104-WEEK CHRONIC TOXICITY-ONCOGENICITY STUDY IN RATS
OECD 453

MPI Research Proposal Number <Number> for <Sponsor>

STUDY DESIGN:

<table>
<thead>
<tr>
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<th>Main Study</th>
<th>12-Month Satellite</th>
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<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
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<tr>
<td>Vehicle Control</td>
<td>50</td>
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<tr>
<td>Low Dose</td>
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<tr>
<td>Mid Dose</td>
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<tr>
<td>High Dose</td>
<td>50</td>
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<tr>
<td>Sentinels*</td>
<td>20</td>
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* Prior to initiation and after 6, 12, and 18 months on study, a health screen will be conducted on the first 5 surviving males and females (Pneumonia Virus of Mice, Reovirus Type 3, Encephalomyelitis Virus, Sendai Virus, Lymphocytic Choriomeningitis Virus, Kilham Rat Virus, Rat Coronavirus/Sialodacryoadenitis Virus, Mycoplasma Pulmonis, Toolan’s H-1 Virus)

DOSE ROUTE/FREQUENCY: Daily via oral gavage

DOSE PREPARATION: Daily

OBSERVATIONS: Twice daily (mortality/moribundity). In addition, a third evening mortality check will be added beginning Week 53.

DETAILED CLINICAL OBSERVATIONS: Once weekly

BODY WEIGHTS: Weekly for first 13 weeks, monthly thereafter

FOOD CONSUMPTION: Weekly for first 13 weeks, monthly thereafter

OPHTHALMOLOGY: All animals pretest and all survivors prior to terminal sacrifice

CLINICAL PATHOLOGY:
- Hematology at 3, 6, 12, and 18 months and at termination (20/sex)
- Clinical chemistries and urinalysis at 3, 6, 12, and 18 months and at termination (10/sex)

NECROPSY: All animals
- Scheduled necropsies at 12 months for satellite groups and 24 months for main study

SLIDE PREPARATION/MICROSCOPIC PATHOLOGY: All found dead animals and all high dose and control animals (full set of standard tissues); all masses and all lesions; target organs in low and mid dose groups

STATISTICAL ANALYSIS: Standard

ANALYTICAL: Standard

STUDY PRICE: $