ACUTE PERIVASCULAR IRRITATION STUDY IN RABBITS

MPI Research Proposal Number <Number> for <Sponsor>

STUDY DESIGN:

<table>
<thead>
<tr>
<th>Group</th>
<th>Initial (M or F)</th>
<th>Necropsy and Microscopic Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Control)</td>
<td>6</td>
<td>Day 2</td>
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<tr>
<td>2 (Test Article)</td>
<td>6</td>
<td>Day 15</td>
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DOSING: Once by intravenous injection into the marginal vein in the right ear and once into the perivascular space around the marginal vein in the left ear

OBSERVATIONS (Mortality/moribundity): Twice daily

DETAILED CLINICAL OBSERVATIONS: Daily (at 1, 4 and 24 hour post dose on Day 1; daily thereafter) including scoring of injection sites for vascular irritation and any other signs of local irritation

BODY WEIGHTS: Days 1, 8, and prior to necropsy

NECROPSY: All animals

SLIDE PREPARATION/MICROSCOPIC PATHOLOGY: microscopic examination of ears, injection sites, gross lesions, and tissue masses from all animals

The region of the ear surrounding and containing the blood vessel into which the injection was made will be fixed in 10% neutral buffered formalin (the injection site, point of needle insertion, and end of needle in the vessel will be marked with an indelible ink marker at the time of injection). Both ears from each animal will be saved and examined. The ears will be distinguished and identified as either right or left.

After appropriate fixation, at least 3 sections (~0.5 cm anterior to the point reached by the needle tip; ~1.5 cm anterior to the point reached by the needle tip; and, needle insertion site) of each ear will be taken transversely through the region of the ear surrounding and containing the injected vein.

STATISTICAL ANALYSIS: None

ANALYTICAL: Sample analysis included; Validation will be conducted under a separate study number (additional cost).

STUDY PRICE: $

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