11-18-88

007760

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: Benefin, Toxicology Chapter of the Registration Standard

To: Chuck Kent, Chief
Registration Branch
Special Review and Reregistration Division

From: John H.S. Chen, D.V.M. 11/18/88
Microbiologist
Review Section I
Toxicology Branch-HFAS
Health Effects Division (TS-769)

Thru: Robert P. Zendzian, Ph.D. 11/18/88
Toxicology Registration Standard Coordinator
Health Effects Division (TS-769)

Albin Kocaialski, Ph.D., Head
Registration Standards and Special Review Section AGK 11/15/88

William Burnam, Acting Director
Health Effects Division (TS-769) 11/18/88

Attached is the Toxicology Chapter of the Registration standard for Benefin. The following portions of this chapter are available. You may obtain a copy from this reviewer.

A. Toxicology Summary
B. Toxicology Profile
C. Data Gaps
D. ADI Reassessment
E. Toxicological Issues
F. Toxicology Summary Tables
H. One Liners

cc: Kocaialski
Zendzian
Coberly

1879

007760

Toxicology Chapter

of the

Benefin

Registration Standard

Prepared by

John H.S. Chan, D.V.M.
Microbiologist
Review Section I
Toxicology Branch II
Health Effects Division

7

TABLE OF CONTENTS

007760

A. Toxicology Summary

Benefin is a preemergent herbicide (N-butyl-N-ethyl-Alpha, Alpha, Alpha-trifluoro-2,6-dinitro-P-toluidine). Benefin is registered for uses on terrestrial non-food crops (i.e., tobacco, ornamental plants, forest trees. and turfgrasses) and may be applied to terrestrial food such as alfafa, clover, lettuce, and peanuts.

Benefin possesses a low order of acute oral, and inhalation toxicity to mammals (category IV and III, respectively). However, no data are available on the ability of benefin to produce acute dermal, primary eye irritation, and primary dermal irritation. A delayed neurotoxicity study is not required for benefin.

Available subchronic oral dosing studies with benefin are not adequate for assessment of subchronic toxicity. No acceptable subchronic dermal study (21-day) is available. This study is required for benefin. A subchronic inhalation study (90-day) will be required if residues of benefin occur in dried tobacco.

Available chronic feeding studies with benefin in rats or dogs, and oncogenicity studies in rats and mice are not adequate for assessment of chronic toxicity and oncogenicity in the rodent and the non-rodent. Chronic toxicity studies in rats and dogs and oncogenic studies in rats and mice are required for benefin.

Available teratology study with benefin in the rat is adequate for assessment of teratogenicity. In this study, the NOEL for maternal toxicity was established at 225 mg/kg/day. The developmental toxicity was established at 1000 mg/kg/day (HDT). The teratology study with benefin in the rabbit was not conducted in accordance with the method recommended by the Pesticide Assessment Guidelines Hazard Evaluation Series 83-2, therefore, a teratology study in the rabbit is required to satisfy this requirement.

Available reproduction study in the rat is not adequate for assessment of reproductive toxicity. A reproductive study in the rat is required for benefin.

Sufficient data are available to satisfy the data requirement for mutagenicity study in the categories of gene mutation and other genetic effects (DNA). In a Salmonella/Mammalian Microsome Mutagenicity Test, benefin did not demonstrate mutagenic activity against the Salmonella typhimurium strains TA1535, TA1537, TA1538, TA100, and TA98 in the presence and absence of metabolic activation at the concentrations from 25 to 750 ug/plate. Although the gene mutation study with benefin in the cultured L5178Y mous lymphoma cells is deficient at the present time, the study can be upgraded to acceptable upon receipt of additonal data under non-activation condition. In the rat hepatocyte unscheduled DNA synthesis assay, benefin did not cause DNA damage and inducible repair in this study. However, the in-vivo sister chromatid exchange assay with benefin in Chinese hamsters is unacceptable. A chromosomal aberration study is required for benefin.

No metabolism study is available for benefin.

Temporary tolerance have not yet been established for residues of benefin in or on the terrestrial food crops.

B. Toxicology Profile

81 Series Acute Toxicity

81-1 Acute Oral

Sufficient data are available to show that technical benefin has a low acute oral toxicity to rats (MRID 00024255) The acute oral LD_{50} for rats was greater than 10 g/kg (combined sexes). Toxicity Category IV.

81-2 Acute Dermal

No acceptable acute dermal toxicity is available for technical benefin. A study is required.

81-3 Acute Inhalation

Sufficient data are available to show that a mist of dimethyl formamide containing 5% benefin has no adverse effect in rats following a single uninterrupted exposure by inhalation route (MRID 00024275). The acute inhalation LC_{50} was greater than 1.33 mg/L/1 hr. Toxicity Category III.

81-5 Primary Eye Irritation

No primary eye irritation study is available for benefin. A study is required.

81-6 Dermal Sensitization

Sufficient data are available to show that the technical benefin is not a sensitizing agent in guinea pigs when 5% suspension were administered dermally (MRID 00144283).

81-7 Acute Delayed Neurotoxicity

No acute delayed neurotoxicity study is available for benefin. However, this test is required only for organophosphate compounds which inhibit cholinesterase. Benefin is not an organophosphate, therefore, a study is not required.

5

82 Series Subchronic Toxicity

82-1 Subchronic Oral

No acceptable 90-day feeding study either in the rat or in the dog is available for benefin. This data requirement is waived based on the requirement for chronic studies in two species.

82-2 Subchronic Dermal (21-day)

No acceptable subchronic study is available for benefin. A study is required.

82-3 Subchronic Dermal (90-day)

No 90-day dermal study is available for benefin. However, the study is not required because the existing acceptable end-uses (present use pattern) should not result in repeated skin contact for extended period.

82-4 Subchronic Inhalation

No subchronic inhalation study is available for benefin. A subchronic inhalation (90-day) study will be required if residues occur in dried tobacco.

82-5 Subchronic Neurotoxicity

No data are available on the subchronic neurotoxicity of benefin. Since an acute neurotxicity study is not required and there is no evidence of neurotoxicity in mammalian species, this study is not required.

83 Series Chronic Toxicity

83-1 Chronic Toxicity

Available data are insufficient to satisfy the data requirements for chronic oral toxicity of benefin (MRID 00037675; 00037678). Chronic toxicity studies are required in two species (rodent and nonrodent).

83-2 Oncogenicity

Available data are insufficient to satisfy the data requirements for oncogenicity of benefin (MRID 0037675; 40301901; 41537401). Oncogenicity stduies in the rat and the mouse are required.

83-3 Teratogenicity

Available data are sufficient to satisfy the data requirements for teratogenicity of benefin in the rat only.

In the rat teratology study (MRID 00147535; 40128001; 40410000; 40410001), pregnant rats were fed 0, 50, 225, 475, and 1000 mg/kg/day of benefin on gestation days 6 through 15. There was no evidence of developmental toxicity observed in any of the dosed groups. However, maternal body weight was decreased at 475 mg/kg/day dose group. The developmental toxicity NOEL was established at 1000 mg/kg/day (HDT). The maternal toxicity NOEL was determined to be 225 mg/kg/day.

No acceptable rabbit teratology study is available for benefin. A rabbit teratology study is required.

83-4 Reproduction

Available data are insufficient to satisfy the data requirements for reproductive toxicity of benefin (MRID 00037676). A study is required.

7

84 Series Mutagenicity Testing

Sufficient data are available to satisfy the data requirements for mutagenicity of benefin in the categories of gene mutation and the other genetic effects (DNA).

In the Salmonella/Mammalian-Microsome Mutagenicity Test (MRID 00160863), benefin did not demonstrate mutagenic activity against the Salmonella typhimurium strains TA1535, TA1537, TA1538, TA100, and TA98 in the presence and absence of metabolic activation at the concentrations tested (i.e., activated condition: 25, 50, 100, 200, & 300 ug/plate; non-activated condition: 125, 250, 500, & 750 ug/plate).

In the gene mutation assay in cultured L5178 mouse lymphoma cells, benefin was nonmutagenic in this assay in the presence of metabolic activation at the concentrations tested (i.e., 0.5 through 100 ug/ml). The results obtained under the non-activated condition are incomplete at the present time. However, the study under the non-activated condition can be upgraded upon receipt of additional data (MRID 160866). A new study is not required.

In the rat hepatocyte unscheduled DNA synthesis, benefin was tested from 50 to 1000 ug/ml. Benefin did not cause DNA damage and inducible repair in this assay at the concentrations tested (MRID 00160865).

Available chromosomal aberration study with benefin (MRID 00160864) is unacceptable. A chromosomal aberration study is required.

85 Series Special Studies

85-1 Metabolism

No metabolism study is available for benefin. A study is required.

85-2 Domestic Animal Safety

Studies not required at this time.

85-3 Dermal Absorption

Studies not required at this time.

9

C. Toxicology Data Gaps and Data Requirements

Technical bufefin is registered for uses on non-food crops and may be applied to terrestrial food such as alfafa, clover, lettuce, and peanuts. The following studies are required for these registered uses (i.e. 158.135 Toxicology Data Requirements):

1. Data Requirements:

81-1 Acute Oral Toxicity
81-2 Acute Dermal Toxicity
81-3 Acute Inhalation Toxicity
81-4 Primary Eye Irritation
81-5 Primary Dermal Irritation
81-6 Dermal Sensitization

82-1 Subchronic Oral Toxicity in Two Species
82-2 Subchronic Dermal (21-day)
82-3 Subchronic Dermal (90-day)
82-4 Subchronic Inhalation

83-1 Chronic Toxicity in Two Species
83-2 Oncogenicity in Two Species
83-3 Teratogenicity in Two Species
83-4 Reproduction and Fertility Effects

84-2 Mutagenicity

85-1 Metabolism

2. Data Gaps

Based on this assessment of the toxicology data base, the following guideline toxicology studies have been identified as data gaps and are required:

81-2 Acute Dermal Toxicity
81-4 Primary Eye Irritation
81-5 Primary Dermal Irritation

82-1 Subchronic Toxicity in Two Species *
82-2 Subchronic dermal (21-day)
82-4 Subchronic Inhalation
83-1 Chronic Toxicity in Two Species
83-2 Oncogenicity in Two Species
83-3 Teratogenicity in rabbit
83-4 Reproduction in Rat

84-2 Chromosomal Aberration

85-1 Metabolism

* This data requirement is waived based on the requirement for chronic studies in two species.

9

007760

D. ADI Reassessment

Temporary tolerances have not yet been established for residues of benefin in or on the terrestrial food crops such as alfafa, clover, lettuce, and peanuts.

The Provisional Acceptable Daily Intake (PADI) for benefin is based on a rat teratology study (MRID 00147535; 40128001; 40410001) with a no-observed-effect level of 225 mg/kg/day for maternal toxicity. Utilizing a safety factor of 3000 , the PADI was calculated to be 0.075 mg/kg/day. Since there are no other toxicology data available to support the PADI (PADI of 0.075 mg/kg/day), the proposed PADI for benefin is submitted to Health Effects Division ADI Committee for verification.

E. Toxicological Issues

There were no toxicological issues at this time. The toxicological data gaps must be filled for a complete evaluation.

TABLE A
GENERIC DATA REQUIREMENTS FOR BENEFIN

Data Requirement	Composition 1/	Use Pattern 2/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? 3/
158.135 Toxicology					
Acute Testing:					
81-1 - Acute Oral Toxicity - Rat	TGAI	AB	Yes	00024255	No
81-2 - Acute Dermal Toxicity - Rabbit	TGAI	AB	No		Yes
81-3 - Acute Inhalation Toxicity - Rat	TGAI	AB	Yes	00024275	No
81-4 - Primary Eye Irritation - Rabbit	TGAI	AB	No		Yes
81-5 - Primary Dermal Irritation - Rabbit	TGAI	AB	No		Yes
81-6 - Dermal Sensitization - Guinea pig	TGAI	AB	Yes	00144283	No
81-7 - Acute Delayed Neurotoxicity - Hen	TGAI	AB	No		No 4/

007760

TABLE A
GENERIC DATA REQUIREMENTS FOR BENEFIN

Data Requirement	Composition 1/	Use Pattern 2/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? 3/
158.135 Toxicology (cont'd)					
Subchronic Testing:					
82-1 - 90-day Feeding - Rodent	TGAI	AB	No	00024651	No 5/
Nonrodent	TGAI	AB	No	00024652	No 5/
82-2 - 21-day Dermal - Rabbit	TGAI	AB	No	00160868	Yes
82-3 - 90-day Dermal - Rabbit	TGAI	AB	No		No 6/
82-4 - 90-day Inhalation - Rat	TGAI	AB	No		Yes 7/
82-5 - 90-day Neurotoxicity - Hen	TGAI	AB	No		No 4/

TABLE A
GENERIC DATA REQUIREMENTS FOR BENEFIN

Data Requirement	Composition 1/	Use Pattern 2/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? 3/
158.135 Toxicology (cont'd)					
Chronic Testing:					
83-1 - Chronic Toxicity - Rat	TGAI	AB	No		Yes
Nonrodent (dog)	TGAI	AB	No		Yes
83-2 - Oncogenicity - Rat	TGAI	AB	No		Yes
Mouse	TGAI	AB	No		Yes
83-2 - Teratogenicity - Rat	TGAI	AB	Yes	00147535 40128001 40410001	No
Rabbit	TGAI	AB	No		Yes
83-4 - Reproduction - Rat	TGAI	AB	No		Yes

TABLE A
GENERIC DATA REQUIREMENTS FOR BENEFIN

Data Requirement	Composition 1/	Use Pattern 2/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? 3/
158.135 Toxicology (cont'd)					
Mutagenicity Testing:					
84-2 - Gene Mutation Bacteria	TGAI	AB	Yes	00160863	No
Mammalian Cells (L5178Y)	TGAI	AB	No	00160866	No 9/
84-2 - Chromosomal Aberration	TGAI	AB	No		Yes
84-2 - Other Genetic Effects DNA	TGAI	AB	Yes	00160865	No
Special Testing:					
85-1 - General Metabolism	PAIRA	A	No		Yes
85-2 - Domestic Animal Safety	Choice	HI	No		No 8/
85-3 - Dermal Absorption	Choice	HI	No		No 8/

1/ Composition: Material to be tested is Technical Grade Active Ingredients; PAIRA = Purified Active Ingredient Radiolabelled;
2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Nonfood; C = Aquatic, Food Crop; D = Aquatic, Nonfood; E = Greenhouse, Food Crop; F = Greenhouse, Nonfood; G = Forestery; H = Domestic Outdoor; I = Indoor; IP = Industrial Preservative.
3/ Unless otherwise specified data must be submitted no later than six months after publication of the standard; 82-1 - 12 months; 82-2 - 7 months; 82-4 - 12 months; 83-2 - 42 months; 83-3 - 12 months; 84-2 - 10 months; 85-1 - 14 months.
4/ Because benefin is not an orhanophosphate, a neurotoxicity study is not required on benefin.
5/ This data requirement is waived because chronic studies are required in two species.
6/ This study is not required because the existing acceptable end-uses should not result in repeated human skin contact for extended period.
7/ A subchronic inhalation study will be required if residues occur in dried tobacco.
8/ These studies are not required under the present use conditions.
9/ The study can be upgraded to acceptable upon receipt of incomplete data.

00760

G. Bibliography

00024253 Worth, H.M. et al. (1965) Toxicological studies with N-Butyl-N-Ethyl-Alpha, Alpha, Alpha-Trifluoro-2, 6-Dinitro-P-Toluidine, Benefin. Received 7/16/65 under 1471-55.

00024275 Worth, H.M. (1964) Toxicity Studies on Mice, Dogs, Rats, and Rabbits. Received 10/1/65 under 1471-55.

00024651 Worth, H.M. et al. (1966) Subacute toxicity of benefin to rats. Received 3/15/66 under unknown admin. no.

00024652 Worth, H.M. et al. (1966) Subacute toxicity of benefin to dogs. Received 3/15/66 under unknown admin. no.

00037675 Gibson, W.R. et al. (1973) A study of the effect on rats from ingestion of benefin for two years. Received 8/5/76 under 1471-92.

00037676 Adams, E.R. (1973) A multigeneration rat reproduction study with benefin. Received 8/5/76 under 1471-92.

00037677 Markam, J.K. et al. (1973) A teratology study on benefin in the rabbit. Received 8/5/76 under 1471-92.

00037678 Gibson, W.R. (1973) A two year toxicity study of benefin administered orally to beagles. Received 8/5/76 under 1471-92.

00144283 Mattingly, C. (1984) A guinea pig sensitization study of benefin, compound 54521. Received under unknown admin. no.

00160863 Rexroat, M. (1985) The effect of benefin (EL-100, compound 54521) on the induction of reverse mutations in Salmonella typhimurium.

00160864 Neal, S. (1985) The effect of benefin (EL-110, compound 54521) on the in vivo induction of sister chromatid exchange in bone marrow of Chinese hamsters.

00160865 Hill, L. (1985) The Effect of benefin (EL-110, compound 54521) on the induction of DNA repair synthesis in primary cultures of adult rat hepatocytes.

00160866 Bewsey, B. (1985) The effect of benefin on the induction of forward mutation at the thymidine kinase locus of L5178Y mouse lymphoma cells.

00160868 Brown, G. (1986) Subchronic (21-day) dermal toxicity study in New Zealand white rabbits with technical benefin.

40128001 Elanco Products Co. (1987) Submission of corrected rat teratology data in support of application for registration of benefin.

40301900 Koenig, G. et al. (1987) Gross pathology findings in a two year oncogenic mouse study with benefin. Interim report.

40410000 Elanco Products Co. (1987) Submission of supplemental data for benefin teratology study.

40410001 Byrd, R. (1987) Response to the Environmental Protection Agency review of a rat teratology study with benefin.

40537401 Koenig, G. et al. (1987) Interim report of histopathologic findings in a two-year oncogenic mouse study with benefin (EL-110, compound 54521).

40569101 Koenig, G. (1987) Benefin data call-in chronic toxicology data from a two-year oncogenic mouse study with benefin to support food crop use.

Tox Chem No. 130

Benefin

File Last Updated _____ Current Date 11/15/88

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	Tox Category	Core Grade Doc. No.
Acute Oral LD_{50} - rat; Lilly Tox. Lab.; 7/1965	Benefin 54521	MRID 00024255	LD_{50} > 10 g/kg	IV	Minimum 003481
Acute Oral LD_{50} - mouse; Lilly Tox. Lab.; 7/1965	Benefin 54521	MRID 00024255	LD_{50} > 5 g/kg	IV	Minimum 003481
Acute Inhalation LC_{50}-rat; Lilly Tox. Lab.; 7/24/64	Benefin 54521	MRID 00024275	LC_{50} > 1.33 mg/L	III	Minimum 003481
Dermal Sensitization - guinea pig; Lilly Res. Lab.; RO1184; 3/14/84	Benefin 54521 98.2% Purity	MRID 00144283	Non-sensitizer (female only) Level tested: 5% in ethanol		Guideline 006287
90-day Feeding - rat; Eli Lilly Labs.; RO524; 3/15/66	Benefin 54521	MRID 00024651	NOEL = 5000 ppm LEL = 10000 ppm (retarded growth and inclusion bodies in hepatic cells) Levels tested: 1250, 2500, 5000, 10000, & 20000 ppm		Supplementary 003482
90-day Feeding - dog; Eli Lilly Labs.; D-96-64; 3/15/66	Benefin 54521	MRID 00024652	NOEL = 500 ppm LEL = 2000 ppm (weight loss, decreased food consumption) Levels tested: 500, 2000, & 8000 ppm		Supplementary 003482
21-day Dermal Toxicity - rabbit; Lilly Res. Labs.; RO2185; 1/15/86	Benefin 54521 (Lot No. 231F74; 97.3% Purity)	MRID 00160868	NOEL = 100 mg/kg Dose levels tested: 100, 325, & 1000 mg/kg (incomplete biochemistry determination)		Supplementary
2-year Feeding -dog; Lilly Res. Labs.; 92-65; 8/5/76	Tech. Benefin 95.6% Purity	MRID 00037678	NOEL = not determined Dose levels tested: 5, 25, & 125 mg/kg (incomplete study)		Supplementary

007760

Tox Chem No. Benefin | File Last Updated _____ | Current Date 11/15/88

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	Tox Category	Core Grade Doc. No.
2-year Feeding - mouse; Eli Lilly Labs.; MO2785 & MO2985;	Benefin 54521	MRID 40301900 40537401 40569101	Interim report: Significant, increased incid. of liver nodules in the females of highest dose group was reported. Levels tested: 0, 6, 36, & 180 mg/kg in B6C3F mice.		Supplementary 006336
2-year Feeding and Oncogenicity - rat; Lilly Res. Labs.; R-0295; 8/5/76	Tech. Benefin (Lot No. X-11424, 95.6% Purity)	MRID 00037675	Systemic NOEL = not determined Oncogenic NOEL = not determined (incomplete study) Levels tested: 0, 0.1, & 0.5% benefin in the diet		Supplementary
Teratology - rabbit; Lilly Res. Labs.; R-0-7-68; 4/8/68	Tech. Benefin (Lot No. 858929, 96.8% Purity)	MRID 00037677	Maternal NOEL = not determined Developmental NOEL = not determined Levels tested: 0, 50, & 100 mg/kg		Supplementary
Teratology - rat; Hazleton Labs.; 6180-101; 6/18/85	Benefin 54521 (Lot No. 231FF4, 97.3% Purity)	MRID 00147535	Maternal NOEL = 225 mg/kg Maternal LEL = 475 mg/kg (decre. body wt.) Developmental NOEL = additonal data required Levels tested: 0, 50, 225, 475, & 1000 mg/kg		Supplementary 005443
Teratology - rat; Hazleton Labs.; 6180--101; 113/87	Benefin 54521 (Lot No. 231FF4)	MRID 40410001 40410000 40128001	Developmental NOEL = 1000 mg/kg Levels tested: 0, 50, 225, 475, & 1000 mg/kg		Guideline 006693
3-Generation Reproduction - rat; Lilly Res. Labs.; R-0305	Tech. Benefin (Lot No. X-11424, 95.6% Purity)	MRID 00037676	Reproductive Toxicity NOEL = not determined Parental Toxicity NOEL = not determined Levels tested: 0.1 & 0.5% of benefin		Supplementary

007760

Tox Chem No. 130 Benefin | File Last Updated _____ | Current Date 11/15/88

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	Tox Category	Core Grade Doc. No.
Mutagenicity - Ames test; Lilly Res. Labs.; 850624AMS2598 & 850708 AMS2598	Tech. Benefin Batch No.231EF4 97.3% Purity	MRID 160863	Nonmutagenic to TA1535, TA1537, TA1538, TA100 & TA98 strains of S. typhimurium Levels tested: 25, 50, 100, 200, & 300 ug/plate with S9 mix; 125, 250, 500, & 750 ug/plate without S9 mix		Acceptable
Mutagenicity - UDS in rat hepatocytes; Lilly Res. Labs.; 850716UDS-2598 &850723UDS2598	Tech. Benefin Batch No. 231FF4 97.3% Purity	MRID 00160865	Benefin did not cause DNA damage and inducible renair in the rat hepatocytes Levels tested: 0.5, 1, 5, 10, 50, 100, 500, & 1000 ug/ml		Acceptable
Mutagenicity - Gene mutation in L5178Y Cells Lilly Res. Labs.; 8501612MLA2598 & 850724-MLA2598; 10/29/85	Tech. Benefin; 54521 (Batch No. 231EF4, 97.3% Purity)	MRID 00160866	Nonmutagenic in L5178Y cells either in the presence or absence of S9 mix (Deficiency: inadequate high dose) Levels tested: 5, 10, 15, 20, 25, 30, 35, & 40 ug/ml without S9 mix; 0.5, 1, 10, 20, 40, 60, 80, & 100 ug/ml with S9 mix		Unacceptable
Mutagenicity - SCE in bone marrow of Chinese hamster; Eli Lilly Res. Labs.; 850722SCE2598; 11/7/85	Tech. Benefin 54521 (Batch No. 231EF4, 97.3% Purity)	MRID 00160864	Benefin did not induce sister chromatid exchange in bone marrow of Chinese hamsters Levels tested: 200, 300, 400, & 500 mg/kg (incomplete study)		Unacceptable