

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Pyridate
Chemical Code # 3939, Tolerance # 52003
SB 950 # N/A

Original: 9/12/94
Revised: 5/1/96

I. DATA GAP STATUS

Combined, rat:	No data gap; no adverse effect
Chronic toxicity, dog:	No data gap; possible adverse effect
Oncogenicity, rat:	See Combined, rat
Oncogenicity, mouse:	No data gap; no adverse effect
Reproduction, rat:	No data gap; no adverse effect
Teratology, rat:	No data gap; no adverse effect
Teratology, rabbit:	No data gap; no adverse effect
Gene mutation:	No data gap; no adverse effect
Chromosome effects:	No data gap; no adverse effect
DNA damage:	No data gap; no adverse effect
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through 143327 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

indicates a study on file but not yet reviewed.

File name: T960501

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

COMBINED, RAT

** 019, 039; 125588, 143323; “Two-Year Feeding Study with Pyridate in Rats (Final Report)” (Til, H.P., et. al., Civo Institutes TNO, Zeist, Netherlands, Report #'s V 83.039/20223, 2/83 and V 89.237, 10/90); Pyridate Technical (CL 11344, Batch 57, 90.3% purity) administered in diet to 75 rats/sex/dose in the diet at 0, 80, 400 or 2500 ppm for 2 years; high mortality were observed in control and mid-dose females without any dose response relationship; significant lower body weights were noted in high dose males from days 7 to 434; gross and microscopic examinations did not indicate any treatment-related abnormality; no evidence of pyridate affecting neoplastic or non-neoplastic lesions was detected; NOEL (M/F) \geq 2500 ppm (no treatment-related effects at HDT); **no adverse effects; Acceptable** (upgraded from unacceptable, Leung, 7/20/94, with food consumption and ophthalmologic exam data). (Miller, 4/5/96)

CHRONIC TOXICITY, DOG

** **020; 125589**; “Chronic Toxicity Study in Dogs with Pyridate Technical” (Bailey, D.E., Hazleton Laboratories America, Inc., Vienna, VA, HLA Study# 2495-100, 5/2/89); 831; pyridate technical (Lot # 2759523, 91.5% purity) administered orally in gelatin capsule to 5 Beagle dogs/sex/dose at 0, 5/10/30, 20/60/80/100, or 60/100/120/140/150 mg/kg/day for 1 year; all initial dose levels were increased as indicated above; No mortality was reported but clinical signs including excessive salivation, ataxia, mydriasis, dyspnea, tremors, increased respiration, and inability to stand were noted in mid and high dose dogs; no treatment-related changes in body weight, food consumption, clinical chemistry, hematology or gross pathology were detected; **possible adverse effect**: histopathology indicated one male dog in the high dose group exhibited degenerative myelopathy of the peripheral (sciatic) nerve; NOEL (M/F)= 80 mg/kg/day (based on incidence of clinical signs); **acceptable**; (Leung, 7/22/94).

ONCOGENICITY, RAT

See Combined, rat

ONCOGENICITY, MOUSE

** 021; 125590; “Oncogenicity Study of Pyridate Administered by Dosed Feed to B₆C₃F₁ Mice11” (Lindamood III, C., et. al., Southern Research Institute, Birmingham, AL, Project ID #

A30-CRM-1, 11/7/91); Pyridate Technical (Batch #s CL 11344/AR-22 and 11344/AR-22, 91.5% purity) administered orally in the diet to 50 mice/sex/dose at 0 (2 groups), 400, 800, 1200/1400/1600, or 7000 ppm for 18 months; pyridate treatment reduced survival in 7000 ppm females (6/100 verses 10/50 for 0 and 7000 ppm, respectively, $p < 0.05$); dose-related reduction in mean body weight without any effect on food consumption was noted in females at 1600 ppm and males and females at 7000 ppm; histopathological examination revealed an increase in the frequency of suppurative inflammation (abscesses) of the ovary in 7000 ppm females; **no adverse effects**; NOEL (M) = 1600 ppm, (F) = 800 ppm (based on reduction in mean body weight); **acceptable**; (Leung, 7/26/94).

REPRODUCTION, RAT

** 24; 125593; "Multigeneration Study with Pyridate in Rats" (Til, H.P., et. al., Civo Institutes TNO; Zeist, Netherlands, Report # V82.235/200696, 8/82); Pyridate Technical (Batch # 57, 90.3% purity) administered in diet to 25 rats/sex/dose at 0, 80, 400 or 2500 ppm for 3 generations; mortalities were reported in 1 control and 1 mid dose female of the F₁ generation and 1 control and 1 low dose female and 2 high dose females of the F₂ generations; **no adverse effects**; body weights were decreased in high dose parental rats in the F₀ and F₁ generations; no treatment-related changes in food consumption, reproduction parameters, hematology, clinical chemistry, gross necropsy and microscopic examination were evident; no malformation at birth was found in any of the pups from any of the three successive generations; parental NOEL = 400 ppm (F₀ and F₁ rats exhibited reduced body weight), reproductive NOEL \geq 2500 ppm (110 mg/kg/day; no signs of toxicity at HDT); **acceptable**; (Leung, 8/12/94).

TERATOLOGY, RAT

** 022; 125591; "Embryotoxicity (including teratogenicity) Study with Pyridate Technical in the Rat" (Nigitz, H.P., Research & Consulting Company AG, Itingen, Switzerland, Project # 055934, 2/28/86); Pyridate Technical (Batch # 2420966, 92% purity) suspended in 4% CMC, was administered by oral intubation once daily to 25-35 pregnant Wistar/Han rats/dose on days 6-15 of gestation at 0, 55, 165, 400 or 495 mg/kg/day; 5/25 and 16/25 pregnant rats from the 400 and 495 mg/kg dose groups, respectively, died during the dosing period; clinical signs including ventral body position, dyspnea, ruffled fur, no reaction to external irritations, and muscle spasms were observed after the first and second treatment; significant decreases in body weight gain and food consumption at two highest dose levels were reported during days 6-11 of gestation; mean body weights of fetuses from the 400 and 495 mg/kg dose groups were slightly reduced and skeletal examination revealed a dose-related increased frequency of either incomplete or lack of ossification of sternebra, phalangeal nuclei, calcanei and vertebra; **no adverse effects**; maternal NOEL = 165 mg/kg/day (unscheduled death), developmental NOEL = 165 mg/kg/day (incomplete or the absence of skeletal ossification); **acceptable**; (Leung, 8/1/94).

TERATOLOGY, RABBIT

** 023, 038; 125592, 143320; “Developmental Toxicity (Embryo/Fetal toxicity and Teratogenic Potential) Study of Pyridate Technical Administered as the Neat Test substance Orally Via Stomach tube to New Zealand White Rabbits” (Hoberman, A.M., Argus Research Laboratories, Inc., Horsham, PA, Project # 512-001, 12/10/87); Pyridate Technical (Batch # 2659427, 93.3% purity) administered neat to 20 artificially inseminated rabbits/dose on days 7-19 of gestation; 0, 150, 300, or 600 mg/kg/day; **no adverse effects indicated**; one control, two low and one high dose pregnant rabbits died as a result of intubation accident; clinical signs included increased incidence of does with dried or absent feces and spontaneous abortions at the high dose level; significant reduction in body weight gain and food consumption was reported at the high dose; fetal external, soft tissue and skeletal evaluations did not demonstrate any malformation or variation that was considered treatment- related; nominal maternal and developmental NOEL = 300 mg/kg/day (based on clinical signs and increased incidence of abortion); **Acceptable** (upgraded from unacceptable, Leung, 8/4/94, with submission of the test article purity data). (Miller, 3/8/96)

GENE MUTATION

025; 125594; “Mutagenicity Evaluation of Pyridate Technical in the Ames Salmonella/Microsome Reverse Mutation Assay” (Hoor, A.J.W., Hazleton Biotechnologies, Netherlands, Assay # E-9550, 9/26/86); Pyridate Technical (Batch # 2556520, 92% purity); tested with Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98, and TA100 in the presence and absence of activation by Aroclor-1254-induced rat liver S9 fraction; triplicate plates; 2 trials; 48 hour incubation; positive controls functional; concentration ranges from 0 (DMS0) to 10000 ug/plate; **no adverse effects; Pyridate Technical did not induce a mutagenic response (increased numbers of revertant colonies); **acceptable**; (Leung, 8/18/94).

CHROMOSOME EFFECTS

** 025; 125595; “Clastogenic Evaluation of Pyridate Technical in an In Vitro Cytogenic Assay measuring Chromosome Aberration Frequencies in Chinese Hamster Ovary (CHO) Cells” (Taalman, R.D.F.M., Hazleton Biotechnologies, Netherlands, Assay # E-9550, 1/87); Pyridate Technical (Batch # 2556520, 92% purity); tested in Chinese Hamster Ovary Cells with and without activation by Aroclor 1254-induced rat liver S9 fraction; 100 cells from each duplicate culture/dose scored for chromosomal aberrations; single trial; Concentrations of 0-50 ug/ml without activation and 0-100 ug/ml with activation; 2- and 9- hour exposure with and without S9 activation, respectively; **no adverse effects**; Pyridate Technical did not induce chromosomal aberrations in the presence or absence of S9 activation; **acceptable**; (Leung, 8/22/94).

DNA DAMAGE

** 025; 125596; “In Vivo - In Vitro Rat Hepatocyte Unscheduled DNA Synthesis Assay” (Curren, R.D., Microbiological Associates, Inc., Rockville, MD, Lab. Study # T8186.381, 8/29/88); Pyridate Technical (Lot # 2759523, 91.5% purity); tested in male Fischer 344 rat hepatocytes; 3 rats/dose; 0 (corn oil), 40, 160, or 800 mg/kg; rats sacrificed at 2-4 and 12-18 hours posttreatment; UDS by autoradiography; 50 cells scored on each of three slides for each rat; positive controls functional; **no adverse effect**; Pyridate Technical did not cause a significant increase in UDS activity in rat hepatocytes at any of the indicated dose levels at either time point; **acceptable**; (Leung, 8/22/94).

NEUROTOXICITY

Not required for this compound at this time.