

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

THIODICARB

Chemical Code # 002202, Tolerance # 00407  
SB 950 # 289

March 23, 1987  
Revised 3/16/88, 8/19/97, and 11/16/98

I. DATA GAP STATUS

Combined toxicity, rat:	No data gap, possible adverse effect
Chronic toxicity, dog:	No data gap, no adverse effect
Oncogenicity, mouse:	No data gap, possible adverse effects
Reproduction, rat:	No data gap, possible adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, possible adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Not required, but studies submitted, no adverse effect

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Toxicology one-liners are attached.

All record numbers through 163514 (Document No. 407-113) were examined. This includes all studies indexed as of 11/16/98.

\*\* indicates an acceptable study.

**Bold face** indicates a possible adverse effect.

## indicates a study on file but not yet reviewed.

File name: t981116.wpd

Revised by B. Davis, 3/16/88, P. Iyer, 8/19/97, and C. Aldous, 11/16/98.

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

## COMBINED, RAT

**\*\*096 131569, "104 Week Dietary Carcinogenicity Study in Rats"** (C. Atkinson et al, Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 450441, 11 July 1994) and Addendum: "Additional Statistical Analysis and Background Tumor Incidences" (Joe Rieth, Rhone-Poulenc Ag Company, NC 27709, 28 March 1995). Thiodicarb technical with 94.5% purity administered ad libitum in the diet to 50 Sprague-Dawley rats per sex per group at concentrations of 0 (Rat and Mouse modified no. 1 Diet SQC Expanded fine ground supplied by Special Diets Services Ltd., Essex, CM8 3AD), 60, 200, and 900 ppm. Treatment was administered for a minimum of 104 weeks and 10 rats/sex/group were subjected to hematology, clinical chemistry and urinalysis at 79 and 104 weeks. Concurrently 15 animals/sex/group were dosed identically for 52 weeks to investigate hematology, urinalysis and clinical chemistry at Weeks 25 and Weeks 52. Body weight gain was reduced (29% in males and 22% in females) at the high dose with no notable difference in food consumption. Plasma cholinesterase was markedly reduced at weeks 79 and 104 (60% and 74%) in males and at week 104 (49%) in females. RBC cholinesterase was reduced (18%) in males and (35%) in females at week 104. Increased hemosiderosis was noted in males at the high dose group and a higher incidence of extramedullary hematopoiesis was noted at 200 and 900 ppm in males. Systemic NOEL = 200 ppm (reduction in body weight gain and decreases in hematological parameters). The additional statistical analysis provides a logistic regression analysis which takes into account the differential survival observed. Background tumor incidences document that the increased incidence of interstitial cell tumors (benign) of the testes is marginally higher than the range observed. Acceptable (P. Iyer, 8/1/97).

**\*\*016-023, 032 37442-49, 37473 "UC 51762, Dimethyl N,N'-(thiobis[(methylimino) carbonoyloxy]]bis[ethanimidothioate] Chronic Toxicity and Oncogenicity Feeding Study in Fischer 344 Rats"** (3/24/80, Carnegie-Mellon #43-18) Thiodicarb, analytical grade, fed at 0, 0.5, 1.0, 3.0, or 10.0 mg/kg/day for two years; histopathology NOEL = 0.5 mg/kg/day; Possible adverse effect-hepatotoxicity (hyperplasia of hepatocytes, neoplastic nodules) and oncogenicity (hepatocellular carcinoma); Acceptable; Hathaway 6/20/86

047 65634 Letter of 5/29/87 from E. H. Fowler summarizing the histopathological examinations of the liver samples, with tables from the full report. Davis 3/10/88

003 24985 A summary of the full report.

## COMBINED, MOUSE

041, 043 (duplicates) 48678 "Thiodicarb: Oral chronic toxicity and oncogenicity study in mice. Report for 52 weeks observation." (12/84, Institute of Environmental Toxicology, Tokyo) Thiodicarb, Batch 34, Code S80258, 92.5% purity, tested in diet at 0, 30, 150, or 600 ppm with a target of 104 weeks to 92 ICR-JCL mice/sex/group; high mortality attributed to lymphomas in females of the 105 ppm group resulted in aborting the study at 68 weeks; no adverse effect; NOEL > 600 ppm for 52 weeks; incomplete, unacceptable as a combined study since it is an

interim report. Van Way & Davis 3/17/87

### CHRONIC DOG

\*\*039 44293 "One Year Feeding Study in Dogs--Thiodicarb Technical" (Hazleton Laboratories, Inc. #2100-126, 4/16/86) Thiodicarb (91.6%) given in the diet at 0, 164, 487, or 1506 ppm for 52 weeks; NOEL = 487 ppm (12.8 mg/kg for males and 13.8 mg/kg for females) based upon cholinesterase depression and anemia at higher doses. No adverse effect; acceptable. Hathaway 7/7/86

043 48684 A summary of the report. Davis 3/20/87

### ONCOGENICITY STUDIES

General Comments on Oncogenicity: The original CDFA review of the mouse oncogenicity study noted a possible effect of hepatic neoplasia but did not identify it as an adverse effect. The study report dismissed this finding on the grounds that it occurred with the same high frequency in all groups including the control, but did remark that the frequency was much higher than historical levels. Since hepatotoxicity and hepatic oncogenicity were demonstrated in the rat combined study, the possibility remains that the high background frequency has masked oncogenicity of thiodicarb in the mouse. Davis, 3/23/87.

### ONCOGENICITY, MOUSE

\*\***072 127156**, "97 Week Dietary Carcinogenicity Study in Mice with 52 Week Interim Kill" (C.J. Perry, C. Atkinson, et al., Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 439056, 8 Sept, 1993), "Supplementary Subchronic Data and Background Tumor Incidences" (Joe Rieth, Rhone-Poulenc Ag Company, NC 27709, 13 April 1995) in support of the Thiodicarb Mouse Oncogenicity Study. Thiodicarb technical with 96% purity was administered ad libitum in the diet to 50 CD-1 mice per sex per group at concentrations of 0 (Rat and Mouse modified No. 1 Diet SQC Expanded fine ground supplied by Special Diets Services Ltd., Essex, CM8 3AD), 5, 70 and 1000 mg/kg/day. Concurrently 15 animals/sex/group designated as interim kill were dosed identically. This group was investigated for hematology at 51 weeks, and after 52 weeks of dosing blood samples were collected for clinical chemistry and at least 10 animals/sex/group were killed and necropsied. Selected organs were weighed and histopathology of liver, kidneys and lungs conducted. Treatment was administered for a minimum of 97 weeks to animals in both the carcinogenicity and remaining interim kill group. At 52 weeks, body weight gain was reduced (46% in males and 15% in females) for the high dose in the carcinogenicity group and 49% in males and 10% in females for the interim kill group with no notable difference in food consumption. After 97 weeks body weight gain was reduced 67% in males at the high dose with no apparent difference in females. Hematocrit, RBC count and hemoglobin was significantly reduced in the high dose group in both males and females with an increase in MCV, MCH and total bilirubin. Also at the high dose liver and spleen weights were increased in both sexes and kidney weights were increased in females. Additionally, liver masses, hepatocyte hypertrophy, pigmented macrophages and single cell necrosis of hepatocytes were seen at the high dose level with an increased incidence of hepatocellular carcinomas noted in both males (14/50) and females (8/50) when compared with the controls. Increased hemosiderosis of the spleen at the high dose and a higher incidence of extramedullary

hematopoiesis was noted in both sexes at 70 mg/kg/day and the high dose. Systemic NOEL = 5 mg/kg/day. **Possible adverse effect (liver tumors)** Acceptable (P. Iyer, 8/12/97).

100 137762 "A 4 Week Dietary Dose Range Finding Study in Mice" (C. Atkinson et al., Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 450148), 8 March, 1991). Thiodicarb technical with 96% purity (Lot No. DA616) was administered ad libitum in the diet to 10 CD-1 mice/sex/group at concentrations of 0 (Rat and Mouse modified No. 1 Diet SQC Expanded fine ground supplied by Special Diets Services Ltd., Essex, CM8 3AD), 30, 1750, 3500 and 7000 ppm. These dietary levels achieved dosages of 6.2, 346, 734 and 1538 mg/kg/day for males and 8.3, 491, 954 and 2030 mg/kg/day for females. Signs of toxicity such as increased liver and spleen weights were noted at 1750, 3500 and 7000 ppm in both sexes and decreased ovary weights at 7000 ppm in females. Reduced body weight gain and food consumption was noted at the 7000 ppm level (both sexes) with reduced body weight gain in males at 3500 ppm. No effects at 30 ppm were noted in either sex. Also changes in cholinesterase levels were not noted at any level and hence this parameter was not examined in the definitive study.

In another study (also in 100 137762) conducted at the Carnegie-Mellon University, CD-1 mice were exposed to thiodicarb in the feed for 7 days at 0, 15, 45 and 90 mg/kg/day. Other than an increase in kidney weights at 45 and 90 mg/kg/day in males no other effects were noted (pp. 31-32).  
No worksheet (P. Iyer, 9/10/96).

101 141472 "RPA 051762 Oral LD50 in the Mouse" The acute oral toxicity of RPA 051762 (96% thiodicarb, 0.18% methomyl and 3.30% sulfur) was evaluated after a single oral administration to OF1 mice 5/group at 52, 68, 90 and 118 mg/kg body weight in males and 52, 118, 130 and 150 mg/kg body weight in females. Also 5 females/group were administered dose levels of 100, 110, 121 and 133 mg/kg body weight and in a third study 5 females were given 70 mg/kg body weight. Animals were examined for moribundity and mortality approximately 1 hour after dosing and at least once more on Day 1 followed by a twice daily check up for 14 days except on weekends when they were examined once daily. Animals were sacrificed and autopsied after day 14 and LD50 values with confidence intervals were calculated separately for each sex from mortality data using the method of Litchfield and Wilcoxon. All mortalities occurred within few minutes to few hours after test substance administration and the major clinical signs observed were tremors and increased salivation. The oral LD50 values were 73 mg/kg for males with a 95% confidence interval of 55-98 and 79 mg/kg in females with a 95% confidence interval of 62-101. No worksheet (P. Iyer, 9/13/96).

070 122709, "Possible adverse effects of mouse oncogenicity study" 5/13/93, Rhone-Poulenc Ag Company, Research Triangle Park, NC 27709. Preliminary data on the gross- and histopathological analysis of the tissues in mice receiving thiodicarb technical at doses 0, 5, 70 or 1000 mg/kg were submitted for review. Enlarged livers and spleens were observed at the high dose. Histologic findings of nephropathy, papillary degeneration, hydronephrosis, lobular hepatitis and bile duct hyperplasia were limited to the high dose as well. Thymus atrophy was also noted in the high dose group males. At 96 weeks the study was terminated and survival for the high dose group was 44% and 26% for males and females compared to 56% for both sexes in the controls. While it appears that the high dose group may have exceeded the MTD for this compound, the 70 mg/kg dose was too low to detect any effects that were statistically significant. Hence the study design does not help obtain a realistic NOEL.  
No worksheet. (P. Iyer 2/27/96).

024-028 37450-4 "UC 51762, Dimethyl N,N'-(thiobis[(methylimino) carbonoyloxy]]bis[ethanimidothioate] Chronic Oncogenicity Feeding Study in Mice (1/25/80,

Carnegie-Mellon #43-10) Thiodicarb (UC 51762) analytical grade, given at 0, 1, 3, 10 mg/kg/day in a two year feeding study; possible hepatic neoplasia; however, data are insufficient to evaluate, Unacceptable--no purity for the test material; data on measured dose levels not supplied; individual data not supplied for body weights and for clinical observations; no organ weights; no Quality Assurance statement. Hathaway 6/26/86

025 37472 Letter from Fowler, DePass, and Frank to Baron addressing certain issues for this mouse oncogenicity study and for the rat chronic study (record numbers 37442-9, 37473), followed by summary tables for all primary neoplasms of mouse study. Hathaway 6/26/86

046, Parts 1-4 57711 Duplicate of the full report (Record numbers 37450-4, 37472 but with the Pathology Report Appendix rearranged so that the pages are consecutive. Davis 3/10/88

047, Parts 1-20 57474 Laboratory notebook pages for diet preparation, diet consumption, cageside observations, and gross pathology at death. Davis 3/14/88

043 48677 "Analysis of the Comments of the California Environmental Health Specialist On the Chronic Oncogenicity Feeding Study in Mice of UC 51762" A response by the C. S. Weil, the study director. Van Way & Davis 3/16/87

043 48679 "Review and Analysis of Hematology and Clinical Pathology Data from Several Studies on Thiodicarb" Pathco, Inc. evaluation of thiodicarb studies to extrapolate to the two year mouse oncogenicity study. Van Way & Davis 3/17/87

003 24984 A summary of the full report.

066 113668, "Thiodicarb - 104 week dietary carcinogenicity study in mice with 52 week interim kill". Study protocol. Rhone-Poulenc Ag Company, Research Triangle Park, NC 27709. Projected beginning Oct 1990, Carcinogenicity draft report August 1993. (P. Iyer, 2/27/96)

#### REPRODUCTION, RAT

031 37470-1 "UC 51762, Dimethyl N,N'-(thiobis[(methylimino) carbonoyloxy]]bis[ethanimidothioate] Inclusion in the Diet of Rats for Three Generations and Dominant Lethal Mutagenesis Studies" (Carnegie-Mellon Institute of Research, Report #42-65, 7/2/79). Thiodicarb = UC 51762, analytical grade (99+% purity) at 0, 0.5, 1.0, 3.0, or 10.0 mg/kg/day in the diet. No compound-related effects on fertility, gestation, gestation-survival, viability (4-day), 14-day and lactation (21-day) indices. NOEL not identified--no reproductive toxicity at any dose level. Unacceptable, incomplete; dose levels too low, no diet measurements, minimal necropsies and histopathology, no clinical observations. Hathaway 7/7/86

043 48680 Rebuttal of 9/12/86 by R. W. Tyl, Bushy Run Research Center. Van Way & Davis 3/6/87.

003 24982 A summary of the full report. Aldous 7/18/85

066 113669, "Two-Generation Reproduction Study with Thiodicarb Technical in Rats" - Study Protocol. Rhone-Poulenc Ag Company, Research Triangle Park, NC 27709. No worksheet (P. Iyer, 2/27/96).

**\*\*068 071 118138, 122776, 122778**, "Two-Generation Reproduction Study with Thiodicarb Technical in Rats", (Susan M. Henwood, Hazleton Wisconsin, Inc., WI. Report # HWI 6224-166, 9 June 1992). "Extrapolated No-Observed-Effect-Level for the Two-Generation Reproduction Study with Thiodicarb Technical in Rats", (Joseph P. Rieth, Rhone Poulenc Ag. Company, 28 April 1993) and 071 122778, "Statistical Derivation of the No-Observed-Effect-Level (NOEL) For a Two-Generation Rat Reproductive Study on Thiodicarb", prepared by ENVIRON Corporation, VA for Rhone-Poulenc, RTP, N.C. Thiodicarb technical (94.5% purity) administered ad libitum in the diet through 2 generations (1 litter in the first generation and 2 litters in the second) to 28 CrI:CD@BR/VAF/Plus@ rats per sex per group at concentrations of 0 (Purina Certified Rodent Chow@ Meal #5002), 100, 300, and 900 ppm. Treatment began 10 weeks before mating. F0 and F1 parental body weights were reduced 6% to 22% (the effect was most pronounced in males). Decreased pup weights are indicated at 100, 300, and 900 ppm with the decrement being most severe in F2b pups. Marginal plasma cholinesterase inhibition (approximately 30%) was noted for F1 parents. **Decreased pup weight gain was noted as a possible adverse effect.** Decreased viability index at 900 ppm. No effect on reproductive parameters. Parental NOEL = 100 ppm (decreased F0 and F1 body weights). Reproductive LOEL = 100 ppm (reduced pup weight gain). A statistically-based estimate of a NOEL provided a NEEL (No-Expected-Effect-Level) = 81 ppm (males); 80 ppm (females). **Acceptable** (P. Iyer, 8/14/97).

### TERATOLOGY STUDIES

General Comments on Teratology: Acceptable studies in three different species are consistent in showing no teratogenicity of thiodicarb.

### TERATOLOGY, RAT

**\*\*407-113 163514** Tyl, R. W., Marr, M. C., and Myers, C. B., "Developmental toxicity evaluation of Thiodicarb administered by gavage to CD@ (Sprague-Dawley) rats", Research Triangle Institute, 1/28/93. RTI ID No. 65C-5345. Twenty-five rats/group were dosed by gavage with 0, 1, 10, or 30 mg/kg/day Thiodicarb Technical, 94.7% purity, on gestation days 6-15 in a standard teratology study. Maternal NOEL = 1 mg/kg/day (cholinergic signs such as lethargy, tremors; modest body weight decrements). Developmental NOEL = 30 mg/kg/day (HDT). Acceptable, with no adverse effects. Aldous, 11/16/98.

**\*\*029 37457-8** "UC 51762 Teratology Study in Rats" (12/28/79, IRDC). UC 51762 = thiodicarb, technical, no purity given, tested at 0, 10, 20 or 30 mg/kg/day on days 6-19 gestation; NOEL = 10 mg/kg/day (minor malformations and variations); not teratogenic; Acceptable. Hathaway 7/2/86.

003 24979 Range-finding study.

**\*\*029 37455** "UC 51762 Rat Teratology Studies" (6/1/79, Carnegie-Mellon #42-48). UC 51762 = thiodicarb, technical, 99+% purity, tested at 0, 0.5, 1.0, 3.0, or 100.0 mg/kg/day in the diet from days 0-20 and also days 6-15 gestation (2 regimens); fetotoxic and materno-toxic NOEL = 3.0 mg/kg/day (increased mean resorptions/litter at 100 mg/kg/day; not teratogenic). Acceptable. Hathaway 7/2/86

003 24981 Report summary.

#### TERATOLOGY, MOUSE

**\*\*029 37456** "Teratology Study in Mice" (2/26/80, IRDC) UC 51762 = thiodicarb, analytic grade, no purity given, tested at 0, 50, 100, or 200 mg/kg/day on days 6-16 by oral gavage; maternal NOEL = 100 mg/kg (overall); not teratogenic. Study Acceptable, but NOEL's should not be used for risk assessment purposes. Hathaway 7/8/86

029 37459 Pilot teratology study. Hathaway 6/30/86

003 24980 Summary of two range finding studies, one of which is 37459. Aldous 7/18/85

#### TERATOLOGY, RABBIT

**\*\*040 45041** "A Teratology Study in Rabbits with Thiodicarb" (WIL Research Laboratories, Inc., 5/16/86) Thiodicarb (93%) given by gavage on days 6-19 of gestation at 0, 5, 20, or 40 mg/kg/day; Maternal toxicity NOEL = 20 mg/kg/day (decreased weight gain and food consumption for days 6-12). Developmental NOEL > 40 mg/kg/day. No adverse effect; acceptable. Parker 7/2/86

043 48683 Report summary. Davis 3/20/87

051 62660 Two range-finding studies. Davis 3/2/88

#### MUTAGENICITY STUDIES

##### GENE MUTATION

General Comments on Gene Mutation: Three studies have been submitted in this category. The bacterial and yeast studies were both negative, but the mouse lymphoma study was clearly positive both with and without activation. Since that study was done in mammalian cells and since it was found to be acceptable, the overall conclusion is that there is a possible adverse effect.

**\*\*030 37467** "Mutagenicity of Thiodicarb in a Mouse Lymphoma Mutation Assay" (7/85, Litton Bionetics #20989) Thiodicarb, 91.48%; Two trials  $\pm$  rat liver activation, 0 to 12.5 ug/ml (-S9), 0 to 10 ug/ml (+S9) with 4 hour exposure. Select with TFT. Acceptable, complete; Possible adverse effect-An increase in mutation frequency  $\pm$  S9 is reported as concentration increases. Gee 4/28/86

030 37460 "Mutagenicity Evaluation of CHF 41-43 in the Ames Salmonella/ microsome Plate Test - Final Report" (4/78, Litton Bionetics #20838) Thiodicarb, unknown purity; TA 1535, TA 1537, TA 1538, TA 98, and TA 100  $\pm$  rat liver S9 at 0, 1, 10, 100, 500 and 1000 ug/plate, 1 plate/dose, 1 trial. No increase in reversion rate reported; Unacceptable, incomplete; single plates, no confirmatory assay, questionable high dose level, no purity or lot number. [EPA: Core minimum] Gee 4/25/86

003 24971 Incomplete version of the report. Aldous 7/17/85

043 48676 Litton Bionetics rebuttal. Van Way & Davis 3/6/87

030 37463 "UC 51762 Technical: Reverse Mutation *Saccharomyces cerevisiae*" (6/1/79, Pharmakon #PH-303-UC-001-79) Thiodicarb (technical?) no purity given; strain D<sub>7</sub> diploid was exposed for 1 hour to 0.0025, 0.00625, 0.025, 0.0625, or 0.25 mg/ml without activation; no increase in isoleucine-independent colonies in one trial. Incomplete, unacceptable--protocol. Gee 4/28/86

003 24973 Report summary. Aldous 7/17/85

### CHROMOSOMAL ABERRATIONS

General Comments on Chromosome Mutagenicity: Three studies have been submitted and all three are negative. One of the three was acceptable. Hence the data gap is filled and there is no adverse effect.

\*\*030 37466 "Clastogenic Evaluation of 91.48% a.i. Thiodicarb in an in vitro Cytogenetic Assay Measuring Chromosomal Aberration Frequencies in Chinese Hamster Ovary (CHO) Cells" (7/85, Litton Bionetics #20990) CHO cells exposed to Thiodicarb, 91.48%, -S9 for 10 hrs at 0, 10, 15, 20, or 30 ug/ml and + rat liver S9 for 2.0 hrs at 0, 10, 20, 30, or 40 ug/ml; 100 cells/ culture, 2 cultures per concentration; no evidence of increase in aberrations; Complete, acceptable. Gee 4/28/86

031 37469 "UC 51762, Dimethyl N,N'-(thiobis[(methylimino) carbonoyloxy]]bis[ethanimidothioate] Inclusion in the Diet of Rats for Three Generations and Dominant Lethal Mutagenesis Studies" (Carnegie-Mellon Institute of Research, Report #42-65, 7/2/79). Thiodicarb = UC 51762, analytical grade (99+% purity) at 0, 0.5, 1.0, 3.0, or 10.0 mg/kg/day in the diet of F2 males from the reproduction study. Bred to 3 lots of naive females at weekly intervals. No evidence for mutagenicity. Unacceptable, incomplete- dose levels too low, too few pregnant females, no diet measurements, high number of week 1 fetal deaths in both negative control groups, no clinical observations. Hathaway 7/7/86

043 48681 Rebuttal of 9/12/86 by R. W. Tyl, Bushy Run Research Center. Van Way & Davis 3/6/87

003 24983 A summary of the full report. Aldous 7/18/85

030 37462 "Micronucleus Test" (5/22/79, Pharmakon #PH-309-UC-001-79) Thiodicarb technical, unknown purity. 4/sex/group given 2 injections i.p. of 0, 5 or 10 mg/kg, TEM for positive control; sacrificed 6 hours after second injection; no formation of micronuclei in PCE from test article is reported; Incomplete, unacceptable (protocol, lack of information on test material). EPA: Core minimum. Gee 4/25/86

043 48674 Complete report, plus two laboratory notebook pages and two invoices. Van Way & Davis 3/6/87

003 24972 Report summary.

## DNA DAMAGE

General Comments on DNA Mutagenicity: Of the four studies submitted in this category, three were negative and one was positive. The original CDFA review noted that the one positive study, mitotic gene conversion in yeast (Record 37465), had two negative companion studies, reverse gene mutation (Record 37463) and mitotic crossing over (Record 37464), using the same strain, the same time period, and same dose levels. In addition, the positive effect in this study was marginal. For these reasons, the reviewer questioned the biological significance of the results. The present reviewers concur and interpret the overall evidence as showing no adverse effect.

\*\*030 37468 "Evaluation of Thiodicarb in the Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay" (7/85, Litton Bionetics #20991) Thiodicarb, 91.48%, exposed 18 - 19 hours to 0, 0.5, 2.5, 5, 10, 25, 50, 100, or 250 ug/ml with <sup>3</sup>H-TdR incorporated as grains/nucleus; to 24% survival at 23 hours. No increase in grain counts. Acceptable, complete. Gee 4/28/86

030 37461 "Primary DNA Damage-Escherichia coli Plate Test" (5/14/79, Pharmakon #PH-305-AM-002-079) Thiodicarb technical, unknown purity; Bacterial strains W3110 and P3478 ± rat liver S9 at 0.001, 0.01, 0.1, 1.0, and 10.0 mg/ml in DMSO; -S9, 20 ul/8mm disk; +S9, 50 ul/8mm well. No evidence of differential growth between strains. Incomplete, unacceptable-no purity and lot information, doses may not be high enough, no evidence for diffusion. Gee 4/25/86

043 48675 Complete report, plus two laboratory notebook pages. Van Way & Davis 3/6/87  
003 24977 Report summary.

030 37464 "Mitotic Crossing Over--Saccharomyces cerevisiae" (6/1/79, Pharmakon #PH-302-UC-001-079) 844. Thiodicarb technical, no purity given; D<sub>7</sub> diploid strain ade2-40/ade2-119, was exposed for 1 hour in suspension to 0.0025, 0.00625, 0.025, 0.0625, or 0.25 mg/ml without activation; no statistically significant increase in percent twin-sectoring colonies is reported. Incomplete, unacceptable--protocol. Gee 4/28/86

003 24975 Report summary.

**030 37465** "Mitotic Gene Conversion Saccharomyces cerevisiae" (6/1/79, Pharmakon #PH-304-UC-001-79) Thiodicarb technical, no purity given; strain D<sub>7</sub> trp 5-12/trp 5-27 diploid strain plated in 30 per concentration after 1 hour exposure to 0, 0.0025, 0.00625, 0.025, 0.0625, or 0.25 mg/ml without activation; concentration-dependent increase in gene conversion to trp independence. Incomplete--missing data; unacceptable--no activation. Gee 4/28/86

003 24974 Report summary.

## NEUROTOXICOLOGY

General Comments on Neurotoxicology: No studies in this category are required. Four studies were submitted and evaluated by CDFA. One was acceptable. No neurotoxicity is indicated.

003 24976 "Special Studies on Neurotoxicity" (Laboratory and date not stated) Thiodicarb (UC 51762), unknown purity, given at 660 mg/kg to 40 white no Leghorn hens by oral gavage; observed 21 days followed by repeat dosing and observation; no adverse effect-one hen had significant numbers of swollen axons but this was not found in other hens in this or other studies.

Incomplete; unacceptable--summary only. Aldous, 7/18/85

003 24978 "Special Studies on Neurotoxicity" (Laboratory and date not stated) Larvin, unknown purity, given at 660 mg/kg to 30 white Leghorn hens by a single gavage; observed 21 days; no adverse effect. Incomplete; unacceptable--summary only. Aldous, 7/18/85

033 37476 "Acute Delayed Neurotoxicity Study in Hens (EPA-8/78)" (IRDC, 9/2/80) Larvin (UC-51762), analytical grade, unknown purity, given at 660 mg/kg after pretreatment with atropine sulfate to 30 white Leghorn hens by oral gavage; observed 21 days; no adverse effect. Incomplete; unacceptable--no purity or stability information, no dosing material analysis, no statistical analysis, no repeat dose after 21 days. Hathaway, 4/28/86

\*\*034 37477 "Evaluation of UC 51762 #40-488 as a Potential Delayed Neurotoxic Agent Following Oral Administration to Hens Protected by Atropine Sulfate" (Food and Drug Research Laboratories, Inc. 6/14/79) UC 51762 #40-488, unknown purity, given at 660 mg/kg after pretreatment with atropine sulfate to 40 white Leghorn hens by oral gavage; observed 21 days followed by repeat dosing and observation; No adverse effect. Complete, acceptable. Hathaway, 6/5/86