SKIN SENSITIZATION STUDY (MAXIMIZATION METHOD) IN GUINEA PIGS

MPI Research Proposal Number <number> for <sponsor>

STUDY DESIGN:

Range-Finding Screens                                      Main Study

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Control</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intradermal Injection</td>
<td>2</td>
<td>2</td>
<td></td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Topical Patch</td>
<td>2</td>
<td>2</td>
<td>Positive Control</td>
<td>5</td>
<td>5</td>
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<tr>
<td></td>
<td></td>
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<td>Test Group</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
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EXPERIMENTAL DESIGN:

*Range-Finding Screens:* Intradermal injections (0.1 mL) and topical patch applications of the test article and vehicle in various mixtures will be administered to determine the highest concentrations that are well tolerated and cause only mild to moderate irritation. The highest non-irritating concentration will be used for the main study.

*Main Study:* Induction of sensitization will be a two-stage procedure with intradermal injections initially administered, followed a week later by a closed topical patch exposure. Intradermal injections of the test article, vehicle and Freund’s Complete Adjuvant in various mixtures will be administered to the Control and Test Groups. The Positive Control Group will be treated in the same manner as the test group but will receive Hexylcinnamic Aldehyde (HCA, a known mild to moderate sensitizer), Freund’s Complete Adjuvant, and water in various mixtures. One week after the intradermal injections, the topical patch induction will be administered to the Control, Positive Control, and Test Groups. The test article in petrolatum or HCA in mineral oil will be applied to the same skin area as the intradermal injections of the appropriate animals.

Two weeks after the topical patch induction, the challenge exposure will be administered. The test article (or HCA) and vehicle will be administered as a topical patch at a non-irritating concentration to different application sites on the appropriate animals. At 24 and 48 hours after patch removal, the challenge application sites will be scored using a Draize scale. A comparison of the skin reactions elicited in terms of incidence and severity will be made to determine whether the test article induces sensitization.

**OBSERVATIONS:** Twice daily in both phases (mortality/moribundity)

**DERMAL SCORING:** 24 and 48 hours after the patch removal in the challenge phase

**BODY WEIGHTS:** On each day of administration and at termination

**NECROPSY:** None

**STATISTICAL ANALYSIS:** Body weights

**STUDY PRICE:** $ (excluding analytical)

To receive information about this study, please contact: Generaltoxicology@mpiresearch.com or call 269-668-3336