ICCVAM Test Method Recommendations for the Reduced LLNA (rLLNA)

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In 1999, U.S. regulatory agencies that require submission of skin sensitization data accepted the LLNA as an alternative to guinea pig tests for assessing skin sensitization potential. In 2007, the U.S. Consumer Product Safety Commission requested ICCVAM to assess the usefulness and limitations of the rLLNA. In the rLLNA, the test substance is tested at the maximum testable dose level only, instead of a minimum of three dose levels used in the traditional LLNA. A retrospective review was conducted of data from 471 traditional LLNA studies (457 unique substances) obtained from 11 sources. Compared to the traditional LLNA, the rLLNA has an accuracy of 99% (465/471), a false positive rate of 0% (0/153), and a false negative rate of 2% (6/318). Based on these data, ICCVAM concluded that the rLLNA is sufficiently accurate to distinguish between skin sensitizers and nonsensitizers. ICCVAM recommended routine use of the rLLNA for determining the sensitization potential of chemicals and products, when dose response information is not needed. ICCVAM recommended a standardized rLLNA protocol, future studies to improve the usefulness and applicability of the rLLNA, and the evaluation of modified rLLNA test methods with LLNA performance standards. An update to OECD TG 429 has been proposed by ICCVAM to include the rLLNA, which should facilitate international acceptance of this modified protocol. Use of the rLLNA should reduce animal use for skin sensitization testing while supporting the protection of human health. This abstract reflects views of the authors and has not been approved by any agencies.