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DATA EVALUATION RECORD

STUDY TYPE: Mammalian cells in culture: cytogenetics assay in Chinese hamster ovary (CHO) cells: OPPTS 870.5375 [84-2]

DP BARCODE: D243979 SUBMISSION CODE: S538757

P.C. CODE: 129112 TOX. CHEM. NO.: [N/A]

MRID NO.: 44496718

TEST MATERIAL (PURITY): Trifloxystrobin technical (96.4%)

SYNONYM(S): CGA-279202 technical

CITATION: Herter, Th. (1994). Cytogenetic Test on Chinese Hamster Cells *In Vitro*, conducted at the Genetic Toxicology Laboratory of Novartis Crop Protection, AG, Basle (Switzerland), Test No. 943076 (Novartis Nexus Number 499-94), dated December 6, 1994. MRID NO. 44496718. Unpublished.

SPONSOR: Novartis Crop Protection Inc. (Formerly CIBA-GEIGY), Greensboro, N.C.

EXECUTIVE SUMMARY: In an *in vitro* mammalian cytogenetic assay (MRID 44496718), duplicate cultures of Chinese hamster ovary (CHO, clone K1) cells were exposed to trifloxystrobin in dimethylsulfoxide (DMSO) in three separate experiments at concentrations ranging from 0.049 to 3.125 *u*g/mL without mammalian metabolic activation, and from 12.5 to 200 *u*g/mL in the presence of activation provided by the post-mitochondrial supernatant (S9 fraction) of Arochlor 1254-induced male rat liver. Higher concentrations of test article could not be applied due to severe cytotoxicity. Non-activated cultures of trials-1 (0.781-3.125 *u*g/mL) and -2 (0.049-0.195 *u*g/mL), were treated for 18 hours before harvesting, whereas those of trial-3 (also 0.49-0.195 *u*g/mL were treated for 42 hours; activated cultures of all trials were exposed for only 3 hours, followed by a 15-hour recovery in fresh non-test article medium for trials-1 (initially exposed to 12.5-50 *u*g/mL) and -2 (25-100 *u*g/mL), and 39 hours for trial-3 (12.5-50 *u*g/mL). In addition to vehicle controls, additional cultures were exposed to the clastogens mitomycin-C (MC, 0.2 *u*g/mL) and cyclophosphamide (CPA, 20 *u*g/mL), to serve as positive controls for, respectively, the non-activated and activated test series. Two hours prior to harvest (18 or 42 hours), all cultures were treated with Colcemid (to arrest cells in metaphase), followed

by conventional cytological procedures for microscope slide preparation. Two hundred metaphases on coded slides from two cultures per dose (100 per replicate) were scored for the standard array of structural chromatid and chromosome aberrations as well as numerical (genomic) changes (metaphase with greater than 21 centromeres), such as polyploidy and reduplication figures. The incidences of aberrations were subjected to Chi-Square analysis.

The highest concentrations selected for cytogenetic analysis were cytotoxic (20-50% relative viability compared to vehicle controls) as determined by mitotic indices. At none of the concentrations in trials-1 and -2 were significant increases over DMSO controls in chromosome aberrations observed, under either activation on non-activation conditions. In trial-3, a statistically significant ($p<0.01$) increase (3.5% of cells with aberrations) was calculated in activated cultures exposed at the HDT, 50 *u*g/mL; however, this value is not considered biologically relevant since it is compared to a rather low concurrent negative control value (0.5%, whereas aberration incidences of 1.5% to 4.5% were registered in trials-1 and -2), and is also within the laboratory's historical solvent control data base. Hence under the experimental conditions of these repeat trials, there was no evidence of clastogenicity in CHO cells treated up to cytotoxic concentrations.

The study is acceptable, and satisfies the FIFRA Test Guideline 84-2 requirement for cytogenetic (*in vitro* chromosome aberration) data.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

NB: This EPA-generated Executive Summary agrees in major respect with the attached CALEPA's 6/4/98 conclusions of the same study.

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