EPA Reviewer: Irving Mauer, Ph.D. Date: _____
Toxicology Branch 2, Health Effects Division (7509C)
EPA Secondary Reviewer: Ching-Hung Hsu, Ph.D. Date: _____
Toxicology Branch 2, Health Effects Division (7509C)

DATA EVALUATION RECORD

STUDY TYPE: In vivo mammalian cytogenetics - micronucleus assay in the mouse; OPPTS 870.5395 [84-2]

DP BARCODE: D243979 SUBMISSION CODE: S538757

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

MRID NO.: 44496714

TEST MATERIAL (PURITY): Trifloxystrobin (96.4%)

SYNONYMS: CGA 279202

CITATION: Herter, Th. (1995). Micronucleus Test, Mouse, conducted at the Genetic Toxicology laboratories of Novartis Crop Protection AG, Basle (Switzerland), Test No. 943078 (Novartis Nexus Number 771-95), dated February 1, 1995. MRID NO.44496714. Unpublished. Greensboro NC

SPONSOR: Novartis Crop Protection Inc., Greensboro, NC

EXECUTIVE SUMMARY: In an in vivo micronucleus assay (MRID No. 44496714), groups of Tif: MAGF/SPF (Sprague Dawley-derived) mice (5M:5F per group) were administered 20 mL/kg volumes of trifloxystrobin (96.4% active ingredient) in 0.5 % aqueous carboxymethyl cellulose (CMC) by oral gavage at single doses of 1250, 2500 or 5000 mg/kg. In addition to vehicle (CMC) control groups of 5M:5F, a group of 5 M and 5 F was given the mutagen, cyclophosphamide (CPA, 64 mg/kg) in a single oral dose. An additional 3M and 3F were also given 5000 mg/kg test article, to serve as reserves in the event of premature deaths at the high dose. High dose animals and vehicle controls were sacrificed (by CO_2 gas) 16, 24 and 48 hours after dosing; all other groups only at 24 hours. At sacrifice, femoral bone marrow was removed from each animal and prepared by conventional cytological (smear) procedures onto coded microscope slides. Polychromatic erythrocytes (1000 PCE per slide) were scored for the presence of micronuclei (MNPCE), and the ratio of PCE to normochromatic erythrocytes (NCE) among the 1000 cells counted was also determined for each slide. Differences between test and vehicle controls were calculated by Chi-Square ($F=1$; $p < 0.05$).

At no dose or sampling time was a statistically significant increase over CMC controls in MNPCE found in animals treated with trifloxystrobin, and no signs of either clinical or cytotoxicity recorded. By contrast, slides from CPA-treated animals showed a large increase in MNPCE compared to negative controls, again with no reported clinical or recorded (cyto-)toxicity.

Although no evidence was presented that the test material (or its active metabolites) were absorbed from the gastrointestinal tract and transported to the target tissue (bone marrow cells) to produce any effect (cytotoxicity or cytogenetic damage), the study is acceptable for regulatory purposes since the limit dose was applied, and thus satisfies the FIFRA Test Guideline requirement (84-2) for in vivo clastogenicity (mammalian cytogenetic) data.

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

NB: Although this EPA-generated Executive Summary agrees that the overall results of this study were reported correctly in the attached CALEPA "one-liner" dated 6/4/98, the latter does not mention the lack of any evidence that test article reached the target tissue, hence the possibility of any "significant adverse health effect" is moot, and cannot be considered as a definite: "NO"!

triflox.14

SignOff Date:	8/3/99
DP Barcode:	D243979
HED DOC Number:	013599
Toxicology Branch:	TOX2