

Effect of Topical Anesthetic Pre-treatment on *In Vivo* Ocular Irritation Hazard

Classification

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The ocular irritation or corrosion potential of substances to which humans may be exposed has been evaluated since 1944 using the Draize rabbit eye test. Due to the potential for pain and distress that may occur in rabbits after application of a severely irritating or corrosive substance, alternative approaches have been proposed and developed to reduce the number of such substances that require animal testing (e.g., a weight-of-evidence approach, use of topical ocular anesthetics prior to test substance administration). This evaluation focuses on the effect of topical application of 0.5% (w/v) tetracaine hydrochloride on the irritancy potential of 97 proprietary formulations, tested in 339 rabbits, evaluated using a sequential testing scheme. In this testing scheme, the first rabbit did not receive topical anesthetic pre-treatment. If a rabbit appeared to exhibit pain or suffering after formulation administration, subsequent rabbits were pre-treated with the topical anesthetic. For all formulations, the final rabbit tested was pre-treated with the topical anesthetic. Irritancy classifications were assigned to each rabbit according to three regulatory hazard classification systems (i.e., EU, EPA, GHS). Although none of the observed differences were statistically significant, rabbits pre-treated with anesthesia appeared to produce slightly more severe responses for all three hazard classification systems than rabbits that were not pre-treated. Further, studies indicated that anesthetic pre-treatment had no impact on the variability of rabbit irritancy classifications for the same formulation. Finally, analyses indicated that anesthetic pre-treatment did not significantly increase the number of days needed for opacity, iris, or conjunctival lesions to fully reverse. Combined, these findings support the routine use of 0.5% (w/v) tetracaine hydrochloride as a pre-treatment in the *in vivo* Draize rabbit eye test. ILS, Inc. staff supported by NIEHS contract N01-ES-35504.

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