

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH  
SUMMARY OF TOXICOLOGY DATA

PYRAZON

Chemical Code # 509, Tolerance # 316

SB 950 # 288

May, 1990

Revised: 5/17/00

I. DATA GAP STATUS

Chronic toxicity, rat:	No data gap, no adverse effect
Chronic toxicity, dog:	No data gap, no adverse effect
Oncogenicity, rat:	No data gap, no adverse effect.
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:	Data gap, no adverse effect indicated
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

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Toxicology one-liners are attached.

All record numbers through 127397 were examined.

\*\* indicates an acceptable study.

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

File name: T000517

Revised by Silva & Kishiyama, 5/17/00

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

### COMBINED, RAT

017 & 018, 045595 & 045596 "Long-Term Dietary Administration of Pyrazon to Rats (Parts I and II)," (B. Hunter, A.V. Barnard, A.E. Street, R. Heywood, D.E. Prentice, J.M. Offer, Huntingdon Research Centre, BSF 87/7766, 4/26/77). Pyrazon technical (no purity indicated) was fed in diet to CFY Sprague-Dawley rats (55/sex/dose) at 0, 150, 450, 1350 or 4050 ppm (40 & 15 rats/sex/dose--main (103-109 weeks) and satellite (78 weeks) groups, respectively). NOEL = 150 ppm for males (Shoulder blades (scapula) were prominent when walking in females at  $\geq$  450 ppm. Bodyweights and bodyweight gains were decreased in both sexes at  $\geq$  1350 ppm. Cholesterol levels were increased in males at 4050 ppm and in females at  $\geq$  1350 ppm. Liver and kidney weights in males (4050 ppm) and thyroid weights in females ( $\geq$  1350 ppm) were increased. Adrenal weights in females were decreased at  $\geq$  1350 ppm. The incidence and severity of muscle atrophy was apparent at  $\geq$  1350 ppm (scapular & thigh) in females. The incidence of thigh muscle atrophy was increased at 4050 ppm in males.) This study is not acceptable and not upgradeable. (Kishiyama & Silva, 5/16/00).

009 041159 "Long-Term Feeding of Pyrazon to Mice (Interim report 0-52 weeks)" (Huntingdon Research Centre, BSF/86/751037, 2-20-76).

### ONCOGENICITY, RAT

063 126376, "Study of the Potential Carcinogenicity of Chloridazon (Pyrazon) in Wistar Rats Dietary Administration for 30 Months," (W. Mellert, BASF Aktiengesellschaft, Germany, Project No. 71S0174/88011; Document #: 93/10818; 8/9/93). Pyrazon technical (Reg. No. 13 033; 95% pure) was fed in diet to Wistar (Chbb : THOM (SPF) rats (50/sex/dose) at 0, 100, 300 and 1000 ppm for 30 months. NOEL > 1000 ppm (Body weight was slightly retarded (no greater than 7%) for high dose males. No other treatment related effects reported.) This study is not acceptable and not upgradeable. The doses for the definitive study were based on preliminary studies. In these studies, effects were observed at 300, 450, 1200 and 1350 ppm. The rangefinding studies performed at these doses used Sprague-Dawley rats, not Wistar strain. Apparently, there is a rat strain difference for toxicological effects of pyrazon. In the definitive study, no effects were observed as high as 2000 ppm. Wistar rats are more resistant to effects of pyrazon than Sprague-Dawley rats. UNACCEPTABLE. (There was no MTD and there were no blood smears collected at 12 and 18 months for differential blood counts). (Kishiyama & Silva, 5/12/00).

035 115526. Supplementary study to 126376. Protocol.

### CHRONIC TOXICITY, RAT

\*\* 062 126375 "Study of the Oral Toxicity of Chloridazon (Pyrazon) in Wistar Rats Dietary Administration for 25 Months," (Mellert, W.; BASF Aktiengesellschaft, Ludwigshafen/Rhein, Germany; Project No. 71SO174/88010; Registration Document #: 93/10819; 8/5/93). Chloridazon (Pyrazon--Reg. No. 13 033; 95% pure) was fed in diet to Wistar (Chbb: THOM (SPF) rats (20/sex/dose) at 0, 100, 300, 1000 and 2000 ppm for 25 months. NOEL = 300 ppm; approximately 16 mg/kg (Males had decreased bodyweights at 2000 ppm (not significant, but > 10%) and females had significantly decreased bodyweights at  $\geq$  1000 ppm. Cholesterol, calcium and urea were increased in females at 2000 ppm. Hematological changes (RBC, HCT, MCV and HGB) were considered due to treatment at 2000 ppm. Thromboplastin time in females was decreased at 2000 ppm. Males at 2000 ppm showed increased keratoconjunctivitis, hyphemia, smeared fur and females at 2000 ppm showed increased incidence of keratoconjunctivitis and reduced physical state.) No adverse effect. ACCEPTABLE (Kishiyama & Silva, 5/9/00).

035 011525. Supplementary study to 126375. Draft Protocol

008 014851 "Chronic Feed Trials with Rats During 15 Weeks Resp. Two Years" (BASF Wyandotte Corp., date unknown) Pyramin, not described, was fed to Sprague-Dawley rats for 2 years in the diet at 0 or 300 ppm, 50/sex/group. No effects were noted, an MTD was not achieved. **Unacceptable**, no description of test article, no analysis of dosing feed, justification of dose levels is not adequate, only one dose level, use animals previously used in a 15 week study, no histopath data. J. Remsen, 7-26-85.

010 041160 Exact duplicate of the above.

**CONCLUSION: The oncogenicity rat (063 126376) and the chronic rat (062 126375) studies contain sufficient data to fill the data gaps for evaluation of pyrazon. Although the oncogenicity, rat study was not acceptable, when combined with the chronic, rat study, the data gap is filled. M. Silva, 5/17/00.**

#### CHRONIC, MOUSE

##### Subchronic:

048 121540 "SUBCHRONIC TESTING - 90-Day FEEDING, RODENT Study on the Oral Toxicity of Chloridazon (Pyrazon) in MICE - Administered Via the Diet over 3 Months," (Schilling, K.; BASF Aktiengesellschaft, Department of Toxicology, Germany; Laboratory Project ID #: 53S0174/88013; BASF Registration Document #: 90/0568; 10/4/90). Chloridazon (Registration #: 13 033; purity = 94.1%) was fed in diet to B6C3F1/CrlBR mice (10/sex/dose) at 0, 300, 1500 and 7500 ppm for 3 months. NOEL (males) = 300 ppm; approximately, 65 mg/kg (Decreased food consumption and body weights occurred in males at  $\geq$  1500 ppm.) NOEL (females) = 1500 ppm; approximately 467 mg/kg (Decreased food consumption in females at 7500 ppm.) The study is unacceptable (no ophthalmology). Therefore, the data are supplemental. (Kishiyama & Silva, 4/18/00).

#### CHRONIC TOXICITY, DOG

The following dog studies (060 126370 & supplemental 061 126373) were performed to illicit a clear toxic effect at the high dose and a clear NOEL for chronic toxicity. Although 060 126370 is acceptable alone, the supplement is not. Both studies were reviewed to obtain an overall picture of the chronic toxicity of pyrazon in dogs, over a broad dose range.

\*\* 060 126370 "Chronic Toxicity with Chloridazon (Pyrazon) in Beagle Dogs Administration in the Diet for 12 Months," (W. Mellert; BASF Aktiengesellschaft, Project #: 33DO174/88059; Registration Document #: 93/10815, 8/5/93). Chloridazon (Pyrazon; Reg. No. 13 033; 95% pure) was fed in diet to beagle dogs (6/sex/dose) at 0, 400, 1200 and 3600 ppm for 12 months. NOEL = 400 ppm; approximately 11 mg/kg (Incidence of vomiting increased, primarily in high dose males. Food consumption was decreased days 0-7 at 3600 ppm (females). Body weight gain was reduced significantly at > 1200 ppm in females.) ACCEPTABLE. (Kishiyama & Silva, 5/2/00).

\*\* 061 126373. "Supplementary Chronic Toxicity with Chloridazon (Pyrazon) in Beagle Dogs Administration in the Diet for 12 Months," (W. Mellert, BASF Aktiengesellschaft, Ludwigshafen /Rhein, Germany; Registration #: 93/10824; Project #: 33DO174/88117, 8/5/93). Chloridazon (Pyrazon, Reg#: 13 033; 95% pure) was fed in diet to beagle dogs (6/sex/dose) at 0, 400, 1200 and 3600 ppm for 12 months (separately reviewed by DPR volume/record #: 316-060/126370). NOEL = 400 ppm (Incidence of vomiting increased, primarily in high dose males. Food consumption was decreased days 0-7 for at 3600 ppm (females). Body weight gain was reduced significantly at  $\geq$  1200 ppm in females.) In this supplemental study (Registration #: 93/10824; 316-061/126373), beagle dogs (6/sex/dose) were fed chloridazon in diet at 0, 6,000 and 8000 ppm for 12-months. NOEL < 6000 ppm (Body weights were decreased in males at 8000 ppm and in females at  $\geq$  6000 ppm. Clinical signs (vomiting and diarrhea) were observed at  $\geq$  6000 ppm. Food consumption was decreased in both sexes at  $\geq$  6000 ppm. Increased inorganic phosphate occurred in both sexes at  $\geq$  6000 ppm. Bilirubin was decreased in males at 8000 ppm. Livers in males and thyroid, adrenals and kidneys in females had weight increases at  $\geq$  6000 ppm. Lymphoid hyperplasia and kidney vacuolization (males at 8000 ppm) were increased at  $\geq$  6000 ppm.) ACCEPTABLE. (Kishiyama & Silva, 5/9/00).

049 121541, "90-Day Feeding/Nonrodent: The Toxicity of Pyrazon (Reg. No. 13 033; 95%) in Beagle Dogs: Administration via the Diet Over 3 Months," ( Hellwig, J.; BASF Aktiengesellschaft, Ludwigshafen/Rhein, FRG; Registration Document #: 92/11648; Project #: 31DO174/88033; 12/8/92). Pyrazon technical (Reg. No. 13 033, purity = 95%) was fed in diet to Beagle dogs (6/sex/dose) at 0, 300, 1000 and 3000 ppm for 90 days. NOEL > 3000 ppm (There were no effects at any dose that were related to treatment.) Not acceptable and not upgradeable (no target organ identified). These data are supplemental. (Silva, 4/19/00)

\*\* 059 126368 "Study of the Toxicity with Chloridazon (Pyrazon) in Beagle Dogs Administration in the Diet for 3 Months," (Mellert, W.; BASF Aktiengesellschaft, Department of Toxicology, Germany; Laboratory Project ID #: 31D0174/88115; BASF Registration Document #: 93/10823; 8/5/93). Chloridazon (Registration #: 13 033; purity = 95%) was fed in diet to Beagle dogs (6/sex/dose) at 0, 4000 and 5000 ppm for 3 months. NOEL < 4000 ppm (Vomiting was observed in all treated animals at  $\geq$  4000 ppm. Food consumption was decreased in females at  $\geq$  4000 ppm, mainly early in the study. Body weight

gain was reduced at  $\geq 4000$  ppm in both sexes. MCV and clotting analyses were significantly decreased in females at 5000 ppm (day 30 only). Females had decreased inorganic phosphate at  $\geq 4000$  ppm. Male potassium levels were increased at 5000 ppm. Relative liver weights were increased significantly at  $\geq 4000$  ppm in males. Kidney weights were also increased at 5000 ppm. Accompanying histopathology was vacuolization of distal renal tubules of females at  $\geq 4000$  ppm.) The study is acceptable. (Kishiyama & Silva, 5/4/00).

008 014850 "Chronic Two Years Lasting Feeding Trial with Dogs" (BASF Wyandotte Corp, date unknown) Pyramin, not described, was administered to Beagle dogs daily in the feed at 0, 600 or 1500 ppm for 2 years, 3/sex/group. No effects were seen, no indication an MTD was reached. **Unacceptable**, only 2 dose levels were used, no justification of dose, no quantitative analysis of dosing solution. J. Remsen, 7-26-85.

010 041161 Exact duplicate of the above.

#### ONCOGENICITY, MOUSE

##### Subchronic Study:

009 041159 "Long-Term Feeding of Pyrazon to Mice (Interim report 0-52 weeks)," (Hunter, B., Graham, C., Street, A.E., Heywood, R., Cherry, C.P.; Huntingdon Research Centre, Cambridgeshire, UK; BSF/86/751037; 2-20-76). Pyrazon (no purity stated; a brown powder; batch Nos. BASF 942 E 679 & 944 E 311) was fed in diet to CFLP mice (68/sex/dose, with 28/dose as satellite group) at 0, 160, 500, 4,000 or 20,000 ppm for 80 weeks (8/sex/dose sacrificed at 26 weeks). Achieved doses were 15, 45, 370 and 2232 mg/kg/day for males and 18, 52, 447 and 2496 mg/kg/day for females. The study includes ophthalmologic exams, urinalysis, hematology and blood chemistry. Gross and microscopic pathology were examined at the 26 week interim kill. The following effects were seen at 20,000 ppm: a lower body weight gain at 52 weeks for males ( $p < .001$ ), a lower body weight gain at 26 weeks for females ( $p < .05$ ), increased water consumption in males and females (statistically significant but within historical controls), increased liver weights in both sexes, elevated SAP and SGPT values, centrilobular hepatocytes had an unusual appearance characterized by granular, eosinophilic cytoplasm with minimal enlargement and an absence of centrilobular fat. **No adverse effects.** The report is considered **supplemental** until a final report is received. M. Silva, 3/21/00.

##### Oncogenicity Study:

\*\* 064 126394 "Carcinogenicity Study with Chloridazon (Pyrazon) in B6C3F1 Mice Administration in the Diet for 24 Months", (W. Mellert, BASF Aktiengesellschaft, Project No. 80SO174/88040, Registration Document #: 93/10820; 8/9/93). Pyrazon technical (Reg. No. 13 033; 95% pure) was fed in diet to B6C3F1/CrlBr mice (50/sex/dose-main group, 24 months & 10/sex/dose-satellite, 12 months) at 0, 200, 1000 and 5000 ppm. Systemic NOEL = 1000 ppm; approximately 152 mg/kg bwt. (Body weight decreased at 5000 ppm (both sexes).) Oncogenic NOEL > 5000 ppm (No treatment-related oncogenicity

was induced at any dose.) No adverse effect. ACCEPTABLE. (Kishiyama & Silva, 5/5/00)

\*\* 013 0 45591 and 014 045592 "Long-Term Feeding of Pyrazon to Mice (Final Report)," (Hunter, B., Graham, C., Street, A.E., Heywood, R., Cherry, C.P. and Prentice, D.E.; Huntingdon Research Centre, BSF 86/77171, 8-25-77). Pyrazon (brown powder, no stated purity, batch Nos. BASF 942 E 679 & 944 E 311) was fed in diet to CFLP mice (40/sex/dose plus an additional 28/sex/dose as a satellite group) at 0, 160, 500, 4,000 or 20,000 ppm. Animals were sacrificed between 81 and 96 weeks when survival reached 25%. The minimum achieved dosage was 14, 44, 351 and 2215 mg/kg/day for males and 18, 48, 423 and 2490 mg/kg/day for females. Chronic NOEL = 4000 ppm (Males at 20,000 ppm had an increased mortality rate. There was an increase in hepatic disease in those dying at 4000 ppm. There was a lower growth rate for males during the first 52 weeks and for females the first 26 weeks at 20000 ppm. Absolute and relative liver weights and SAP and SGPT values were increased in both sexes at 20000 ppm. Histopathologically increased centrilobular hepatocytes with granular, eosinophilic cytoplasm (minimal enlargement) and an absence of centrilobular fat occurred in both sexes at  $\geq$  4000 ppm.) Oncogenic NOEL > 20,000 ppm (No treatment-related effects occurred at any dose.) **No oncogenic effects due to treatment.** There were sufficient survivors late in the study for onco evaluation. Acceptable for oncogenicity evaluation, with numerous deficiencies. M. Silva, 4/11/00.

#### REPRODUCTION, RAT

\*\* 065 126397 "2-Generation Reproduction: Reproduction Toxicity Study with Pyrazon (Chloridazon) in Rats," (J. Hellwig; BASF Aktiengesellschaft, Ludwigshafen/Rhein; FRG; Project #: 71R0174/88032; Registration Document #: 93/10632; 6/29/93). Pyrazon (Chloridazon, Reg. #: 13 033; purity = 95%) was fed in diet to Wistar Chbb: THOM (SPF) rats (24/sex/generation/dose) at 0, 100, 400 or 1600 ppm for 2 generations. F0 parental generation was mated twice to produce the F1a and F1b litters. Systemic NOEL = 400 ppm (Triglycerides were reduced for F0 & F1 males and F1 females. Liver weight increased for high dose F0 females. Both F0 and F1 parents had liver pathology (hydropic swelling and focal fibrosis) but not always in both sexes at 1600 ppm.) Reproduction NOEL > 1600 ppm (There were no treatment-related effects at any dose.) ACCEPTABLE (minor deficiencies). (Kishiyama & Silva, 5/1/00).

011 041165 "Effect of Pyrazon on Reproductive Function of Multiple Generations in the Rat," (Palmer, A.K. and Allen, T.R.; Huntingdon Research Centre, BSF/73/76519, 6-27-77). Pyrazon (purity not stated) was fed in diet to CFY SPF rats (20/sex/dose) at 0, 150, 450 or 1350 ppm for 3 generations (1 litter/gen). NOEL (maternal and reproductive) > 1350 ppm (HDT). There were minimal body weight effects that were not statistically significant. **Unacceptable** (The study had numerous deficiencies, such as: no justification of dose levels, no histopathology, no description of randomization and selection of pups, no clinical signs were reported & dose analyses do not include homogeneity or stability. Not performed according to FIFRA Guidelines.) No adverse effect in this study as performed. M. Silva, 3/22/00.

003 940788 This is text only, identical to 011 41165.

## TERATOLOGY, RAT

\*\* 037 115531, "Chronic Testing - Teratogenicity - The Prenatal Toxicity of Chloridazon (Pyrazon) in Rats after Oral Administration (Gavage)," (J. Hellwig; BASF Corporation Aktiengesellschaft, Republic of Germany, BASF Registration Document #: 90/0163; Laboratory Project ID#: 34R0174/88035, 5/30/90). Chloridazon technical (94.1% pure) was administered by gavage to mated female Wistar (Chbb:Thom (SPF)) rats (25/dose) at 0 (distilled water + 0.5% CMC), 10, 50 and 250 mg/kg body weight on days 6 through 15 post coitum. **Maternal NOEL** = 10 mg/kg (There were significant decreases in food consumption and body weight change, particularly at 250 mg/kg. Clinical signs showed increased piloerection at 250 mg/kg.) **Developmental NOEL** = 250 mg/kg (There were no treatment-related effects at any dose.) ACCEPTABLE. (Kishiyama & Silva, 4/27/00).

008 034207 "Testing for Possible Teratogenic Effect by Oral Application on Rats" (BASF Wyandotte Corp., date unknown) Pyramin, not described, was given to presumed pregnant Sprague-Dawley rats in the feed at 0, 1000 or 5000 ppm in the feed, 12 or 13 per group. Food consumption and body weights were decreased at 5000 ppm, but there is insufficient information to determine a NOEL. **Unacceptable** with no description of test article, only 2 dose levels, the length of dosing period is not stated, too few per group, no analysis of feed, no justification of dose. J. Remsen, 7-26-85.

010 041164 Exact duplicate of the above.

## TERATOLOGY, MOUSE

015 045593 "Trial Report on the Pre-, Peri- and Postnatal Toxicity of 5 -amino- 4-chloro- 2-phenyl -3 (2H) -pyridazinone in the Mouse," (Hofmann, H.Th. & Peh, J.; BASF Medical Biology Research Laboratories, 3/19/75). This study was conducted according to 1966 FDA guidelines, Section II and III. Teratology Section (II): Technical pyrazon was fed in diet to mated NMRI mice (21/dose) at 0, 5000 or 10000 ppm (days 1-18 of gestation). NOEL (maternal) = 10000 ppm (HDT). NOEL (fetal) < 5000 ppm. Body weights and fetal length were reduced in treated animals at statistically significant level. Peri- and Postnatal Sections (III): Mated NMRI mice (10/dose) were fed in diet throughout gestation at 0, 5000 or 10000 ppm technical pyrazon, then dosed or given control diet through day 21 of lactation. Mice were then sacrificed day 22 of lactation. **Developmental Toxicity Study: Maternal NOEL** = 5000 ppm (There was an increased percent dead implantations. **Developmental NOEL** < 5,000 ppm (Fetal weights and length were significantly decreased in both treated groups at  $p < 0.01$ .) **Peri-/Postnatal Developmental Study: Maternal NOEL** = 5000 ppm (Dams at 10,000 ppm had reduced absolute and relative spleen, heart and kidney weight. Macroscopic findings showed intestinal convolution, acute cardiac dilation, general congestion hyperaemia and emaciation.) **Pup NOEL** = 5000 ppm (Pup deaths were increased and the vitality index (%) was decreased in pups at 10000 ppm.) These data are supplemental. M. Silva, 4/11/00.

008 034206 "Testing for Possible Teratogenic Effect by Oral Application on Mice" (BASF Wyandotte

Corp., date unknown) Pyramin, not described, was given to presumed pregnant NMRI mice in the feed on days 1 - 18 of gestation at 0, 1,000, or 5000 ppm, 10/group. No effects were seen, however the information is insufficient to determine a NOEL. **Unacceptable** due to too few animals, no justification of dose selection, no analysis of dose, too few doses, no individual data, summary only. J. Remsen, 7-26-85.

010 041163 Exact duplicate of the above.

008 014848 "Testing for Possible Teratogenic Effect by Intraperitoneal Application on Mice" (BASF Wyandotte Corp., date unknown) Pyramin, not described, was injected i.p. into presumed pregnant NMRI mice daily on days 11 - 15 of gestation at 0, 60 or 150 mg/kg, 20, 20 and 8 mice per group, respectively. These dose levels were equal to 1/5 and 1/2 of the LD 50. No maternal or fetal effect was seen. **Unacceptable** due to summary only, only 2 dose levels, not enough animals, unusual route of administration with no justification, test article not described, dosing period was too short, no individual data. J. Remsen, 7-26-85.

010 041162 Exact duplicate of the above.

#### TERATOLOGY, RABBIT

036 115530, "Chronic Testing - Teratogenicity - Pyrazon/Rabbit Project Number 067768", (H. Becker, E. Mueller & Ch. Terrier; RCC, Research Consulting Company AG, Itengen/Switzerland; BASF Registration Document #: 87/0413; 10/16/87). Chloridazon technical (95.3% pure) was administered by gavage to mated Chinchilla (Kfm: CHIN, hybrid, SPF Quality) rabbits (16/dose) at 0 (distilled water + 4% CMC), 55, 165 or 495 mg/kg body weight on days 6 through 18 post coitum. Body weight change and food consumption were reduced only at initiation of dosing (days 1 & 2) at  $\geq$  165 mg/kg. Developmental NOEL > 495 mg/kg. No treatment-related fetal abnormalities occurred at any dose. Currently this study is not acceptable but is possibly upgradeable upon submission of the dose-rangefinding study. The results of that study need to be evaluated in order to determine whether optimal doses were used for the definitive test. No adverse effects indicated. (Kishiyama & Silva, 4/27/00).

#### GENE MUTATION

\*\* 035 115527 "Mutagenicity Testing - Pyrazon Gene Mutation Ames Salmonella Mammalian Microsome and Reverse Mutation Assay - E. Coli WP2 uvrA", (G. Englehardt, BASF Aktiengesellschaft, Ludwigshafen/Rhein, Germany Project No. 40M0174/884171; Document #: 89/0173; 5/17/89). Chloridazon technical (purity = 94.1%) at concentrations of 0, 20, 100, 500, 2500 and 5000  $\mu$ g/plate was evaluated for mutagenicity using *Salmonella typhimurium* strains TA 98, TA 100, TA1535 and TA 1537 and *Escherichia coli* strain WP2 uvrA (+/-S9 mix). The increase in revertants was marginal (TA 100), non dose related (TA 1537) and was not observed in repeat tests. ACCEPTABLE. (Kishiyama & Silva, 4/20/00).

## CHROMOSOME EFFECTS

\*\* 035 115528, "Mutagenicity Testing - Pyrazon Structural Chromosomal Aberration - Mice Micronucleus *In Vivo* Test", (G. Englehardt, BASF Aktiengesellschaft, Ludwigshafen/Rhein, Germany, Project Number 26M0099/8635; Document #: 87/0424; 11/17/87). Chloridazon technical (purity = 95.3%) at 0 (0.5% CMC), 150, 300 or 600 mg/kg body weight was evaluated for mutagenicity using the bone marrow (femora) of oral gavage-treated NMRI mice. Sacrifice for 150 and 300 ppm (5/sex/dose) was at 24 hours and at 600 mg/kg (15/sex) sacrifice was at 16, 24, and 48 hours (5/sex/dose/time point). Clinical signs showed increased "abdominal position" and irregular respiration in all chloridazon-treated groups and general health was poor at  $\geq 300$  mg/kg. The number of micronucleated polychromatic erythrocytes did not increase in any treated group. ACCEPTABLE (Kishiyama & Silva, 4/24/00).

**016 045594** "Study on the Mutagenic Effect of 5-amino-4-chloro-2-phenyl-3(2H)-pyridazinone on the Male Mouse Following Repeated Oral Administration" (BASF Medical Biology Research Laboratories, 2-13-75). Technical pyrazon (no purity given) was administered by gavage to male NMRI mice (22/dose) on 5 consecutive days at 0 (0.5% CMC), or 570 mg/kg. Males were then mated with 3 females per week for 8 weeks to assess dominant lethal effects. The third week of mating there was a statistically significant increase in the number of dead implants and premature absorptions (attributed to 1 male). **Possible mutagenic effect of equivocal significance. Unacceptable and not upgradeable** (Purity of test article is not given, an MTD was not reached, 3 dose levels not used, no positive control, no individual data to evaluate). M. Silva, 4/17/00

003 940789 This is an incomplete report of 016 45594 which was reviewed by J. Remsen, 7-25-85. It had insufficient information for assessment.

## DNA DAMAGE

\*\* 035 115529, "Mutagenicity Testing - Pyrazon/Other Genotoxic Effects Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay Project Number HBC 20991", (M.A. Cifone, Hazleton Biotechnologies Company, Kensington, MD; BASF Registration Document #: 86/0257;10/31/86). Chloridazon technical (no stated purity) was used on primary rat hepatocytes at 0 (1% DMSO), 5.04, 10.1, 25.2, 50.4, 101, 252, 504, and 1010  $\mu\text{g/ml}$  to determine the potential for DNA damage. Chloridazon treatments did not significantly increase net nuclear grain count after 18 hours of exposure under study conditions. The positive controls functioned as expected. ACCEPTABLE. No adverse effect. (Kishiyama & Silva, 4/26/00).

## NEUROTOXICITY

Not required at this time.