Subject: FR Notice Comments - 72FR27815 - LLNA
Date: Friday, June 15, 2007 1:43 PM

Dear Dr Stokes,

Safepharm Laboratories Ltd., UK (SPL) has conducted Local lymph node assays on behalf of sponsoring companies since 1997. The assays have been conducted on a wide variety of chemicals and chemical preparations. Since August 2002 the use of other animal models for evaluation of skin sensitisation potential for regulatory purposes (e.g. methods that require the use of guinea pigs) has been permissible in the UK only if a valid scientific reason can be provided as to why a LLNA cannot be conducted. In effect, the LLNA is the only method that can be used in the UK for assessment of skin sensitisation potential forregulatory purposes. We therefore support the proposed activities of ICCVAM-NICEATM as detailed in the Federal Register vol. 72, No. 95, p.27815-27817, 17 May 2007 in response to the U.S. CPSC nomination of January 10, 2007.

We have witnessed concerns in some areas of the chemical industry, with regard to the applicability of the LLNA for testing of preparations, mixtures and irritant substances, and also with regard to the fact that the LLNA has not always provided results consistent with existing knowledge of the test substance or related test substances. We do not know if all of these concerns are justified, but they can only serve to reduce confidence in the predictive capability of the assay. This is not desirable when the assay offers significant scientific and animal welfare advantages over guinea pig models for many product types, and in a country where the assay is effectively the only available method for evaluation of skin sensitisation potential for regulatory purposes. An assessment of the applicability domain of the assay in its current form and the use of the assay for testing mixtures, preparations, aqueous solutions, irritant substances and metals is therefore very much welcomed. It seems very appropriate to initiate a review of the current peer-reviewed literature and available data, in order to prepare a comprehensive background review document, conduct a review of the validation status of the LLNA for its various uses and to develop relevant performance standards.

It is noted that at its 26th meeting held on 26-27th April 2007 at the European Centre for the Validation of Alternative Methods (ECVAM), the non-commission members of ECVAM Scientific and Advisory Committee (ESAC) considered the reduced version of the LLNA (rLLNA) to be scientifically validated, but only when used as a screening test to distinguish between sensitisers and non-sensitisers and with due regard to the conditions set forth in the official ESAC statement of 27th April 2007. This statement was based on the outcome of a review of LLNA data for 211 chemicals[1]. The review of existing and newly-provided LLNA data proposed by ICCVAM-NICEATM therefore presents an ideal opportunity to assess further the validity of the rLLNA for screening purposes.

As a contract research organisation, SPL is unable to provide data for review by ICCVAM-NICEATM without the permission of its Sponsors, although we

consider it may be possible to provide a summary of study outcomes, coupled to general product type, should this be of interest to ICCVAMNICEATM.

In conclusion, Safepharm Laboratories Ltd. welcomes the proposed activities of ICCVAM-NICEATM in response to the U.S. CPSC nomination of January 10, 2007, and will be pleased to explore ways in which our experience may be of use in the process.

Yours sincerely,
Robert L. Guest
Head of Alternative and Acute Toxicology
Safepharm Laboratories Ltd.

[1] I Kimber, RJ Dearman, CJ Betts, GF Gerberick, CA Ryan, PS Kern, GY Patlewicz, DA Basketter (2006). The local lymph node assay and skin sensitization: a cut-down screen to reduce animal requirements? Contact Dermatitis 2006: 54:181-185