1. The submitted test method and supporting validation data should have been subjected to a transparent and independent peer review process.

   Validation results have been published academically in a research paper.[3] It has been evaluated by an independent specialist.[1]

2. The data generated by the test method should adequately measure or predict the endpoint of interest. For replacement test methods, the data should show a linkage between the proposed test method and an existing test method, and/or the proposed test method and effects in the target or model species.

   Shows high sensitivity and specificity for control toxins assessed using LLNA, which is the gold standard of toxin tests, and compares favorably with conventional toxin tests. Theoretical basis differs from that of guinea pig maximization test. Functionality equivalent to the internationally-recognized LLNA as an alternative test for immunotoxic skin sensitization.

3. The test method should generate data useful for hazard/risk assessment purposes.

   This test method is useful for hazard assessment.

4. The submitted test method and supporting validation data should adequately cover a spectrum of chemicals and products representative of those administered by the regulatory program or agency for which the test method is proposed, and the applicability and limitations of the test method should be clearly described.

   Covers an adequate spectrum of high-purity chemical substances.

   This test method is useful for sensitization assessment.

   This test method provides functionality equivalent to LLNA in the assessment of sensitizing substances.

   This test method is designed for soluble substances and is not suitable for testing solid substances.

   Sensitization assessment was implemented using 31 substances (participating laboratories).

Assessment of inter-laboratory discrepancies was implemented using 14 substances and has otherwise been performed for an adequate spectrum of substances.

5. The test method should be sufficiently robust (relatively insensitive to minor changes in protocol) and transferable among properly-equipped laboratories with adequately-trained staff.

The protocol must be followed faithfully to obtain accurate results.

Care is required when implementing this test method, since any reduction in the number of doses administered or failure to use sodium lauryl sulfate could result in an increase in false negatives.

This test method is sufficiently robust, as long as time is monitored carefully until system and ATP measurements are made.

This test method is easily transferable.

6. The test method should be both time and cost effective as well as likely to be used in a regulatory context.

In comparison with LLNA and given that no radioisotopes are used, this test method is both more time and cost effective. Also, it is not limited to specific laboratories. Therefore, it is easily used in a regulatory context.

7. Justification should be provided (scientific, ethical, economical) for the new or updated test method in light of existing test methods.

Since no radioisotopes are used, there are no restrictions placed on laboratories or test technicians, and major reductions in the cost of waste disposal and environmental-protection measures provide significant ethical and economic justification.

Since no intravenous injections are made, the test procedure itself is simplified and the suffering of test animals is reduced.

8. This test method should be acceptable for use in regulatory documentation on safety assessment.

This test method is design to assess skin sensitization, which it is capable of detecting on a par with existing LLNA test methods. It is useful in the assessment

of potential skin sensitization by drugs, quasi drugs, cosmetic products, cosmetic ingredients, and chemical substances.

Based on the above, the JaCVAM Regulatory Acceptance Board has determined that correct application in accordance with all precautions stipulated by the LLNA: DA test method for assessing skin-sensitization potency as an alternative to animal testing is a scientifically-valid means of assessing the skin-sensitization potency of chemical substances.