CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Quinclorac

Chemical Code 5104, Tolerance 52216

4/27/00, updated: 05/09/2014

I. DATA GAP STATUS

Combined, rat:	No data gap; no adverse effects
Chronic toxicity, dog:	No data gap; no adverse effects
Oncogenicity, mouse:	No data gap; no adverse effects
Reproduction, rat:	No data gap; no adverse effects
Teratology, rat:	No data gap; no adverse effects
Teratology, rabbit:	No data gap; no adverse effects
Gene mutation:	No data gap; no adverse effects
Chromosome effects:	No data gap; **possible adverse effects**
DNA damage:	No data gap; no adverse effects
Neurotoxicity:	No study on file[1]
Immunotoxicity:	No data gap, no adverse effect

Toxicology one-liners are attached.

All record numbers through 258929 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.
File name: T050914
Vidair, 4/27/00, updated by Pan &Leung, 05/09/2014.

[1]New active ingredient, quinclorac, submitted as an herbicide for non-food use. These studies are not required at this time.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

COMBINED, RAT

52216-015, -016, -017; 168797, 168798, 168799; "Study of the Chronic Toxicity and Oncogenic Potential of Reg. No. 150 732 in Rats, Administration via the Diet over 24 Months" (Schilling, K. et al., Dept. of Toxicology, BASF Aktiengesellschaft, 6700 Ludwigshafen/Rhein, FRG, Doc. 88/0409 and 91/10734, Project No. 71S0282/8519, 9/14/88). Test article Reg. No. 150 732 (Batch IIIN55=97.4% pure, Batch III/2N57=98.3% pure) was administered to 50 rats/sex/dose level in their feed for 24 months at 0, 1000, 4000 and 8000 ppm. Two additional groups of 20 or 10 rats/sex/dose level were fed 0, 1000, 4000, 8000 and 12000 ppm of test article for 24 months (satellite group #1) or 12 months (satellite group #2), respectively. Mean test article intake by main group males was 55/221/444/675 and females was 66/262/529/832 mg/kg/day for 1000/4000/8000/12000 ppm (the high dose values from satellite group #1 animals). The test article did not induce mortality or abnormal clinical signs. Mean food consumption was also unaffected. Mean water consumption was generally higher in treated animals, but the increases relative to controls were never statistically significant. Only satellite group #1 females fed 12000 ppm exhibited mean bodyweights that were significantly lower than controls ($p<0.05$) for more than a single time point (5 time points between days 518 and 658). Measured parameters of hematology, clotting times and ophthalmology were normal. Urinalysis detected a general decrease in protein as the dose of test article was increased, but this was attributed to increased water consumption and increased urination. The single consistent change in serum chemistry was a drop in bilirubin in treated males of satellite group #1 from day 95 through day 725. However, the decreases were usually not statistically significant, no dose-response was evident, and females were unaffected, making the toxicological significance of these changes doubtful. Gross pathological examination of main group animals demonstrated liver foci in 23/25/28/33* males (* $p<0.05$), testes foci in 4/2/15/10 males (** $p<0.01$), and ovarian masses in 1/3/6/6/ females, all corresponding to 0/1000/4000/8000 ppm. However, lack of a clear dose-response and the absence of histological correlates suggest that these findings were not treatment-related. Absolute and relative organ weights were largely unaffected by the test article. Gross and microscopic pathology of satellite group animals (including absolute and relative organ weights) were normal, demonstrating that 12000 ppm also had no effect. Lastly, macroscopic and microscopic neoplastic lesions (both benign and malignant) were unaffected by test article administration, with regard to both the total number of neoplasms and the number of animals with neoplasms. **No adverse effects indicated. Chronic NOEL: (M) = 12000 ppm** (675 mg/kg/day, based on the absence of effects in males fed 12000 ppm), **(F) = 8000 ppm** (832 mg/kg/day based on lower mean bodyweights in females fed 12000 ppm). **Study acceptable** (Vidair 12/8/99).

52216-017; 168800; "Response to Reviewer's Comments for Chronic Toxicity/Oncogenicity Study in Rats on Quinclorac (FACET Herbicide)" (Hildebrand, B., Dept. of Toxicology, BASF Aktiengesellschaft, Ludwigshafen/Rhein, FRG, Doc. No. 91/5139, December, 1990). The author first addressed the reasons for choosing 8000 and 12000 ppm as the highest dose levels, in light of the result that 12000 ppm was a NOEL for males. In a previous 3 month feeding study in rats, 12000 ppm caused reduced bodyweights in both males and females. 8000 ppm was chosen for the carcinogenicity study to ensure that enough animals would be alive after 2 years. The average daily test article intake in the satellite animals fed 12000 ppm was 1226-826 mg/kg in males over

the first 49 days and 1226-961 mg/kg for females, with 2 year average intakes of 675 (males) and 832 (females) mg/kg. These levels are close to the 1000 mg/kg limit stated in the guidelines (870.4100, 8/98). The issue of autolysis and tissue loss in pathology samples was stated not to have been a problem. The historical control incidences of acinar cell hyperplasia and neoplasms were given. The incidences of these alterations in the treated male Wistar rats of the subject study fell within the ranges of historical controls. An incident was described where a pancreatic tumor completely replaced the left adrenal gland, making only one adrenal gland available for examination. Lastly, an explanation for increased adrenal weights (not statistically significant) in treated males was provided. One of the adrenals contained a pheochromocytoma, and one was the above-mentioned pancreatic tumor, mistakenly counted as an adrenal gland. When these were excluded, mean adrenal weights were no different in treated and control animals. **Study supplemental** (Vidair 12/9/99).

52216-017; 168801; "Review of the Supplemental Toxicology Evaluation of Pancreatic Lesions from the Chronic/Oncogenicity Study of Quinclorac in the Wistar Rat" (Tobia, A. and Mascianica, M., BASF Corporation, P.O. Box 13528, Research Triangle Park, NC, Doc. No. 91/5124, 9/6/91). The objectives of this review of a 2 year rat oncogenicity/chronic toxicity study (Record #168798) were to summarize the findings for non-neoplastic and neoplastic lesions of the exocrine pancreas, and to compare those findings to historical controls. For acinar cell hyperplasia and acinar cell adenoma/carcinoma, re-evaluation of the data for main and satellite group animals demonstrated no significant differences between treated and control animals in the incidences of these alterations, as tested by the Fisher's Exact Test, at $p = 0.05$ or $p = 0.01$ levels of probability. There was also no dose-response for any group. Lastly, incidences of acinar cell hyperplasia and acinar cell adenomas/adenocarcinomas fell within the ranges of historical controls (historical control values: male hyperplasia up to 26%; female hyperplasia up to 5%; male adenomas up to 18%; female adenomas up to 8%; male adenocarcinoma up to 5.1%; female adenocarcinoma up to 2%). It was concluded that the 2 year oncogenicity study showed that the test article was not oncogenic in rats. **Study supplemental** (Vidair 12/9/99).

CHRONIC TOXICITY, DOG

52216-018; 168802; "Report on the Study of the Toxicity of Registration Number 150 732 in Beagle Dogs After 12-month Administration in the Diet." (Hellwig, BASF Aktiengesellschaft, Dept. of Toxicology, 6700 Ludwigshafen, West Germany, Project No. 33D0150/8445, November, 1987). Six Beagle dogs/sex/dose level were administered Reg. No. 150 732 (Batch N32, 96.5% pure; Batch N55, 97.4% pure) in their feed for one year at 0, 1000, 4000 and 12000 ppm. Mean daily intake of the test article was 33/132/462 (males) and 33/131/445 (females) mg/kg, corresponding to 1000/4000/12000 ppm. The single mortality (a male fed 12000 ppm) was due to tracheal obstruction in the seventh month. There were no other treatment-related clinical signs. Bodyweight gains were markedly affected by the high dose only; mean gains/losses over the one year period in high dose animals were (–)1% and (+)1% for males and females, respectively, compared to (+)27% and (+)21% for control males and females. Since food consumption was not significantly lower in high dose animals relative to controls, and high dose animals did not suffer more diarrhea or vomiting than controls, the test article may have decreased the efficiency with which food was processed. Female liver was the only organ exhibiting a statistically significant increase in absolute weight (114%/112%/131% of control corresponding to 1000/4000/12000 ppm; ** $p<0.01$). Single cell necrosis was observed in the livers of high dose males (2/6) and females (2/6). Increased mean relative kidney weights in both males (106%/119%**/155%** of

control for 1000/4000/12000 ppm; ** p<0.01) and females (108%/112%/137%** of control; ** p<0.01) were associated with hydropic degeneration with vacuolar formation in epithelial cells of the pars recta of the nephron in high dose males (2/6) and females (2/6). In contrast, increased mean relative brain, adrenal, and thyroid weights in treated males and females were ascribed to lower bodyweights, since organ histopathology was normal. Lastly, hypoplasia of the prostate was noted in 2/6 males fed 4000 ppm and 1/6 fed 12000 ppm. **No adverse effects indicated. NOEL (M/F) = 1000 ppm** (33 mg/kg/day, based on higher relative mean kidney weight in males fed 4000 ppm and on elevated relative liver weight and single cell necrosis (2/6) in females fed 4000 ppm). **Study acceptable** (Vidair 12/14/99).

ONCOGENICITY, MOUSE

52216-015; 168797; "Study of the Potential Carcinogenic Effect of Reg. No. 150 732 in Mice Dietary Administration for 78 Weeks (88/0411), Supplement, Supplementary Study (88/0412)" (Schilling, K., BASF Aktiengesellschaft, Dept. of Toxicology, D-6700 Ludwigshafen/Rhein, FRG, Project ID No. 80S0282/8520, 9/14/88). Sixty mice/sex/dose level were administered test article Reg. No. 150 732 (purity 97.4% and 98.3% for Batches IIIN55 and III2N57, respectively) in their feed at 0, 1000, 4000 and 8000 ppm. Fifty animals from each group were fed the test article for 18 months, while 10 animals from each group comprised satellite groups which were sacrificed after 6 months. Mean test article uptake for main group animals was: males 0/170/711/1444 and females 0/213/869/1828 mg/kg/day for 0/1000/4000/8000 ppm. A few months before the end of this study, sixty mice/sex/dose level were begun on diets containing 0 or 250 ppm of the same batch of test article, lasting for 18 months (main groups, 50 animals/sex) or 6 months (satellite groups, 10 animals/sex). Mean test article uptake for the main group animals was: males 42 and females 60 mg/kg/day for the 250 ppm level. There was no test article-induced mortality or clinical signs. Mean bodyweights of animals fed ≥ 1000 ppm were sporadically lower than control bodyweights for multiple weeks, ranging from 82% to 92% of controls (p<0.01) by day 546 without changes in food consumption. These lower bodyweights were considered the cause of the scattered lower mean absolute organ weights in animals fed ≥ 1000 ppm (18 month sacrifice). There were no other consistent treatment-related effects on any parameters of hematology, gross pathology or histopathology, including no induction of benign or malignant neoplasms. **No adverse effects indicated. Chronic NOEL (M/F) = 250 ppm (M: 42 mg/kg/day, F: 60 mg/kg/day; based on lower mean bodyweights of animals fed ≥ 1000 ppm). **Study acceptable** (Vidair 12/6/99).

REPRODUCTION, RAT

** 021, 024, 025, 026; 168806, 168813, 168814, 168815; "Report on the Reproduction Study with Registration Number 150 732 in Rats; Continuous Dietary Administration over 2 Generations (2 Litters in the First and 1 Litter in the Second Generation) – Consists of 2 Volumes, a Supplement and a Pathology Report"; (J. Hellwig; BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen/Rhein, FRG; Reg. Doc. #88/0321; 7/21/88); Twenty four rats/sex/group were treated in the diet with 0, 1000, 4000, or 12000 ppm of Reg. No. 150 732 (batch nos. N55 III (purity: 97.38%)and N57 III/2 (purity: 98.29%) for 2 generations. The treatment period for the F0 generation included at least 10 weeks prior to mating, the mating period, and 3 weeks each for gestation and lactation (F1a litter). After a 10 day interlude, the F0 parents were remated and maintained on their respective diets during the 3 week gestation and lactation periods (F1b litter). Twenty four rats/sex/group were selected from the F1a litter and treated for at least 14 weeks prior to mating, during the mating period and an additional 3 weeks each for gestation and lactation (F2 litter). The F0 and F1 parental females demonstrated lower mean body weights than the control females during the gestation and/or lactation periods (p<0.05

or p<0.01). In addition, the F1 parental males and females exhibited lower mean body weights during the premating period (p<0.05 or p<0.01). Microscopic examination revealed an increased incidence and severity of interstitial nephritis in the kidneys of the F0 and F1 females. There were no treatment-related effects upon any of the reproductive parameters. Developmentally, the F1a and F1b pups had lower mean body weights beginning at 7 or 14 days of lactation (F1a) or 21 days of lactation (F1b) (p<0.05 or p<0.01). The mean body weights for the F2 pups were less than those of the controls from the time of birth (p<0.05 or p<0.01). **No adverse effect indicated.**
Parental NOEL: 4000 ppm ((M) F0: 343.3 mg/kg/day, F1: 379.8 mg/kg/day, (F) F0: 307.5 to 778.5 mg/kg/day, F1: 306.6 to 753.5 mg/kg/day) (based upon the lower mean body weights for the parents in both generations and higher incidence of interstitial nephritis in F0 and F1 females);
Reproductive NOEL: 12000 ppm ((M) F0: 1026.3 mg/kg/day, F1: 1208.8 mg/kg/day, (F) F0: 914.2 to 2168.3 mg/kg/day, F1:944.0 to 2152.0 mg/kg/day) (based upon the highest dose tested);
Developmental NOEL: 4000 ppm ((M) F0: 343.3 mg/kg/day, F1: 379.8 mg/kg/day, (F) F0: 307.5 to 778.5 mg/kg/day, F1: 306.6 to 753.5 mg/kg/day) (based upon the lower mean body weights of the pups in both generations). **Study acceptable.** (Moore, 1/10/00)

TERATOLOGY, RAT

52216-020; 168805; "Report on the Study to Determine the Prenatal Toxicity of Registration Number 150 732 in Rats After Oral Administration (Gavage)" (Hellwig, J., BASF Aktiengesellschaft, Dept. of Toxicology, 6700 Ludwigshafen/Rhein, FRG, Project No. 34R0150/8453, Doc. No. 87/0167, 5/12/87). Twenty five mated females rats/dose level were administered Reg. No. 150 732 (Batch No. N32, 96.5% pure) by oral gavage on days 6-15 post coitum at 0 (0.5% carboxymethyl cellulose), 24.4, 146 and 438 mg/kg. At day 20, all animals were sacrificed and their fetuses delivered by cesarean section. Three dams from the high dose group died, one on each of days 11, 13 (sacrificed moribund) and 14 post coitum. All three had severe ulcerations of the glandular stomach. No clinical signs were exhibited in the other dose groups. Food consumption by high dose animals was significantly lower than that of controls for days 7-8 (p<0.01), 9-10 (p<0.01) and 11-13 (p<0.05). However, mean bodyweights and uterus weights were unaffected throughout, although the mean bodyweight gain of high dose animals was significantly lower than controls at a single time point (days 6-8, p<0.01, analysis of trend). The mean number of corpora lutea, live implantations, live fetuses and dead implantations per pregnant female were not significantly different in treated versus control dams. There were no dead fetuses. Fetal weights and lengths, along with placental weights, were not affected by test article administration. Mean fetal retardations in organs after evisceration, in % fetuses/litter, were 0.89/0.44/1.84/2.94 corresponding to 0/24.4/146/438 mg/kg. Mean fetal anomalies in organs by the Barrow/Taylor method were, in % fetuses/litter, 0/0/1.09/2.50. Neither increase in retardations or anomalies in treated animals relative to controls was statistically significant. **No adverse effects indicated. Maternal NOEL: 146 mg/kg (based on lower mean food consumption and increased mortality in animals fed 438 mg/kg). **Developmental NOEL: 438 mg/kg** (based on the absence of effects in fetuses of the 438 mg/kg group). **Study acceptable** (Vidair 12/20/99).

TERATOLOGY, RABBIT

**52216-019; 168803, 168804; "Report on the Study of the Prenatal Toxicity of Registration Number 150 732 in Rabbits After Oral Administration (Gavage)" (Hellwig, J., BASF Aktiengesellschaft, Dept. of Toxicology, D-6700 Ludwigshafen, FRG, Project No. 38R0282/8511, Doc. No. 88/0099, 12/23/86). Fifteen pregnant female Himalayan rabbits per dose level were administered Reg. No. 150 732 (Batch N57III/2, purity 98.3%) once per day by oral gavage on days 7-19 post insemination (p.i.). On day 29 p.i., all animals were sacrificed and fetuses were

delivered by cesarean section. Dose levels were 0 (0.5% carboxymethyl cellulose), 70, 200 and 600 mg/kg. Both mean bodyweights and mean bodyweight gains for high dose animals were significantly ($p<0.05$) lower than controls, with bodyweight losses recorded during the feeding period (days 7-19 p.i.). Mean food consumption was only affected during administration of the test article (days 7-19 p.i.), averaging 86% and 47% of control values for the 200 and 600 mg/kg dose levels, respectively. There were six deaths, all in the high dose group. These included 2 animals sacrificed after aborting, one sacrificed moribund, and one dying after an error in dosing. Clinical signs associated with the treatment were limited to poor general state, diarrhea and reduced defecation, all in the 600 mg/kg group. At necropsy, the following were detected in does: light cortex of the kidney in 0/0/0/5 does corresponding to 0/70/200/600 mg/kg, watery feces in the large intestines of 0/0/0/5 does, and incarcerated placenta in 0/0/0/2 does. A marginal decrease in the mean number of live fetuses per litter was detected in high dose animals (5.36/5.31/5.77/4.38 corresponding to 0/70/200/600 mg/kg), along with an increased mean number of resorptions (0.5/0.69/0.23/1.88), the latter being due to increased early resorptions. Mean fetal weights and mean placental weights in high dose animals were largely unaffected (92% and 93% of control for fetal and placental weights, respectively). Fetal skeletal variations including fused sternbrae, irregularly shaped sternbrae, accessory sternbrae, accessory ribs and shortened twelfth rib(s) were elevated in high dose fetuses (fetal incidences in %: 12/19/9/31% corresponding to 0/70/200/600 mg/kg). In contrast, fetal malformations and retardations were unaffected. **No adverse effects. Maternal NOEL: 200 mg/kg/day** (based on reduced bodyweights, reduced food consumption, increased mortality, increased clinical signs, and increased abnormal findings at necropsy in does administered 600 mg/kg/day); **Developmental NOEL: 200 mg/kg/day** (based on an increased incidence of skeletal variations in fetuses from does administered 600 mg/kg/day). **Study acceptable** (Vidair 12/16/99).

GENE MUTATION

52216-027; 168816; "Report on the Study of Reg. No. 150 732 in the Ames Test (Standard Plate Test with *Salmonella typhimurium*) dated May 4, 1984" (BASF Aktiengesellschaft, Crop Protection Division, Doc. No. 84/0156, 5/4/84). *S. typhimurium* tester strains TA1535 and TA100 (reverted to histidine autotrophy by base substitution) and tester strains TA1537 and TA98 (reverted by frameshift mutations) were exposed to test article Reg. No. 150 732 (Test Substance No. 84/150; <u>puritiy not indicated</u>) at 0 (DMSO vehicle), 20, 100, 500, 2500 and 5000 ug/plate, with or without activation by an S9 microsomal fraction (source of S9 not given). The time interval of bacterial exposure to the test article, as well as the time allowed for colony formation, were not given. Each condition was tested once and assayed in three replicate plates. Positive controls were functional. Bacterial toxicity exhibited by TA100 at 2500 and 5000 ug/plate (in the presence of S9) indicated that the test article was present at sufficiently high concentrations. The test article had no effect on the reversion frequency. **No adverse effects indicated. Study unacceptable (missing information)** (Vidair 12/29/99).

**52216-027; 168817; "Report on the Study of Registration Number 150 732 in the Ames *Salmonella*/mammalian microsome mutagenicity test and reverse mutation assay-*E. coli* WP uvrA (standard plate test and preincubation test dated August 30, 1988)." (Engelhardt, G., BASF Aktiengesellschaft, Dept. of Toxicology, Z470, 6700 Ludwigshafen/Rhein, Project ID No. 40M0282/854179,Doc. No. 88/0358, 8/18/88). *S. typhimurium* tester strains TA1535 and TA100 (reverted to histidine autotrophy by base substitution), strains TA1537 and TA98 (reverted by frameshift mutation), and *E. coli* tester strain WP2 uvrA (reverted to tryptophan autotrophy by base

substitution) were exposed to test article Reg. No. 150 732 (Batch No. III/2N57; 98.3% purity) at 0 (vehicle only), 20, 100, 500, 2500 or 5000 ug/plate, with or without activation by an S9 microsomal fraction. Exposure was at 37°C for 48 hours, with or without an additional 20 min 37°C pre-incubation period (in which the bacteria, S9 fraction and test article were incubated together prior to the addition of agar). Each condition was tested once and assayed in three replicate plates. The test article had no effect on the reversion frequency of any tester strain. Positive controls were functional. There may have been some cytotoxicity in the *E. coli* cultures at 2500 and 5000 ug/plate. **No adverse effects indicated. Study acceptable** (Vidair 12/30/99).

52216-027; 168818; "Addendum to MRID 41063528 (Reg. Doc. # 88/0358)-Report on the Study of Reg. No. 150 732 in the Ames *Salmonella*/Mammalian Microsome Mutagenicity Test and Reverse Mutation Assay-*E. coli*" (Engelhardt, G., BASF AG, Dept. of Toxicology, 6700 Ludwigshafen, Doc. No. 88/5520, 8/18/88). The EPA criticized the author of the bacterial mutagenicity study reported in Record # 168817, for using too high a concentration of S9 fraction in the test mix (30% versus 4% recommended by the EPA). The author responded that a 30% level had been accepted by the EPA in the past, and that he believed the 4% value was a recommendation by the EPA rather than a strict rule. The EPA also asked for the results of the chemical analysis of the dosing material. The author responded by reporting that toxicity occurred in the background bacterial lawn for TA1537 (-S9) and TA100 (+S9), suggesting that the upper practical limit of test article exposure had been achieved. Stability data were presented, demonstrating by HPLC analysis that the test article was stable for at least 1 day in DMSO and at least 2 days in an aqueous solution. **Study supplemental** (Vidair 12/30/99).

52216-027; 168819; "Report on the Study of Reg. No. 150 732, Batch N55 in the Ames Test" (Engelhardt, G., BASF Aktiengesellschaft, Dept. of Toxicology, 6700 Ludwigshafen, Germany, Document No. 88/0172, 7/19/85). *S. typhimurium* tester strains TA1535 and TA100 (reverted to histidine autotrophy by base substitution), and tester strains TA1537 and TA98 (reverted by frameshift mutation) were exposed to test article Reg. No. 150 732 (Batches N55 and N15; purity not indicated) at 0 (vehicle only), 20, 100, 500, 2500 or 5000 ug/plate, with or without activation by an S9 microsomal fraction. Exposure was for 48 hours at 37°C. Batch N55 was tested in all 4 tester strains in two identical trials, with 3 replicate plates per condition. Batch N15, synthesized by an obsolete purification process, was used as a positive control in a single trial comparison to N55 in TA1535, again with 3 replicates per condition. Positive controls were functional. Test article Batch N55 had no effect on the reversion frequency. As found previously, Batch N15 did cause a small increase in reversion at 2500-5000 ug/plate of from 2.4-2.6 fold that of controls in the absence of S9 to from 4.0-5.7 fold in the presence of S9. There may have been some bacterial toxicity exhibited by TA100 in the presence of S9 at 2500 and 5000 ug/plate, as suggested by the decreased numbers of revertant colonies. **No adverse effects indicated. Study not acceptable but may be upgradeable with submission of test article purity** (Vidair 12/31/99).

52216-027; 168820; "Report on the Study of Reg. No. 150 732 Batch N57 and Batch N15 in the Ames Test" (Engelhardt, G., BASF Aktiengesellschaft, Dept. of Toxicology, 6700 Ludwigshafen, Germany, Document No. 88/0173, 12/2/85). *S. typhimurium* tester strains TA1535 and TA100 (reverted to histidine autotrophy by base substitution), and tester strains TA1537 and TA98 (reverted by frameshift mutation) were exposed to test article Reg. No. 150 732 (Batches N57 and N15; purity not indicated) at 0 (vehicle only), 20, 100, 500, 2500 or 5000 ug/plate, with or without activation by an S9 microsomal fraction. Batch N15 was synthesized by an obsolete purification process, and had been used to induce a low level of mutations in previous studies (see Record

#168819). Exposure was for 48 hours at 37°C. Batch N57 was evaluated in one trial in all 4 tester strains, along with N15 administration to TA1535. In a second trial, both batches were compared in TA1535. Both trials were conducted with 3 replicate plates per condition. Positive controls were functional. Batch N57 had no effect on the reversion frequency. Batch N15 induced reversion in both trials in TA1535, ranging from 2.2-8.5 fold over control reversion frequencies at 2500 and 5000 ug/plate. **No adverse effects indicated. Study unacceptable but upgradeable with purity of test article** (Vidair 1/4/00).

** 027; 168821**; "**Report on a Point Mutation Test Carried Out on CHO Cells (HGPRT locus) with the Test Substance Reg. No. 150 732 (BAS 514…H)"; (R. Jackh; BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen/Rhein, FRG; Project No. 50M0282/854185; Doc. No. 90/0008;1/8/90); Chinese hamster ovary cells (K1) were exposed to Reg. No. 150 732 (Quinclorac) (technical grade) (purity: 97.38%) at concentrations ranging from 0.0464 to 2.15 mg/ml for 4 hours at 37° C with and w/o activation. Two trials were performed with duplicate cultures for each treatment level. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. There was no treatment-related increase in mutation frequency. **No adverse effect indicated. Study acceptable.** (Moore, 3/8/00)

52216-032; 168831; "Report on a Point Mutation Test Carried out on CHO Cells (HGPRT Locus) with the Test Substance Reg. No. 150 732 (BAS 514 H)" (Jäckh, R., BASF Aktiengesellschaft, Dept. of Toxicology, Ludwigshafen, W. Germany, Document No. 86/0214, 7/18/86). Chinese hamster ovary (CHO) cells strain K1, each cell containing a wild type HGPRT gene, were exposed to test article Reg. No. 150 732 (Batch No. N32; 96.5% pure) in Ham's F12 medium without added serum for 4 hours at 37°C, with or without activation by an S9 microsomal fraction. Treatment levels ranged from 0.0464 to 2.15 mg/ml. Following 9 days of incubation in normal medium, HGPRT^{-} mutations were detected by measuring colony formation in medium containing 6-thioguanine. No mutant colonies were detected from among the 5 replicate flasks/dose level used in the trial with activating S9 fractions, whereas the positive control was functional. In the absence of activation, mutant colonies were detected at different dose levels in each of the three trials. In no case was a dose-response observed, suggesting that the mutant colonies did not result from exposure to the test article. Therefore, the data suggest that the test article is not mutagenic under the conditions of this study. **No adverse effects indicated. Study acceptable (Vidair 2/16/00).

CHROMOSOME EFFECTS

028; 168823; "Comparative *In Vitro* Cytogenetics Investigations in Human Lymphocytes with Reg. No. 150 732, batch CH 384 121 and Reg. No. 150 732, batch N32"; (G. Engelhardt; BASF, Department of Toxicology, D-6700 Ludwigshafen/Rhein, FRG; Project No. 30M0383/8368; Doc. No. 87/0555; 1/9/87); Human lymphocytes were treated with Reg. No. 150 732 (Quinclorac) (technical grade) (batch no. N32) (purity: 96.5%) or Reg. No. 150 732 (batch no. CH 384 121) (purity: >98%) at a concentration of 1000 µg/ml under conditions of non activation at 37° C for 24 hours following 48 hours of stimulation with phytohemagglutinin (PHA). The cells were cultured in the presence of Colcemid (1.33 µg/ml) the last 2 to 3 hours of the incubation period. There were duplicate cultures for each treatment level. A treatment-related increase in the incidence of chromosomal aberrations was noted for both test materials ($p<0.01$**). Possible adverse effect indicated**: increased incidence of chromosomal aberrations. **Study supplemental** (study was not performed according to guideline requirements). (Moore, 3/24/00)

** 029; 168825; "Report on the Cytogenetic Study *In Vivo* of Reg. No. 150 732 in Chinese Hamsters; Bone Marrow Chromosome Analysis: Single Oral Administration"; (G. Engelhardt; BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen/Rhein, FRG; Doc.

No. 88/0186; 6/13/88); Two trials were performed. In Trial 1, five hamsters/sex/group were dosed with 0, 2000, 4000 or 8000 mg/kg of Reg. No. 150 732 (Quinclorac) (technical grade) (purity: 98.3%) by gavage and euthanized 24 hours after dosing. An additional 5 animals/sex/time point were dosed by gavage with 8000 mg/kg and euthanized at 6 or 48 hours post dose. Five animals/sex received 40 mg/kg of cyclophosphamide as the positive control and were euthanized 24 hours after dosing. Only the 8000 mg/kg treatment group along with the negative and positive control groups were included in the second trial. Each animal was treated ip with 3.3 mg/kg of Colcemid two hours prior to sacrifice. One hundred metaphases/animal were examined for chromosomal aberrations. The animals treated with the test material exhibited signs of irregular respiration, apathy and poor general appearance. One female in the 8000 mg/kg treatment group, trial #2, died. In trial #1, there were an increased number of metaphases with aberrations including gaps in the 8000 mg/kg treatment group at 24 hours ($p<0.01$) (but not significant excluding gaps). Upon reexamination in trial #2, the number of aberrant metaphases with and without gaps was not significantly greater than that of the controls. **No adverse effect indicated. Study acceptable.** (Moore, 2/15/00)

**** 030; 168827; "**Report on the *In Vitro* Cytogenetic Investigations in Human Lymphocytes with Reg. No. 150 732"; (G. Engelhardt; BASF Aktiengesellschaft, Department of Toxicology, Z 470, D-6700 Ludwigshafen/Rhein, FRG; Doc. No. 86/0371; 11/25/86); Human lymphocytes (whole blood) were treated with Reg. No. 150 732 (Quinclorac) (technical grade) (purity: 96.5%) at concentrations ranging from 125 to 1500 μg/ml (non activation) or 250 to 2500 μg/ml (activation) at 37° C for 24 hours (non activation) or 2 hours, followed by an additional 22 hours of incubation (activation), following 48 hours in culture with phytohemaglutinin. The cells were cultured in the presence of Colcemid (1.33 μg/ml) the last 2 to 3 hours of the incubation period. There were duplicate cultures for each treatment level. An Aroclor 1254-derived rat liver S9 fraction was used to metabolize the test material. A treatment-related increase in the incidence of chromosomal aberrations was noted for the non-activated cultures ($p<0.01$). The highest treatment level examined in the activated samples demonstrated an increase in the incidence of aberrant chromosomes with gaps ($p<0.05$). However, there was a treatment-related reduction in the mitotic index indicative of increasing cytotoxicity. The chromosomal aberrations may have been a secondary consequence of the cytotoxicity. **Possible adverse effect indicated:** increased incidence of chromosomal aberrations. **Study acceptable.** (Moore, 2/16/00)

**52216-031; 168828; "Report on the Cytogenetic Investigations in NMRI Mice After a Single Oral Administration of Registration Number 150 732-Micronucleus Test" (Engelhardt, G., BASF Aktiengesellschaft, Dept. of Toxicology, Z470, 6700 Ludwigshafen/Rhein, FRG, Project No. 26M0150/8452, Doc. No. 86/0018, 2/3/86). Fifteen male and fifteen female NMRI mice were administered Reg. No. 150 732 (Batch No. N32; 96.5% pure) at 2000 mg/kg, while 5 animals/sex were administered 1000 mg/kg, 500 mg/kg, or vehicle only (0.5% carboxymethyl cellulose). Positive controls (5 animals/sex) received 40 mg/kg of cyclophosphamide. Administration was by single-dose oral gavage. At 16, 24, and 48 hours after administration (highest dose animals), or at 24 hours after administration (1000 and 500 mg/kg, negative control, positive control), 5 animals/sex were sacrificed and smears prepared from the bone marrow of their femora. One thousand polychromatic erythrocytes per animal were evaluated for micronuclei. Normochromatic erythrocytes in the same fields were also scored. Animals administered the test article exhibited irregular respiration, piloerection, and apathy (the two highest dose levels only). Necropsy of all sacrificed animals revealed no abnormalities. The percentages of polychromatic or normochromatic erythrocytes containing micronuclei were similar in treated animals and negative controls. Positive controls were functional. At 1000 and 2000 mg/kg the test article caused a small inhibition of erythropoiesis as shown by small decreases in the ratios of polychromatic to normochromatic erythrocytes. In summary, the test article was neither clastogenic nor a disrupter

of mitotic spindle function under the conditions of this study. **No adverse effects indicated. Study acceptable** (Vidair 2/15/00).

DNA DAMAGE

028; 168824; "Report on the Evaluation of Reg. No. 150 732 (ZNT No. 84/150) in the *In Vitro* Rat Primary Hepatocytes Unscheduled DNA Assay, Dated June 1986"; (M.A. Cifone; Litton Bionetics, Inc., Kensington, MD; Project No. 20991; Doc 86/0135; 6/6/86); Primary rat hepatocyte cultures were exposed to Reg. No. 150 732 (Quinclorac) (technical grade) (purity not reported) at concentrations ranging from 101 to 2020 µg/ml for 18 to 19 hours at 37° C. Vehicle control (DMSO: 1%) and positive control (2-AAF, 0.05 µg/ml) cultures were included in the assay. There were 3 cultures/treatment level with the results of a single trial being reported. There was no treatment-related increase in unscheduled DNA synthesis. **No adverse effect indicated. Study unacceptable**, possibly upgradeable with the submission of test material purity. (Moore, 3/27/00)

** 028; 168894; "*In Vivo/In Vitro* Unscheduled DNA Synthesis in Rat Hepatocytes with Reg. No. 150 732/BAS 514 H"; (R. Fautz; Cytotest Cell Research GMBH & Co., D-6101 Robdorf, FRG; Doc. No. 91/10965; 10/24/91); Five male rats/group were dosed with 0, 100 or 1000 mg/kg of Reg. No. 150 732 (Quinclorac) (technical grade) (purity: 97.38%) and euthanized 16 hours after dosing. An additional 5 animals were treated with 1000 mg/kg and euthanized 4 hours post dose. The 5 animals in the positive control group were treated with 100 mg/kg of 2-acetylaminofluorene (2-AAF) and euthanized 16 hours after dosing. Upon recovery of the hepatocytes, a primary culture was established and the cells were exposed to ^{3}H-thymidine (5 µCi/ml) for 4 hours, followed by further incubation overnight with unlabeled thymidine. There were 3 cultures/animal in one trial. There was no treatment-related increase in unscheduled DNA synthesis. **No adverse effect indicated. Study acceptable.** (Moore, 2/14/00)

52216-032; 168895; "Mutagenicity Evaluation of BAS 514..H in the Rec-Assay with *Bacillus Subtilis*" (Hoorn, A.J.W., Hazleton Biotechnologies, Landjuweel 11, 3905 Pe Veenendaal, Netherlands, Report No. 87/0025, 10/16/86). *Bacillus subtilis* indicator strains H17 (rec+) and M45 (rec-) were tested for growth inhibition in response to Reg. No. 150 732 (Batch No. N57 III/2, 98.3% purity) at concentrations ranging from 1 to 10,000 ug per plate. Exposure was at 37°C for 24 to 48 hours, in the presence or absence of an S9 microsomal activating system. Each dose level was tested in 3 replicate plates. Three independent trials were run under both activating and nonactivating conditions. Two of three trials under nonactivating conditions showed similar zones of growth inhibition in the rec+ and rec- strains at the highest dose tested (10,000 ug/plate). One of three trials under activating conditions gave a similar result. Positive controls (100 ug/plate of sterigmatocystin for activated and 5 ul/plate of methylmethanesulfonate for nonactivated) showed consistently larger zones of inhibition in the rec- strain compared to the rec+ strain, consistent with these chemicals' ability to kill the bacteria by damaging their DNA. These data indicate that the test article is equally toxic to both rec+ and rec- strains, and suggest that the toxicity is not due to DNA damage. **No adverse effects indicated. Study acceptable (Vidair 2/16/00).

NEUROTOXICITY

No study submitted.

SUBCHRONIC STUDIES

**52216-011; 168793; "Report on the Study of the Subchronic Toxicity of Reg. No. 150 732 in Rats after 3 Months' Administration in the Diet – Volumes I & II (86/0057), Amendment I (88/0163) and Amendment II (88/0229)"; (B. Kuhborth; BASF Aktiengesellschaft, Department of

Toxicology, D-6700 Lugwigshafen, FRG; Reg. Doc. No. 88/5145; Ten rats/sex/group were dosed in the diet with 0, 1000, 4000, or 12000 ppm of Reg. No. 150 732 (Quinclorac) (technical grade) (purity: 96.5%) for 3 months ((M): 0, 76.8, 302.3, 929.9 mg/kg/day, (F): 0, 86.7, 358.0, and 1035.4 mg/kg/day). The 12000 ppm treatment group demonstrated lower mean body weights and food consumption although the values were not statistically significant from those of the controls. Various hematological and clinical chemistry parameters for the high dose animals were statistically different from those of the control animals. However, no treatment-related effects were apparent at a dose level equivalent to the limit test level. There were no treatment-related lesions noted in the microscopic examination. There was no target organ. **No adverse effect evident. NOEL:** (M/F) 4000 ppm (based upon reduced food consumption and lower mean body weights of the 12000 ppm treatment group (apparent diminished palatability of the diet)) ((M): 302.3 mg/kg/day, (F) 358.0 mg/kg/day). **Study acceptable.** (Moore, 12/10/99)

52216-012; 168794; "Report on the Study of the Oral Toxicity of Reg. No. 150 732 in Mice after 3 Months' Administration in the Diet, and Pathology Report"; (K. Schilling; BASF Aktiengesellschaft, Department of Toxicology, D-6700 Lugwigshafen/Rhein, W. Germany; Reg. Doc. No. 88/0337; 4/25/86); Ten mice/sex/group were treated in the diet with 0, 4000, 8000 or 16000 ppm of Reg. No. 150 732 (purity: 98.29%) for 3 months ((M): 0, 1000.4, 2202.4, 4555.5 mg/kg/day; (F): 0, 1467.4, 2735.5, 5953.1 mg/kg/day) . No mortalities resulted from the treatment. The mean body weights of the males in the 8000 and 16000 ppm treatment groups were lower than that of the controls ($p<0.01$). The mean body weights of the females in these groups as well as the 4000 ppm treatment group were lower than that of the controls ($p<0.05$, 4000 ppm, $p<0.01$, 8000 and 16000 ppm). Food consumption was not apparently affected by the treatment. The kidney was a possible target organ. The mean blood urea level for the males was greater in the 8000 and 16000 ppm treatment groups. The mean kidney weights for the males were less in all three treatment groups (4000 and 8000 ppm, $p<0.05$, 16000 ppm, $p<0.01$). Although the blood urea levels for the females in the treated groups were greater than that of the control, the differences were not statistically significant. The mean kidney weight of the 16000 ppm females was lower than that of the control ($p<0.01$). Histopathological examination of the kidneys did not reveal any apparent treatment-related lesions. **No adverse effect indicated. NOEL:** (M/F) < 4000 ppm ((M) <1000.4 mg/kg/day, (F) <1467.4 mg/kg/day) (based upon the lower mean kidney weights for the males and the lower mean body weights for the females of the 4000 ppm treatment group). **Study unacceptable, not upgradeable** (ophthalmology and complete clinical chemistry evaluations were not performed). (Moore, 12/13/99)

552216-013; 168795; "Report on the Study of the Oral Toxicity of Reg. No. 150 732 in Mice after 3 Months' Administration in the Diet, and Pathology Report"; (K. Schilling; BASF Aktiengesellschaft, Department of Toxicology, D-6700 Lugwigshafen, W. Germany; Reg. Doc. No. 88/0338; 8/11/88); Ten mice/sex/group were treated in the diet with 0 or 500 ppm of Reg. No. 150 732 (purity: 98.29%) for 3 months ((M): 0, 85.4 mg/kg/day, (F): 0, 129.8 mg/kg/day). No mortalities resulted from the treatment. There were no treatment-related clinical signs nor treatment-related effects upon mean body weight or food consumption. The hematology parameters and clinical chemistry parameters were not affected by the treatment. Macroscopic examination of the liver revealed slight yellow discoloration in one female in the treated group and yellow foci in one male and one female of the treated group. Two females in the treated group had several foci in the stomach. No histopathological examination was performed. **No adverse effect indicated. NOEL not determined; Study supplemental** (study was performed to ascertain a subchronic dietary NOEL). (Moore, 12/14/99)

52216-014; 168796; "Subacute 21-Day Repeated Dose Dermal Toxicity Study with Quinclorac in Rabbits"; (L. Ullmann *et. al.*; RCC, Research & Consulting Company AG, Itingen, Switzerland; Reg. Doc. No. 90/0021; 4/19/90); Ten New Zealand white rabbits/sex/group were treated dermally with 0 or 1000 mg/kg of Reg. No. 150 732 (Quinclorac) (technical grade) (purity: 98.29%) for six hours/day, 7 days/week for 3 weeks. An additional five rabbits/sex/group were treated in the same manner with 40 or 200 mg/kg/day of the test material. There were no mortalities nor treatment-related effects upon the mean body weights. Although some of the values in the hematology and clinical chemistry results for treated animals were statistically significant from the corresponding control values, there were no apparent treatment-related effects. There were no treatment-related effects upon the eyes. The mean kidney weight of the males in the 1000 mg/kg/day treatment group was greater than that of the control ($p<0.05$). However, no treatment-related microscopic lesions were evident in the kidney nor any of the other organs examined. A target organ was not identifiable. **No adverse effect indicated. Systemic and Dermal NOEL (M/F): 1000 mg/kg/day (HTD); **Study acceptable.** (Moore, 12/9/99)

IMMUNOTOXICITY

52216-0082, 258929, "BAS 514 H (Quinclorac): Immunotoxicity study in female C57BL/6J RJ Mice administration via the diet for 4 weeks"; 857; Mice; Experimental Toxicology and Ecology, BASF SE, Germany, Buesen, R., Strauss, V., Rey Moreno, M.C., Fabian, E., and van Ravenzwaay, B., Test facility project ID: 43C0081/01S005: 12/17/2010; BAS 514 H (Quinclorac), Batch No.479-480, 99.9% (w/w) pure, a beige solid, was administered to 8 female mice by diet at 0, 500, 1500 or 5000 ppm [mean test substance intake: 176, 439 and 1760 mg/kg/day for the 500, 1500 and 5000 ppm groups, respectively] for 28 days. An additional group of 8 female mice were given 10 mg/kg of cyclophosphamide monohydrate by gavage for 4 weeks. All mice were administered 0.5 mL sRBC (sheep Red Blood Cells, 4 x 10^8/mL) via intraperitoneal injection 6 days before blood sampling and necropsy. The mice were observed for vitality, general appearance, body weight and food consumption. At the end of the 28-day treatment period, all mice were euthanized, and organ weights were measured. A female mouse in the positive control group was sacrificed moribund on day 21 of study due to severe findings. Tremors, poor general condition and hunched posture were observed prior to its sacrifice. No test substance treatment related changes in body weight, bodyweight gains, food consumption, were observed. Reduced food consumption in the positive control treated females throughout the study period, reduced body weight and bodyweight changes at days 21 and 28 was observed. Reduced absolute and relative thymus weight in the positive control group, decreased spleen germinal centers in high dose group, reduced and absent germinal centers and reduced thymus cortex cellularity in the positive control group was observed at necropsy and histopathology examinations. Immunotoxicity examinations with anti-SRBC IgM ELISA showed reduced antibody titers in serum samples from positive control group, no such effects were seen in test substance treated groups. **NOEL (No Observed Effect Level) for immunotoxicity: 5000 ppm (1760 mg/kg/day) in female mice after 28 day treatment, due to no effect at the HDL; for general toxicity: 1500 ppm (439 mg/kg/day) due to decreased spleen germinal centers observed in the high dose group mice at histopathology examination. **Acceptable** (Pan& Leung, 4/22/2014).