

US EPA ARCHIVE DOCUMENT

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

MEMORANDUM

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: California Department of Food and Agriculture - EPA
Toxicology review for Bromacil (Tox. Chem No. 111).

FROM: Linda L. Taylor, Ph.D.
Section II, HFAS
HED (TS-769C)

Linda L. Taylor 4/30/89

THRU: K. Clark Swentzel
Acting Section II Head, HFAS
HED (TS-769C)

K. Clark Swentzel 1/31/89

and

Marcia van Gemert, Ph.D.
Acting Chief, Toxicology Branch/HFAS/HED (TS-769C)

Marcia van Gemert 1/3/89

TO: William Burnam, Ph.D.
Acting Division Director
Health Effects Division (TS-769C)

The following responses are provided for each specific deficiency identified by the Medical Toxicology Branch of the California Department of Food and Agriculture:

STUDY TYPE: Combined chronic/oncogenicity; Reference: Two-Year Feeding Study in Charles River CD Rats - Haskell Laboratory, 2/18/66; Sherman, H. and Kaplan, A.M. Appl. Pharm. 34, 189-196 (1975); Pesticide Petition No. 6F0499, MRID 00022077.

Deficiency: inadequate presentation of histopathology, inadequate number of animals, no analysis of diet, no individual clinical observations, animals with tumors not identified, use of formulated product.

EPA Response: This study was considered by the Peer Review Committee (memo dated July 18, 1988) and was considered inadequate and of little use in the weight-of-evidence determination, based on insufficient number of animals and high mortality during the study. The Agency does have data regarding the identity of the animals with tumors. The Peer Review Committee recommended that the rat study be repeated (memo dated July 18, 1988 to Registration Division)

CONCLUSION: EPA has previously determined that this is a data gap.
CORE-GRADE: Changed from Minimum to Supplementary following Peer Review Committee Report (July 13, 1988).

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STUDY TYPE: Chronic dog; Reference: Long-Term Feeding Tests with 5-Bromo-3-sec-butyl-6-methyluracil - Haskell Laboratories, February 18, 1966.

Deficiency: inadequate number of dogs at risk, use of formulated product, no diet analysis, no justification of dose selection and no effects noted at any dose level.

EPA Response: The original Agency review of this study, which was performed in 1966 (prior to any guidelines), also identified deficiencies in this study but considered the study acceptable. Subsequent Agency review (Toxicology Chapter of the Registration Standard) determined that this study was inadequate and listed the chronic dog study as a data gap (EPA Registration Standard for Bromacil, dated September 30, 1982).

CONCLUSION: EPA determined previously (1982) that this is a data gap.
CORE-GRADE: Not applicable (see EPA response above).

STUDY TYPE: Reproduction in rats; Reference: same as above.

Deficiency: inadequate number of animals, no analysis of diet, inadequate histopathology, technical grade not used. only one dose was used and no effects were reported.

EPA Response: The original Agency review of this study was performed in 1966 (prior to guidelines). Although this was not a data gap identified in the EPA Registration Standard on Bromacil in 1982, TB reviewer reclassified this study as Supplementary in presentation of Tox Branch position on Bromacil to the Agency's Peer Review Committee on September 9, 1987. In a personal communication with Dr. Bruce Jaeger (SACE), the Registrant has indicated to the Agency that this study, as well as the rat oncogenic, chronic dog, and mutagenicity studies on Bromacil will be repeated.

CONCLUSION: EPA has determined that this study is a data gap.
CORE-GRADE: Changed to Supplementary.

STUDY TYPE: Mutagenicity; numerous studies listed on pages 5-7 of the SUMMARY OF TOXICOLOGY DATA prepared by the California Department of Food and Agriculture are not re-referenced here.

Deficiency: For the most part, there are no individual data, assay not repeated, dose level used not justified, only summary data available.

EPA Response: Although two mutagenic studies (incorporation into nucleic acid; bacteriophage E. coli) were classified as not acceptable (and remain as such), other studies were available in the published literature, and these were used in the Registration Standard on Bromacil (1982). At that time, published mutagenicity studies were considered in the Agency's review and they were found to adequately address the subject of mutagenic potential of Bromacil. This was not identified as a data gap. Historically, the Agency has not classified individual published studies as acceptable, due to, among other things, the lack of raw data and detailed information on methods. However, in this case a number of published studies were available and were considered along with other data.

CONCLUSION: Mutagenicity data package will be re-evaluated when the Registration Standard is updated.

CORE-GRADE: Unchanged (the two studies that were available for review remain unacceptable).

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

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SUMMARY OF TOXICOLOGY DATA

BROMACIL (HYVAR)

SB 950-020, Tolerance # 210

December 8, 1986
Revised December 9, 1987
Revised June 20, 1988

I. DATA GAP STATUS

Combined (chronic + onco rat): Data gap, inadequate study, possible adverse effect indicated *see Review*

Chronic dog: Data gap, inadequate study, no adverse effect indicated

Onco mouse: No data gap, possible adverse effect.

Repro rat: Data gap, inadequate study, no adverse effect indicated

Terato rat: No data gap, no adverse effect

Terato rabbit: No data gap, no adverse effect

Gene mutation: Data gap, inadequate studies, possible adverse effect indicated *- published data*

Chromosome: Data gap, inadequate studies, no adverse effect indicated

DNA damage: Data gap, inadequate studies, no adverse effect indicated ^L

Neurotox: Not required at this time

Data for Bromacil (SB-020), and its dimethylamine (SB-537), lithium (SB-538) and sodium (SB-539) salts are grouped for evaluation of possible adverse effects in accordance with California Administrative Code Section 6198.5b. Data for Bromacil, but not for its salts, are on file.

Note, Toxicology one-liners are attached
** indicates acceptable study
Bold face indicates possible adverse effect

Toxicology summary for Bromacil prepared 12/8/86 by J. Gee, updated and group summaries prepared 12/9/87 by M. Harnois, revised 6/20/88 by J. Gee.

FILE: T880620

Handwritten notes:
12/10/88
J. Gee
M. Harnois

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II. TOXICOLOGY SUMMARY

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COMBINED (CHRONIC + ONCO) RAT

016 037341 "Long-term Feeding Tests with 5-Bromo-3-sec-butyl-6-methyluracil." (Haskell Lab., 2/18/66). Bromacil, 82.0 to 83.4%, formulated product; fed in the diet to CD rats for 2 years, 36/sex/group, at 0, 50, 250 or 1250 ppm; diet prepared weekly; NOEL = 250 ppm (body weight). Possible adverse effect on thyroid; unacceptable (inadequate presentation of histopathology, inadequate number of animals, no analysis of diet, no individual clinical obs, animals with tumors not identified, use of formulated product.) Not upgradeable. Gee, 1/10/86.
EPA 1-liner: Minimum. NOEL = 250 ppm (0.025%) (weight retardation).

009 3899 "Substitute Chemical Program. Initial Scientific and Minieconomic Review of Bromacil." (USEPA, 1975. Summary of Sherman, H., et al., Report 12-66, EPA Pesticide Petition No. 6F0499, Vol. I (1963). Rats were fed Bromacil (80% wettable powder, 83.0% a.i.) at 0, 50, 250 or 1250 ppm for 2 years; states there appeared to be a dose-related effect on the thyroid with focal light cell hyperplasia and focal follicular cell hyperplasia being slightly more frequent - no data. Not clear if this is the same study as 037341.

005 46353 Summary of 037341 in publication: Sherman, H. and Kaplan, A. M., "Toxicity Studies with 5-Bromo-3-sec-butyl-6-methyluracil," Toxicology and Applied Pharmacology 34: 189-196 (1975).

CHRONIC DOG

016 037340 "Long-term Feeding Tests with 5-Bromo-3-sec-butyl-6-methyluracil." (Haskell Lab, 2/18/66.) Bromacil, 82.0 to 83.4%; fed to 3/sex/group, Beagle dogs (> 1 year of age at start), for 2 years at 0, 50, or 1250 ppm; 1/sex sacrificed after 1 year in high dose group; no adverse effect reported. NOEL > 1250 ppm. Reviewed (Gee, 1/10/86) as unacceptable (inadequate number of dogs at risk, use of formulated product rather than technical with no analysis of diet, no justification of dose selection with no evidence for MTD with no toxic effects on hematology, clinical chemistry or urinalysis changes reported, no ophthalmological exam, all required organs not taken for histology). Review of study (Harnois, 11/5/87 for response to letter, CDFA vol. 021) found study not upgradeable because of the several deficiencies. Gee, 1/10/86.
EPA 1-liner: Acceptable. NOEL = 0.025% (some decline in body weight)

009 3899 Summary of 037340

005 46355 Summary of 037340 in publication: Sherman, H. and Kaplan, A. M., "Toxicity Studies with 5-Bromo-3-sec-butyl-6-methyluracil," Toxicology and Applied Pharmacology 34: 189-196 (1975).

ONCOGENICITY RAT

See under Combined Rat above.

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ONCOGENICITY MOUSE

** 013 to 015 037337 to 037339 "Long-term Feeding Study in Mice with 5-Bromo-3-sec-butyl-6-methyluracil." (Haskell Lab, 12/01/80.) Bromacil, 95%, diet adjusted for purity; fed in the diet to 80/sex/group at 0, 250, 1250 or 5000 ppm for 18 months; LD50 stated as 5,175 mg/kg; diet prepared weekly; chronic NOEL < 250 ppm (amyloid in several organs; atrophy of immune system organs and pancreas; liver, testes and kidney necrosis; lung fibrosis and dust cells and other effects observed in one or both sexes at the lowest dose level). Effects at higher doses included liver cellular hypertrophy and cellular necrosis, testicular atrophy, atrial thrombus, aortic root necrosis. Adverse effects. Oncogenic NOEL = 1250 ppm. (increased liver adenomas + carcinomas in males at high dose). Initially reviewed (Gee, 1/2/86) as unacceptable (no chronic NOEL, autolysis of animals). Review of study (Harnois, 11/5/87; for response to letter, CDFA vol. 021) allowed study to be upgraded to acceptable as an oncogenic study since the chronic effects did not prevent the observation of an oncogenic effect. (Harnois, 11/5/87)
EPA 1-liner: Minimum. NOEL < 250 ppm (testicular abnormalities as focal atrophy of seminiferous tubules. At 5000, increased liver weight and carcinomas were observed.)

004 26469 Summary with no data but sponsor identified liver and testicular effects at mid- and high-doses. Possibly same study as 037337.

REPRODUCTION RAT

016 037342 "Long-term Feeding Tests with 5-Bromo-3-sec-butyl-6-methyluracil." (Haskell Lab, 2/18/66) Bromacil (formulated), 82 to 83.4%; fed in diet to 12/sex/group selected from combined feeding study (see 037341) for F0; 0, or 250 ppm only; NOEL > 0.025% (250 ppm) for reproduction in rats. Unacceptable, not upgradeable (inadequate number of animals, no analysis of diets, inadequate histopathology (not done on parental animals), formulated product rather than technical, one dose only with no evidence of MTD). No adverse effect reported. Gee, 1/10/86.
→ EPA 1-liner: Minimum. No difference than controls (only dose tested - 0.025%).

009 3899 Summary of 037342.

005 46354 Summary of 037342 in publication: Sherman, H. and Kaplan, A. M., "Toxicity Studies with 5-Bromo-3-sec-butyl-6-methyluracil," Toxicology and Applied Pharmacology 34: 189-196 (1975).

The Registrant has indicated that a new rat reproduction study will be conducted (CDFA vol. 021).

TERATOLOGY RAT

** 024 65988 "Teratogenicity Study on INN-976 in Rats." (Haskell Laboratory, Project No. 605-87, 1/5/88) INN-976, 95.1%, was given to mated Cr1:CD BR rats by gavage on days 7-16 of gestation at 0, 20, 75, 200 or 500 mg/kg, 25/group. No adverse effects noted. Maternal NOEL = 20 mg/kg

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(decreased weight gain and food consumption, significant increase in absolute and relative liver weights), Developmental NOEL = 75 mg/kg (increase in fetal variations of the skeleton) Acceptable. Shimer, 4/6/88 and Gee, 6/20/88.

017 037361 "Teratology and Acute Toxicology of Selected Chemical Pesticides by Inhalation." (SRI, 1/78) Bromacil, no purity stated, 10₃ Sprague-Dawley rats per group exposed by inhalation to 0, 38, 78 or 165 mg/m³ for 1-3 hours/day, days 7 through 14 of gestation (doses equivalent to nominal 1.83, 3.75, and 7.92 mg/kg). No adverse effects reported; developmental NOEL > 165 mg/m³, maternal NOEL > 165, reproductive NOEL > 165 (some reduction in average number of caudal ossification centers compared with untreated (no data for vehicle control group)); unacceptable not upgradeable (inadequate number of females, no individual information, no comments on visceral exam, no evidence of maternal toxicity and no justification of dose selection.) Gee, 1/2/86.
EPA 1-liner: Minimum. Teratogenic NOEL > 165 mg/m³, fetotoxic NOEL > 165
Changes in parents were not significant.

TERATOLOGY RABBIT

** 025 65989 "Teratogenicity Study of INN-976 in Rabbits." (Haskell Laboratory, project No. 527-87, 12-18-87) Bromacil, INN-976, Lot # 180-806 3T Batch 31, 95.1%, was given to inseminated New Zealand White rabbits by gavage on days 7-19 of gestation at 0, 30, 100, 300 or 500 mg/kg, 20/group. Maternal NOEL = 100 mg/kg (significant weight losses and reduced food consumption); Developmental NOEL = 100 mg/kg (increased number of resorptions, reduced number of live fetuses). No adverse developmental effects. Acceptable. Shimer, 4/6/88 and Gee, 6/20/88.

017 037343 "Reproduction Study - Rabbits." (Hazleton Labs, 6/14/66) Bromacil (80%) was fed to New Zealand White rabbits at 0, 50 or 250 ppm from day 8 to 16 of gestation, 9 per group. Three or 4 were sacrificed, rest allowed to deliver. No adverse effect reported. Unacceptable, not upgradeable (inadequate number of animals, no mention of visceral exam, 1/3 for skeletal, protocol, dose selection.) Gee, 12/31/85.
EPA 1-liner: Minimum. Fetotoxic, maternal and teratogenic NOEL > 250 ppm (HDT).

009 3899 "Substitute Chemical Program. Initial Scientific and Minieconomic Review of Bromacil." USEPA, 3/75. Summary of study by Hazleton.

005 46351 Summary of 037343 in publication: Sherman, P. and Kaplan, A. M., "Toxicity Studies with 5-Bromo-3-sec-butyl-6-methyluracil," Toxicology and Applied Pharmacology 34: 189-196 (1975).

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MUTAGENICITY, GNMU

Microbial systems

017 037357 "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, 5/77) Escherichia coli WP2; Bromacil, no purity stated, tested at 0, 1, 5, 10, 50, 100, 500 or 1000 ug/plate for trp reversion; number of plates is not given, report states three trials but data are not clear; mouse liver to activate; no increase in reversion rate; unacceptable but possibly upgradeable (no individual data, no evidence assay was repeated, dose range is not justified in terms of cytotoxicity (no data) or solubility.) Gee, 1/2/86.
No EPA 1-liner.

017 037390 "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, 5/77.) Salmonella typhimurium; Bromacil, no purity given, strains TA1535, TA1537, TA1538 and TA100, tested with and without mouse liver activation at 0, 1, 5, 10, 50, 500 or 1000 ug/plate, no increase in reversion rate is reported. Unacceptable, not upgradeable (no individual plate counts, TA98 not included, concentration range not justified by cytotoxicity or solubility, no evidence of a repeat trial, no comment on cytotoxicity.) Gee, 1/2/86.

017 037346 "Survey of Pesticides for Mutagenicity by the Bacterial-plate Assay Method." Publication in Environmental Mutagen Society Newsletter 6: 6-8 (1972). Hyvar X was negative in Salmonella strains. Unacceptable, not upgradeable (summary report only).

017 037352 and 37353 "Absence of Mutagenic Effects of 3- and 6-Alkyl-5-bromouracil Herbicides on a Bacteriophage." Publication: Nature 209: 1241-1242 (1966), J. W. McGahen and C. E. Hoffmann. JR(G), 12/32/85. Negative at 20 ug/ml for mutagenic effect on bacteriophage AP72 of Escherichia coli. Unacceptable, not upgradeable (too low treatment level)
EPA 1-liner: Not adequate. Bromacil - negative mutagen. 5-Bromouracil - mutagenic.

009 3899 "Substitute Chemical Program. Initial Scientific and Minieconomic Review of Bromacil." USEPA, 3/75. Summary of a publication: J. Agr. Food Chem. 20: 649-656 (1972), K. J. Anderson et al. "Evaluation of Herbicides for Possible Mutagenic Activity." Salmonella was tested with negative results.

Also, summary of 037352 - negative.

Also, summary of J. W. McGahen and C. E. Hoffmann, "Action of 5-Bromo-3-sec-butyl-6-methyluracil as Regards Replacement of Thymine in Mouse DNA." Nature 199: 810-811 (1963) - negative.

All studies are unacceptable, not upgradeable (summary data only).

017 45731 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI, 84.) Saccharomyces cerevisiae strain D3 for reverse mutation. Report is missing every other page so study cannot be evaluated. Report states results were negative (No data, Page with reference is missing.). Insufficient data, unacceptable. Gee, 12/8/86.

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Other systems

017 037349 "Mutagenesis Screening of Pesticides: Drosophila." (WARF Institute, Madison, 2/81) Summary. Drosophila males were fed Bromacil, 2000 ppm, and mated for sex-linked recessive lethal assay. More lethals were recorded with Bromacil. Unacceptable. Need full report. Gee, 12/31/86.

017 45728 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI, 1984.) Report is missing every other page. It reports on the results of a number of tests including mouse lymphoma L5178Y mutation assay in which, from the 2 tables included, a positive response was found. The complete report should be submitted. Unacceptable as is. Gee, 12/8/86.

Summary: The possible adverse effect is based on the Drosophila and mouse lymphoma studies.

MUTAGENICITY, CHROMOSOME

- 017 037355 "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, 5/77) Mouse dominant lethal, Bromacil, no purity stated; 20 males/group were fed 0, 1250, 2500 or 5000 mg/kg for 7 weeks, then mated 1:2 for 8 weekly periods; TEM as positive control; no adverse effect reported, NOEL > 5g/kg. Unacceptable (no individual data, no purity of test article, no analysis of diet reported and no food consumption.) LD50 stated as 3.04 g/kg. Possibly upgradeable. Gee, 12/31/85. No EPA 1-liner.

017 037351 "Detection of Chemical Mutagens by the Dominant Lethal Assay in the Mouse." (Childrens Cancer Research Foundation, 1972) Publication: Toxicology and Applied Pharmacology 23: 288 - 325 (1972). Swiss mice; 174 compounds were tested, 7 or 8 per group were injected once i.p. with 150 mg/kg or five times by gavage, then mated over 8 weekly periods to 3 females per week. Negative for Bromacil. Unacceptable (summary data only). Gee, 12/31/85.

017 45729 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI, 1984) Mouse micronucleus test. Report is missing every other page so results cannot be evaluated. Report states results were negative. Insufficient information for evaluation, unacceptable. Gee, 12/8/86.

MUTAGENICITY, DNA/OTHER

017 037356 "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, 5/77) Unscheduled DNA synthesis in WI-38, Bromacil, no purity stated, contact-inhibited cells were exposed to 0, 10^{-7} , 10^{-6} , 10^{-5} , 10^{-4} or 10^{-3} M for 3 hours without activation and 1 hour with mouse liver S9; incorporation of 3 H-thymidine into DNA was measured by liquid scintillation spectrometry of purified DNA; no increase in incorporation was reported; unacceptable but upgradeable (inadequate details on extraction of DNA, amount of DNA recovered, method of correcting CPM to DPM, passage number of WI-38). Gee, 1/2/86.

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017 037359 "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, 5/77) Bacillus subtilis strains H17 and M45; Bromacil, no purity stated; tested at 0 or 1 mg/disk without activation only; no vehicle control and vehicle identity not clear; unacceptable (single concentration and no evidence of more than one plate, no activation included, inadequate details in methods, no purity of test article.) No evidence of cytotoxicity = no test. Gee, 1/2/86.
No EPA 1-liner.

017 037358. "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, 5/77) Escherichia coli strains W3110 and P3478; Bromacil, no purity stated, tested by diffusion test at 0 or 1 mg/disk, no activation only, vehicle control not identified; no evidence for repeat trial or replicates; no difference in growth; unacceptable (single concentration, no activation, no purity of test article, solvent not clear, no repeat.) No evidence of cytotoxicity = no test. Gee, 1/2/86.

017 037360 "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, 5/77) Saccharomyces cerevisiae D₃; Bromacil; no purity stated, tested at 0, 50, 100, 500, 1000 or 5000 ppm for 4 hours; mouse liver S9 for activation; two trials; no consistent increase in recombination reported; unacceptable but possibly upgradeable (no purity of test article, vehicle and number of plates not clear, concentrations not justified.) Gee, 1/2/86.
No EPA 1-liner.

017 037350 "Mutagenesis Screening of Pesticides: Drosophila." WARF Institute, Madison, 2/81. Drosophila melanogaster; Bromacil tested at 2 and 3 ppm for capacity to induce chromosomal rearrangement or non-disjunction as part of a sex-linked recessive lethal test; no adverse effect reported. Unacceptable. Gee, 12/31/85.

017 037347 "Genetic Effects of Herbicides: Induction of Mitotic Gene Conversion in Saccharomyces cerevisiae." (Univ. of Freiburg) Publication: Mutation Res. 22: 111-120 (1974). Bromacil and 31 other pesticides were tested in Saccharomyces cerevisiae D₃ at 1000 ppm for 16 hours with no effect reported. Unacceptable. Gee, 12/31/85.

017 037348 "Pesticide-induced Complete and Partial Chromosome Loss in Screens with Repair-defective Females of Drosophila melanogaster." (Bowling Green State University. Publication: Environmental Mutagenesis 5: 835 - 846 (1983). Bromacil was fed to males at 10,000 ppm in sugar water and tested for complete or partial chromosomal loss. No adverse effects. Unacceptable (summary report, inadequate data). Gee, 12/21/85.

017 45730 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI, 1984.) Sister chromatid exchange in Chinese hamster ovary cells. Report is missing every other page. Unacceptable (pages missing). Table without activation does not show an effect. Insufficient data for evaluation. Gee, 12/8/86.

MUTAGENIC EFFECTS, MISC.

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017 037345 Publication: Waters, M. D. et al., "Study of Pesticide Genotoxicity," in: Fleck, R. A. and Hollaender, A., eds., Genetic Toxicology; An Agricultural Perspective. Plenum Press, NY, NY, 1982, pp. 275 - 326. Summary of a series of in vitro genotoxicity tests conducted at SRI and WARF Institute. Bromacil was one of the herbicides included. A "+" was indicated for mouse lymphoma L5178Y forward mutation assay for TK+/- cells (presumably 45728) and for Drosophila sex-linked recessive lethal test (presumably the same as 037349). A "-" was indicated for Salmonella and E. coli mutation assays and for Saccharomyces mutation test, for E. coli pol A and B. subtilis DNA and Salmonella typhimurium differential growth, for Saccharomyces mitotic recombination crossing-over, for unscheduled DNA synthesis in WI-38 cells, for sister chromatid exchange in Chinese hamster cells, for mouse micronucleus test and for mouse dominant lethal test. The review discusses the fact that the initial battery with Bromacil was negative and that the mouse lymphoma test was performed only after the positive finding with Drosophila. The authors suggest that it may be a gene mutagen in eukaryotic systems and not cause chromosomal damage.

NEUROTOXICITY

Not required at this time.

RS EPA 025 data - mutagenicity

05013518

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one line - 00013309 - NTA separate

05016657

05014905

05004007

also NTA incor into nucleic acids - acceptable

4-12-83