

### **(3TX31) P388 Murine Leukemia Resistant To Paclitaxel (Taxol<sup>®</sup>) NSC 125973**

Origin of Tumor Line: Developed at Southern Research Institute, Birmingham, Alabama under contract to the National Cancer Institute. A line of the sensitive P388 leukemia was injected i.p. daily for five (5) days with 15 mg/kg/inj of paclitaxel for three (3) generations and then every other generation for a total of eight (8) treatment generations. Resistance was noted at the fourteenth (14) transplant generation. This resistance persisted for at least three (3) months without additional injections of paclitaxel.

**Animals:** (refer to protocol 8)

Propagation: CD<sub>2</sub>F<sub>1</sub> mice.

Testing: CD<sub>2</sub>F<sub>1</sub> mice.

Weight: Mice should be within a 3 gm weight range with a minimum weight of 18 gm for males and 17 gm for females.

Sex: One sex is used for all test and control animals in one experiment.

Source: One source, if feasible, for all animals in one experiment. Exceptions to be noted as comments.

**Experiment size:** (refer to Protocol 9)

General testing: Six (6) animals per test group.

Control Groups: Number of control animals varies according to the number of test groups

**TUMOR TRANSFER:** (refer to Protocols 2,5, and 6)

**PROPAGATION**

Suspension: Prepare a suspension of diluted ascitic fluid so that a 0.1 ml portion contains 1x10<sup>6</sup> cells. Prudence dictates that each generation be treated with paclitaxel i.p. days 1-5 at a dose of 15 mg/kg/inj as duration of resistance in an untreated line is unknown.

Time: Day 11-13

Site: Implant i.p. 0.1 ml of suspension containing 1x10<sup>6</sup> cells.

**TESTING**

Suspension: Prepare a suspension of diluted ascitic fluid so that a 0.1 ml portion contains 1x10<sup>6</sup> cells.

Time: Day 11-13.

Site: Implant i.p. 0.1 ml of suspension containing 1x10<sup>6</sup> cells.

**Testing Schedule:** (refer to Protocols 3 and 4)

Day 0: Implant tumor. Run bacterial cultures (refer to Protocol 7). Prepare materials. Record deaths daily.

Day 1: Check cultures. Discard experiment if contaminated. Weigh and randomize animals. Treat as instructed.

Day 2: Recheck cultures. Discard experiment if contaminated.

Day 5: Weigh animals and record. Toxicity day.

Day 7: Control early-death day.

Day 18: Control no-take day.

Day 30: End and evaluate experiment unless otherwise instructed.

**Quality Control:** (refer to Protocol 7)

The acceptable untreated control median survival time is 11-13 days.

**Negative Control:** To insure that the experiment utilized a resistant tumor generation, every experiment should contain one test group injected with 15 mg/kg/inj of paclitaxel i.p. days 1-5.

**Evaluation:** (refer to Protocol 11)

The parameter measured is median survival time. Compute mean animal body weights for Day 1 and Day 5, compute T/C for all test groups with >65% survivors on Day 5. A T/C Value of <86% indicates toxicity. An excessive body weight change difference (test minus control) may also be used in evaluating toxicity.

**Criteria for Activity:**

An initial T/C  $\geq 125$  is considered necessary to demonstrate activity.