

Murine Local Lymph Node Assay (LLNA)

WuXi AppTec is a global leader in providing discovery, testing and manufacturing services for the pharmaceutical, biotechnology and medical device industries. Research-driven and customer-focused, with operations in China and the U.S., WuXi AppTec offers a broad and integrated portfolio of services designed to assist our customers with cost-effective and efficient outsourcing solutions.

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As part of its comprehensive biocompatibility/safety testing services, WuXi AppTec is pleased to offer a recognized alternative to guinea pig sensitization assays.

With advancements in the study of allergic contact sensitization, an alternative method to the frequently used guinea pig sensitization studies was developed. Since 1995, regulatory agencies (EPA and FDA), based on the recommendations of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and ISO 10993-10: 2002(E), have considered the murine local lymph node assay (LLNA) an acceptable method to screen for allergic contact sensitization. With its extensive experience in extract sensitization testing, WuXi AppTec adapted and modified the LLNA for testing of medical devices (extracts). In this assay, the ability of a material to potentially elicit a delayed-type hypersensitivity response is evaluated by the ability to cause mitotic proliferation of lymphocytes within the draining auricular lymph nodes. [Note: If this test is performed on devices containing metal, the possibility exists that the FDA may not accept the data.]

The Standard Assay

The standard assay utilizes three (3) groups of mice – test article, positive control and negative control (n=15 total). Adult female CBA strain mice are treated topically with solutions or extracts applied to the dorsum of the ears bilaterally. The response is compared to appropriate concurrent positive and negative controls. Measurement of the degree of cell proliferation is quantified by incorporation of ³H-thymidine into DNA of replicating lymph node lymphocytes. Interpretation is based on a statistically significant difference in the stimulation index (SI) between the test and negative control groups. Assay performance requires that the positive control's SI be greater than 3.0.

Comparison to Guinea Pig Maximization Sensitization (GPMS)

	GPMS	LLNA
On-Test Time	28 days	6 days
Adjuvant	Yes	No
Dose Response	No	Yes
Induction Phase I	Yes	Yes
Induction Phase II	Yes	No
Challenge Phase	Yes	No
Testing Endpoint	Subjective	Quantitative



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