

## 9.0 Other rLLNA Scientific Reports and Reviews

### 9.1 Reports in the Peer-Reviewed Literature

A search of the terms “reduced LLNA,” “cut-down LLNA,” “limit dose LLNA,” and “limit test LLNA” in the MEDLINE<sup>®</sup>, TOXLINE<sup>®</sup>, and Web of Science<sup>®</sup> search engines through December 2007 produced one relevant published report in addition to that of Kimber et al. (2006). Three related presentations (two posters and one platform) were included in the 2007 SOT Annual Meeting held in Charlotte, NC, from March 25-29. One of the posters (Basketter et al. 2007) and the platform presentation (Basketter 2007) detailed the evaluation that resulted in the Kimber et al. (2006) publication and are therefore not discussed below. The information in the second poster, Chaney et al. (2007), described the impact of reducing the number of animals per dose group on the performance of the rLLNA and is summarized below from the subsequent publication (Ryan et al. 2008; published online ahead of print as Ryan et al. 2007).

#### 9.1.1 Ryan et al. (2008)

Ryan et al. (2008) evaluated the impact of reducing the number of mice (from five animals to two) on the performance characteristics using the rLLNA. Nineteen sensitizing and five non-sensitizing substances were evaluated with 33 sensitizer datasets and eight non-sensitizer data sets.

SI values were determined for all possible two-animal combinations for the control- and high-dose groups. With 10 possible data combinations per experimental group, there were 100 possible sets of four values (two control animals and two high-dose animals) for each data set. The 100 possible SI values, each based on a unique set of four values, were plotted for each data set, and the percentage of combinations that resulted in an  $SI \geq 3$  was calculated. Of the sensitizers evaluated, at least 96% of the combinations yielded an  $SI \geq 3$  for 76% (25/33) of the data sets. Thirteen or fewer percent ( $\leq 13\%$ ) of the possible combinations of non-sensitizers (excluding three data sets for sodium lauryl sulfate) had an  $SI \geq 3$ . For the data sets with threshold SI values (2–4.9), however, 90% or more of the combinations resulted in  $SI \geq 3$  for only 20% (4/20) of the sensitizers. Thirteen of the 20 (65%) sensitizer data sets had less than 75% of the combinations producing  $SI \geq 3$ . The authors concluded that the decreased sensitivity produced by using two mice per group was inappropriate for using the rLLNA to identify skin sensitization hazard.