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Deriving an Allowable Exposure Limit for Isobornyl Acrylate for Skin Sensitization in Skin-Contacting Consumer Products

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Isobornyl acrylate ([IBOA]; CAS No. 5888-33-5) is a chemical of concern used widely in medical devices and consumer products that have the potential for skin contact. Recently, there have been numerous reports of individuals with allergic dermal reactions to IBOA-containing adhesives used on continuous glucose monitors (cGM) with direct skin contact. In addition to use as an adhesive, IBOA is found in consumer products, such as thermoplastics and paints. The objective of our research was to derive an allowable exposure limit (AEL) for IBOA in skin-contacting consumer products to protect the average consumer from the skin-sensitizing properties of IBOA. We conducted a literature search to identify experimental studies that provided dose-response data for IBOA skin sensitization, including mouse local lymph node assay (LLNA) data and patch testing of patients using cGMs. For patch-test studies, the concentrations used and the details of the patch-testing system were recorded, so that doses could be expressed in terms of µg/cm^2 – recognized as the relevant dose metric for skin sensitization. The point of departure for each type of study was identified and an AEL was derived in µg/cm^2. Patch test dose-response data were aggregated from several studies and the response rate at each dose was plotted in order to define a no observed response level and minimal observed response level. Based on the available LLNA data, IBOA would be classified as a weak sensitizer (with an AEL greater than 2.6 µg/cm^2). However, concentrations of IBOA found in cGMs responsible for allergic dermal reactions suggest dermal sensitization is possible at a much lower dose than what would be expected based on the results of the LLNA. The results of three chemical characterization studies on cGMs showed IBOA exposure concentrations in product extracts ranging from 0.2 to 6 µg/cm^2. Patch-test studies on cGM users showed dermal reactions to IBOA at concentrations of 0.001% to 0.1%, equivalent to 0.8 µg/cm^2 to 78.7 µg/cm^2. Whether the reactions were induction or elicitation is unclear, although some appeared to follow the time course typical of induction. Because the no-effect concentration of 0.2 µg/cm^2 may be difficult to achieve and represent worst-case exposure conditions, we also identified a minimal response level of 0.8 µg/cm^2, which appeared to be protective against responses (particularly severe reactions) in the great majority of the individuals studied. From the available data, a concentration of 0.2 µg/cm^2 was identified as the lowest-known concentration of IBOA that elicited allergic dermal reactions among the reported cGM cases. Such an exposure concentration may be difficult to achieve or demonstrate with common testing methodology, particularly when IBOA is present as an adhesive and may have a relatively small surface area. Moreover, due to the differences in the nature of exposure between cGM devices and skin-contacting consumer goods, this AEL was considered to be overly conservative when used for consumer products. cGM adhesives are applied to skin adjacent to where the sensor of the cGM penetrates the skin, affecting the integrity of the skin, whereas consumer goods are in contact with intact skin. It is also unknown whether the exposures in the cGM cases represented induction or elicitation of skin sensitization. Notably, a far less restrictive AEL of 2.6 µg/cm^2 can be derived from the LLNA study data, which is the standard approach used for most chemicals. However, due to the substantial number of cases of allergic reaction occurring in cGM patients at exposure concentrations below the LLNA-derived value, it may not be protective enough for some consumer goods with long contact times or those that may come into contact with damaged skin. Therefore, an alternative AEL of 0.8 µg/cm^2 was derived that would be protective for the substantial majority of patch-tested cGM users. While this AEL may still be considered conservative for most consumer products in contact with intact skin, it is considered protective for induction of skin sensitization and likely protective of elicitation of skin sensitization in the average consumer.