and sensitizer, ii) activation of keratinocytes, iii) activation of dendritic cells, iv) proliferation of T cells[5].

The expression of skin sensitization begins with the formation of a complex by the binding between a sensitizing substances and protein. This reaction occurs by covalent bonding with thiol group (-SH) of cysteine and/or amino groups ($-NH_2$) of lysine in proteins. Industrial stakeholders have been developing new products with understanding the principles of what mechanism causes skin sensitization and predicting future potential risks, not limited to substances that are already classified as sensitizers in Annex VI of the CLP regulation, but also other potential sensitizers.

---

[3] OECD Test Guideline No. 442C In Chemico Skin Sensitisation

[4] *OECD Series on Testing and Assessment*, 168, 1 (2014).

[5] J Chem Inf Comput Sci. 1994 Jan-Feb;34(1):154-61

Industrial stakeholders diligently evaluate both performances and risks to determine the maximum concentration required for function, while minimizing the amount of potential skin sensitizing substances in their products. However, it is not possible to eliminate the potential skin sensitizers because skin sensitization is the chemical reaction with human skin proteins. For example, the anti-oxidation and/or antiseptic function in the products is important in terms of hygiene and longer product life.

If the concentration of a functional substance will be below the limit concentration needed for performance, the mixture will not be able to perform its intended function. It is of concern that eliminating important functions will cause other problems. (e.g. insufficient stability for products delivered to remote areas, etc.). Careful attention should be paid to prevent conflicts with the original purposes (e.g. quality, long life, stable supply, etc.)

(ⅳ) Type of use and Applications

The following products and applications will be relevant: adhesives and glue, plastics, resins and polymerization reagents (including hardeners and cross-linking reagent), carpets, textiles, dyes, inks, toners and printing materials for paintings, office printers, and commercial printers, photographic and printing chemicals, preservatives agent, antioxidant, antiseptic, antimicrobial reagent. Even though sensitizers are used in such products this does it does not mean that these products will cause skin sensitization.

(v) Alternatives, cost, and transition period

Even if it is possible to confirm that one performance of a substitute product is equal to or higher than that of a substitute substance, the performance of the product as a whole must be examined because the function is due to chemical reactions. Alternative technologies typically could take 10 years or more through the process of feasibility research and development, scale-up, manufacturing, performance evaluation by customer, and certification. Considering the product life cycle, including the holding period of spare and repair parts, from the perspective of a circular economy, we believe that a sufficient transition period is necessary for substitution.

3. Conclusion

JBCE supports the risk management approach based on chemical substances and mixtures. Although the use of higher-hazard substances and mixtures should be restricted, a sufficient scientific evaluation and transition period should be taken into account. Regarding allergens and skin sensitizers, it is important to properly inform users rather than simply ban the products. When chemical products are used correctly, EU citizens also benefit from their use.

About JBCE

Created in 1999, the Japan Business Council in Europe (JBCE) is a leading European organisation representing the interests of more than 90 multinational companies of Japanese parentage active in Europe.

Our members operate across a wide range of sectors, including information and communication technology, electronics, chemicals, automotive, machinery, wholesale trade, precision instruments, pharmaceutical, steel, textiles and glass products.

Building a new era of cooperation between the European Union (EU) and Japan is the core of our activities, which we perform under several committees focusing on: Corporate Policy, Corporate Social Responsibility, Digital Innovation, Environment & Energy, Standards and Conformity, and Trade.

About JBCE - JBCE - Japan Business Council in Europe

EU Transparency Register: 68368571120-55

Contact: info@jbce.org