Retrospective Analysis of Dermal Absorption Triple Pack Data

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Prior to registration and sale, agrochemicals must be characterized for potential risks associated with exposure through all possible routes, including the dermal route. Dermal toxicity is primarily driven by the ability of a substance to penetrate the skin and subsequently pass into the systemic circulation. An estimate of dermal absorption is possible using the "triple pack", a study design that combines results from in vivo rat, in vitro rat, and in vitro human studies to calculate an estimated human dermal absorption factor (DAF). To assess the feasibility of deriving a DAF using only in vitro data, we conducted a retrospective evaluation to compare the DAF derived from each of the three methods (rat in vivo, rat in vitro, and human in vitro). Additionally, the DAF derived from the human in vitro study was compared to the DAF generated from the triple pack approach. In over 70% of the 30 agrochemicals evaluated, the ratio of in vitro to in vivo absorbance in rat skin was greater than one, indicating that the in vitro rat method generated a similar or higher DAF value than the in vivo method. Consistent with other studies that have demonstrated greater permeability of rat skin compared to human skin, absorption through in vitro human skin was similar to or less than that observed in rat skin for all 30 agrochemical formulations evaluated. For most of the chemicals evaluated, the human in vitro method provided a similar or higher estimate of dermal absorption than the triple pack approach. In cases where the human in vitro method provided a lower DAF value, most were within less than 1% to 4% of the values obtained from the triple pack approach, indicating the human in vitro and triple pack approach provided similar estimates of dermal penetration in these cases.

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