SUMMARY

Chromosome Aberration Assay in Chinese Hamster Ovary Cells
Study Number AC10GK.331.BTL (2008)
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Sponsor: Albemarle Corporation, Baton Rouge, LA

2,2'-(1,2-Ethanediyl)bis(4,5,6,7-tetrabromo-1H-isoindole-1,3(2H)-dione) (EBTBP) was tested in the chromosome aberration assay using Chinese hamster ovary (CHO) cells in both the absence and presence of an Aroclor-induced S9 activation system. A preliminary toxicity test was performed to establish the dose range for the chromosome aberration assay. Both preliminary toxicity and definitive chromosome aberration assays were performed using the population doubling method. The study was conducted according to Good Laboratory Practices and according to OPPTS guidelines.

Based on a preliminary toxicity assay, the doses chosen ranged from a) 5 to 100 µg/mL for the non-activated and S9-activated 4-hour exposure groups, and b) 5 to 750 µg/mL for the non-activated 20-hour continuous exposure group. All cells were harvested 20 hours after treatment initiation. Visible precipitate was observed in treatment medium at dose levels ≥ 100 µg/mL. In the non-activated and the S9-activated 4-hour exposure groups, the highest dose level evaluated was 100 µg/mL. The percentage of cells with structural or numerical aberrations in the non-activated and the S9-activated 4-hour exposure groups was not significantly different from the solvent control at any dose level ($p>0.05$, Fisher's Exact test).

The non-activated 20-hour exposure assay was repeated due to inconsistent toxicity as expressed by cell growth inhibition. Dose levels tested were 0, 5, 10, 25, 50, 100, 250, 350, 500 and 750 µg/mL. Visible precipitate was observed in treatment medium at dose levels ≥ 50 µg/mL. Due to excessive mitotic inhibition at dose levels with ≥ 50% reduction in cell growth, selection of doses for microscopic analysis was based on mitotic index, e.g. the lowest dose with at least 50% reduction in mitotic index and two lower doses. The percentage of cells with structural or numerical aberrations in the non-activated 20-hour exposure group was not significantly different from the solvent control at any dose level ($p>0.05$, Fisher's Exact test).

Based on the results of this study, 2,2'-(1,2-Ethanediyl)bis(4,5,6,7-tetrabromo-1H-isoindole-1,3(2H)-dione) did not induce structural or numerical chromosome aberrations in CHO cells in either non-activated and S9-activated test systems.