The Updated ICCVAM Recommended Murine Local Lymph Node Assay (LLNA) Protocol

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In 1999, ICCVAM recommended the LLNA as a valid test method to assess the skin sensitization potential of most substances. ICCVAM concluded that the LLNA provided several advantages compared to guinea pig methods, including elimination of potential pain and distress, use of fewer animals, less time required to perform, and availability of dose-response information. In 2002, the LLNA was adopted by OECD as TG 429, assuring its international acceptance as a test for skin sensitization potential. In March 2008, ICCVAM and NICEATM convened an international independent peer review panel (Panel) on the LLNA to evaluate alternative versions that are not based on radioactivity and new applications. ICCVAM considered the Panel's conclusions and recommendations, comments from SACATM (ICCVAM's advisory committee) and the public, and recommended updates to the protocol. These included: reducing the required number of animals from five to four per group; adding rationale for collection of individual animal data; adding guidance for use of a concurrent positive control group; and adding guidance on evaluating local irritation and systemic toxicity to establish the appropriate highest dose to test. The updated ICCVAM recommended test method protocol for the LLNA has been forwarded to US Federal agencies for their consideration as a standardized protocol for the purposes of skin sensitization hazard classification. A proposal to update OECD TG 429 has been submitted. ILS staff supported by NIEHS contract N01-ES-35504.