

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Pyroxsulam

Chemical Code # 6030, Tolerance # 53115  
SB 950 # NA

Original date: 2/17/11

I. DATA GAP STATUS

<b>Chronic toxicity, rat:</b>	No data gap, no adverse effect indicated
<b>Chronic toxicity, dog:</b>	No data gap, no adverse effect indicated
<b>Oncogenicity, rat:</b>	No data gap, no adverse effect indicated
<b>Oncogenicity, mouse:</b>	No data gap, no adverse effect indicated
<b>Reproduction, rat:</b>	No data gap, no adverse effect indicated
<b>Teratology, rat:</b>	No data gap, no adverse effect indicated
<b>Teratology, rabbit:</b>	No data gap, no adverse effect indicated
<b>Gene mutation:</b>	No data gap, no adverse effect indicated
<b>Chromosome effects:</b>	No data gap, no adverse effect indicated
<b>DNA damage:</b>	No data gap, no adverse effect indicated
<b>Neurotoxicity:</b>	No data gap, no adverse effect indicated

Toxicology one-liners are attached.

All record numbers through 253227 were examined.

\*\* indicates an acceptable study.

Bold face indicates a possible adverse effect.

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

File name: T021711

Revised by R. Pan, 2/17/11.

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

### COMBINED, RAT

\*\*53115-0059 253218, "Two-Year Chronic Toxicity/Oncogenicity and Chronic Neurotoxicity Study in Fisher 344 Rats", 835; Fisher 344 Rats; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 031014, 11/2/05; Stebbins, K. and Brooks, K. ; XDE-742; 98.0%, Lot# E0952-52-01, groups of 65 Fisher 344 Rats /sex received diets containing 0, 10, 100 or 1000 mg/kg/day XDE-742 for up to one or two years ( 10 rats/sex/dose were necropsied after one year for chronic toxicity, 5 rats/sex/dose were necropsied after one year for chronic neurotoxicity, 50 rats/sex/dose were necropsied after two years for oncogenicity study). [Time-weighted average dosages for males were: 0, 10.1, 101.0, or 1012 mg/kg/day, those for females were: 0, 10.2, 101.6, or 1018 mg/kg/day]. No treatment related difference in mortality, body weight or feed consumption was observed. Increased incidence of perineal soiling of urine was observed in high dose males and females over the two year period compared to the control groups. Increase of absolute and relative liver weight was observed in high dose males at the end of 12 month and in high dose females at the end of 24 month. Statistically significant decrease of alanine aminotransferase and increased cholesterol concentrations were observed in high dose males at 3, 6, 12 and 24 month. No treatment related increase of neoplasms was observed in male or female rats at any dose level. No adverse effects. **No observed effect level (NOEL):** 10 mg/kg/day for male and female mice for the 2-year chronic toxicity study [Time-averaged dosages 10.1 and 10.2 mg/kg/day for males and females, respectively.] based on perineal soiling. **Acceptable** (Pan, 12/24/10).

### CHRONIC TOXICITY, RAT

No study on file.

### CHRONIC TOXICITY, DOG

\*\*53115-0057 253209, "XDE-742: One-Year Dietary Toxicity Study in Beagle Dogs", 831; Beagle Dogs; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 031012, 9/21/04; Stebbins, K.E., Dryzga, M. D. ; XDE-742; 98.0%, Lot# E0952-52-01, groups of 4 Beagle Dogs /sex received diets containing 0, 0.05, 0.3, or 2.0% XR-742 for one year. [Mean test substance intake for males were: 0, 13.2, 93.0, or 619.6 mg/kg/day, those for females were: 0, 17.1, 88.7, or 589.1 mg/kg/day]. No mortality. There were no test substance related clinical signs, body weight or feed consumption changes. Treatment related increase of cholesterol and alkaline phosphatase concentrations were observed in high dose males and females compared with the control males and females. Statistically significant increase of absolute and relative liver weight was observed in high dose males and females. **No observed effect level (NOEL):** 0.3% (93.0 and 88.7 mg/kg/day for male and female Beagle Dogs, respectively) for the one-year dietary toxicity study. **Acceptable** (Pan, 12/16/10).

### ONCOGENICITY, RAT

No study on file.

### ONCOGENICITY, MOUSE

\*\*53115-0058 253217, "XDE-742: 18-Month Dietary Oncogenicity Study in CD-1 Mice", 832;

mice; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 031015, 12/15/05; Johnson, K., et al. ; XDE-742; 98.0%, Lot# E0952-52-01, groups of 50 mice/sex received diets containing 0, 10, 100 or 1000 mg/kg/day XDE-742 for up to 18 months. [Time-weighted average dosages for males were: 0, 10, 100, or 932 mg/kg/day, those for females were: 0, 10, 101, or 1012 mg/kg/day]. No treatment related difference in mortality. There were no test substance related clinical signs, body weight or feed consumption changes. Statistically significant increase of absolute and relative liver weight, higher incidence and number of hepatic "Mass-Nodules", and higher incidence of foci of altered hepatocytes were observed in 1000 mg/kg/day group males. Slightly decreased absolute and relative kidney weights were observed in both males and females. **No observed adverse effect level (NOAEL):** 100 mg/kg/day for male and 1000 mg/kg/day for the female mice for the 18-month dietary toxicity study [Time-averaged dosages 100 and 1012 mg/kg/day for males and females, respectively.] **Acceptable** (Pan, 12/20/10).

### REPRODUCTION, RAT

\*\* 53115-0056; 253208; "XDE-742: Two-Generation Dietary Reproductive Toxicity Study in CD Rats"; (E.W. Carney, C.L. Zablony, K.E. Stebbins; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, MI; Study ID. 041012; 9/19/05); CD rats/sex/group received with 0, 100, 300 or 1000 mg/kg/day of XDE-742 (Pyroxsulam technical) (lot no. E0952-52-01; purity: 98%) in the diet for two generations. Twenty seven rats/sex/group in both the F0 and F1 generations were treated for 10 weeks prior to mating, during mating, and during the 3 weeks of gestation and 3 weeks of lactation. The F1 generation was derived from the offspring at the time of weaning. The F0 and F1 parental generations did not demonstrate any treatment-related effects upon mean body weight or food consumption. In the necropsy examination, no treatment-related effect on organ weights was evident. No treatment-related lesions were noted in the histological examination. There were no treatment-related effects upon the reproductive parameters or the development of the offspring of either generation. **No adverse effect indicated. Parental NOEL:** (M/F) 1000 mg/kg/day (based upon the lack of treatment-related effects at the highest dose tested); **Reproduction NOEL:** 1000 mg/kg/day (based upon the lack of treatment-related effects at the highest dose tested); **Developmental NOEL:** 1000 mg/kg/day (based upon the lack of treatment-related effects at the highest dose tested); **Study acceptable.** (Moore, 12/13/10)

### TERATOLOGY, RAT

\*\* 53115-0052; 253204; "XDE-742: Oral Gavage Developmental Toxicity Study in Crl:CD(SD) Rats "; (E.W. Carney, B. Tornesi; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, MI; Study ID. 051053; 10/13/05); Twenty six time-mated female CD rats/group were dosed orally by gavage with 0, 100, 300, or 1000 mg/kg/day of XDE-742 (Pyroxsulam technical) (lot no. E0952-52-01; purity: 98.0%) from day 6 through day 20 of gestation. The vehicle was aqueous 0.5% Methocel A4M. There was no treatment-related effect upon the dams' mean body weight gain or food consumption. An increased incidence of skeletal malformations was noted for the fetuses in the 300 mg/kg group. However, the incidence of skeletal malformations for the 1000 mg/kg group fetuses was not apparently affected by the treatment. Therefore, this observation was not deemed to be treatment-related. **No adverse effect indicated. Maternal NOEL:** 1000 mg/kg/day (based upon the lack of treatment-related effects on the highest dose tested); **Developmental NOEL:** 1000 mg/kg/day (based upon the lack of treatment-related effects on the highest dose tested); **Study acceptable.** (Moore, 12/9/10)

### TERATOLOGY, RABBIT

\*\* 53115-0051; 253203; "Oral Prenatal Developmental Toxicity Study of XDE-742 in Rabbits "; (E.D. Slotter; WIL Research Laboratories, LLC, Ashland, OH; Study No. WIL-406015; 12/21/05); Twenty six time-mated female New Zealand White rabbits/group were dosed orally by gavage with 0 (aqueous 0.5% (w/v) methylcellulose), 30, 100, or 300 mg/kg/day of XDE-742 (Pyroxsulam technical); lot no. E0952-52-01; purity: 98.0%) from day 6 through day 28 of

gestation. One female in the 30 mg/kg group was found dead on day 19 due to a dosing error. One doe each in the 100 and 300 mg/kg groups was found dead on day 18. Their cause of death was not ascertained. One female in the 30 mg/kg group aborted on day 26. There was no apparent treatment-related effect upon the maternal mean body weight gain or food consumption. In the fetal examination, 6 and 3 of the fetuses in the 100 mg/kg group suffered lobular dysgenesis of the liver and lobular agenesis of the lungs, respectively. However, these fetuses were from one litter each. In addition, only one fetus each had these malformations in the 300 mg/kg group. **No adverse effect indicated. Maternal NOEL:** 300 mg/kg/day (based upon the lack of treatment related effects on the does in the 300 mg/kg group); **Developmental NOEL:** 300 mg/kg/day (based upon the lack of treatment effects on the fetuses in the 300 mg/kg/day group). **Study acceptable.** (Moore, 12/2/10)

### GENE MUTATION

\*\* 53115-0060; 253219; "Evaluation of XDE-742 in the Chinese Hamster Ovary Cell/Hypoxanthine-Guanine-Phosphoribosyl Transferase (CH)/HGPRT) Forward Mutation Assay"; (S.D. Seidel, M.R. Schisler, J.M. Grundy; Toxicology & Environmental Research and Consulting, The Dow Chemical Co., Midland, MI; Study ID No. 041003; 8/23/04); Chinese Hamster Ovary (CHO-K<sub>1</sub>BH<sub>4</sub>) cells were exposed to XDE-742 (Pyroxsulam technical) (lot no. EO952-52-01; purity: 98%) at concentrations ranging from 12.5 to 200 ug/ml for 4 hours at 37° C under conditions of both non-activation and activation 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 the mutation frequency of the 6-thioguanine-resistant colonies. The positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 12/2/10)

\*\* 53115-0067; 253226; "*Salmonella typhimurium/Escherichia coli* Reverse Mutation Assay (Standard Plate Test and Preincubation Test) with XDE-742/BAS 770H"; (G. Engelhardt, E. Leibold; Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany; Project No. 40M0298/034051; 12/4/03); *Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 and *Escherichia coli* strain WP2 uvrA were exposed to concentrations of XDE-742/BAS 770H (batch no. EO952-52-01; purity: 98%) ranging from 20 to 5000 ug/plate in the 1<sup>st</sup> trial, from 500 to 2000 ug/plate in the 2<sup>nd</sup> trial and from 62.5 to 2000 ug/plate in the 3<sup>rd</sup> trial. All three trials were performed with and without rat liver activation. In the 1<sup>st</sup> and 2<sup>nd</sup> trials, the strains were exposed to the test material, which had been plate incorporated, for 48 to 72 hours at 37° C. In the 3<sup>rd</sup> trial, the strains were preincubated with the test material for 20 minutes prior to being incubated for 48 to 72 hours, using the plate incorporation method. There were triplicate plates per treatment level. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. **No adverse effect indicated.** There was no increase in the incidence of revertant colonies under conditions of either activation or non-activation. Positive controls were functional. **Study acceptable.** (Moore, 12/7/10)

### CHROMOSOME EFFECTS

\*\* 53115-0061; 253220; "Evaluation of XDE-742 in an *In Vitro* Chromosomal Aberration Assay Utilizing Rat Lymphocytes"; (G.D. Charles, M.R. Schisler; Toxicology & Environmental Research and Consulting, The Dow Chemical Co., Midland, MI; Study ID. 041005; 8/23/04); Primary lymphocyte cultures, procured from the whole blood of male Sprague-Dawley rats

(stimulated with PHA for 48 hours), were treated with 3.125 to 200 ug/ml of XDE-742 (Pyroxsulam technical) (lot no. EO952-52-01; purity: 98%) for 4 hours (both non-activation and activation), followed by 20 hours of incubation and with 1.56 to 200 ug/ml of the active ingredient for 24 hours (non-activation). An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. A treatment-related increase in chromosomal aberration was not evident under either conditions of non-activation or activation. The positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 12/8/10)

\*\* 53115-0062; 253221; "Evaluation of XDE-742 in an *In Vitro* Chromosomal Aberration Assay Utilizing Rat Lymphocytes"; (P.J. Spencer, J. Grundy; Toxicology & Environmental Research and Consulting, The Dow Chemical Co., Midland, MI; 7/12/04); Six CD-1 mice/sex/group were dosed orally by gavage with 0 (aqueous 0.5% methocel), 500, 1000 or 2000 mg/kg/day of XDE-742 (Pyroxsulam technical) (lot no. EO952-52-01; purity: 98%) for 2 consecutive days. Twenty-four hours after the second dose, all of the surviving animals were euthanized. In addition, 6 animals/sex were dosed with 120 mg/kg of cyclophosphamide (positive control) and euthanized at 24 hours post-dose. Bone marrow samples from the femurs of each animal were examined and the percentage of polychromatic erythrocytes (PCE) which were micronucleated was determined in 2000 PCEs per mouse. The percentage of PCE's in the erythrocyte population was calculated as well. There was no treatment-related increase in the percentage of micronucleated PCEs. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 12/9/10)

### DNA DAMAGE

\*\* 53115-0063; 253222; "XDE-742: Measurement of Unscheduled DNA Synthesis in Mouse Liver Using an *In Vivo/In Vitro* Procedure"; (C. Beevers; Covance Laboratories Ltd, Harrogate, North Yorkshire HG3 1PY, England; Study No. 295/169; 12/4/06); Six CD-1 male mice/group/time point were dosed with 0 (aqueous 0.5% (w/v) methylcellulose), 1000 or 2000 mg/kg of XDE-742 (Pyroxsulam technical) (batch no. TSN103826; purity: 98%) and euthanized at 2 to 4 (Assay 1) or 12 to 14 (Assay 2) hours after dosing. For positive controls, 6 males/group were treated with 10 mg/kg of dimethylnitrosamine (Assay 1) and euthanized 2 to 4 hours post-dose or 200 mg/kg of Fast Garnet GBC (Assay 2) and euthanized at 12 to 14 hours after dosing. Upon recovery of the hepatocytes, a primary culture was established and the cells were exposed to <sup>3</sup>H-thymidine (10 uCi/ml) for 4 hours, followed by further incubation overnight with unlabeled thymidine. Two cultures/animal in each trial, 50 cells/culture, were evaluated for the number of net grains/nucleus. There was no treatment-related increase in unscheduled DNA synthesis. The positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 12/10/10)

### NEUROTOXICITY

#### Chronic Neurotoxicity Study in Rats

\*\*53115-0064 253223, "XDE-742: Chronic Neurotoxicity Study in Fisher 344 Rats", 827; Fisher 344 Rats; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 031014, 11/2/05; Maurissen, J. ; XDE-742; 98.0%, Lot# E0952-52-01, groups of 10 Fisher 344 Rats /sex received diets containing 0, 10, 100 or 1000 mg/kg/day XDE-742 for one year (5 rats/sex/dose were necropsied after one year for chronic neurotoxicity). [Time-weighted average dosages for 65 males (including those for the chronic toxicity/oncogenicity studies) /dose were: 0, 10.3, 101.8, or 1024 mg/kg/day, those for 65 females (including those for the chronic toxicity/oncogenicity studies)/dose were: 0, 10.1, 101.3, or 1014 mg/kg/day]. No mortality. There were no test substance related clinical signs, body weight or feed consumption changes. Functional Observation Battery observations, Motor Activity counts, gross and histopathologic observations did not show treatment related neurotoxicity. **No**

**observed effect level (NOEL):** 1000 mg/kg/day for male and female rats for the 1-year chronic neurotoxicity study [Time-averaged dosages 1024 and 1014 mg/kg/day for males and females, respectively.] **Acceptable** (Pan, 12/27/10).

## METABOLISM STUDY

### Metabolism, Rat

\*\*53115-0065; 253224; "XDE-742: Metabolism and Pharmacokinetics of  $^{14}\text{C}$ -XDE-742 in Male Fischer 344 Rats Following Single and Repeated Oral Administration"; (S.C. Hansen, A.J. Clark, D.A. Markham, A.L. Mendrala; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, MI; Study ID. 041019; 12/13/05); Five groups of 4 male Fischer 344 rats/group were dosed once orally by gavage with 10 (Groups 1, 3, 4) or 1000 mg/kg (Group 2) of XDE-742-Het-2- $^{14}\text{C}$  (Inv. no. 1901, purity: 99.5%, specific activity: 36.6 mCi/mmol) or for 14 days with 10 mg/kg/day of unlabeled XDE-742 technical (lot no. 0952-52-1, purity: 98.0%), followed by a single dose of 10 mg/kg (Group 7) of the radiolabeled compound. A sixth group of 3 males was dosed iv with 10 mg/kg of the radiolabeled compound. Three males in Group 5 were dosed orally by gavage with 10 mg/kg of XDE-742-pyridine-2,6- $^{14}\text{C}$  (inv. no. 1905, purity: 100%, specific activity: 43.7 mCi/mmol). Urine and fecal samples were collected for up to 48 hours post-dose. The excretion profile was characterized and the pharmacokinetic parameters and the distribution of radiolabeling in specified tissues at 48 hours post-dose was determined and radiolabeled moieties were isolated and identified. In the excretion profile, 58 to 62% (urine plus cage wash) and 45 to 51% of the administered dose was recovered in the urine and feces, respectively, for the three groups (Groups 1, 5 and 7) dosed orally with single or multiple doses of 10 mg/kg of the test material. The position of the radiolabel did not affect the profile. Recovery of radiolabel in the expired air was negligible. In the iv study (Group 6), 17 to 18% of the dose was excreted via the biliary pathway. At the higher dose level Group 2), excretion via the feces increased to 69% (from 45 to 51%) with a concomitant decrease in the recovery of radiolabel from the urine. The liver was the predominant site of recovery in the tissues when dosing via the oral route was used. When the test material was administered via the iv route, a higher recovery of radiolabel was found in the kidneys. The GI tract with contents was the one other tissue in which a significant fraction of radiolabel was recovered. The parent compound was the principal radiolabeled entity which was recovered in the urine and feces (83.7 to 89.7% of the administered dose). The one other radiolabeled moiety which was identified was 2'-demethyl-XDE-742 which constituted 15 to 16% of the administered dose at 10 mg/kg and 3 to 4% of the dose at 1000 mg/kg. The unidentified radiolabeled compounds constituted less than 5% of the administered dose. The pharmacokinetic values (plasma) for the oral route were as follows; C<sub>max</sub>: 19.8 ug/ml, t<sub>max</sub>: 0.5 hours, T<sub>1/2</sub> (alpha): 1.33 hours, and T<sub>1/2</sub> (beta): 11.0 hours. **Study acceptable.** (Moore, 12/16/10)

## SUBCHRONIC STUDIES

### Subacute Toxicity Study in Rats

\*\*53115-0047 253199, "XR-742/BAS 770H: 90-Day Dietary Toxicity Study with a 28-Day Recovery in Fisher 344 Rats", 821; rats; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 021107, 3/25/03; Stebbins, K., et al. ; XR-742/BAS 770H; 98.0%, Lot# E0952-52-01, groups of 10 rats/sex received diets containing 0, 10, 100 or 1000 mg/kg/day XR-742/BAS 770H for 90 days. Two

additional groups of 10 rats/sex received 0 and 1000 mg/kg/day test diets for 90 days followed with 28 days of control diets in the recovering period. [Time-averaged dosages for males were: 0, 10.3, 103, or 1030 mg/kg/day, those for females were: 0, 10.2, 102, or 1020 mg/kg/day]. No mortality. Perineal urine soiling was observed in up to 50% of females from 1000 mg/kg/day groups. Statistically significant body weight decrease in 1000 mg/kg/day females was observed compared with control females from day 29 to day 92(main study) or day 113 (recovery group). At the end of the recovery period (day 120), the body weight decrease in 1000 mg/kg/day females was not statistically significant compared with control females. Body weight decreases in 1000 mg/kg/day group males were not statistically significant compared with control males. Statistically significant feed consumption increases in 1000 mg/kg/day males and females were observed compared with control rats from day 93 to day 100 (recovery group). Statistically significant increase of relative liver weight was observed in 1000 mg/kg/day group males at the end of the main study. In female, statistically significant increases of relative weights of kidney, liver, and brain were observed in 1000 mg/kg/day group at the end of the main study compared with control females. Statistically significant decreases of absolute weights of heart, ovary and thymus were observed in 1000 mg/kg/day group females at the end of the main study compared with control females, reflecting the body weight decrease. There were no statistically significant differences in absolute or relative organ weights between the control and high dose group animals at the end of the recovery period. Statistically significant decrease of ALT (alanine aminotransferase) concentration and increase of cholesterol concentrations were observed in 1000 mg/kg/day males at the end of the main study compared with the control males. At the end of the recovery period, there were no statistical significant differences for these parameters between the control and high dose males. **No observed adverse effect level (NOAEL):** 100 mg/kg/day for male and female rats for the 90-day dietary toxicity study with 28-day recovery period [Time-averaged dosages 103 and 102 mg/kg/day for males and females, respectively.] **Acceptable** (Pan, 11/30/10).

### **Four-week Dose Toxicity Study in Rats**

\*\*53115-0046 253198, "XR-742: 28-Day Dietary Toxicity Study in Fisher 344 Rats", 821; rats; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 011044, 8/16/01; Stebbins, K., Day, S. ; XR-742; 96.7%, Lot# 200100558-14B, groups of 5 rats/sex received diets containing 0, 10, 100, 500 or 1000 mg/kg/day XR-742 for 28 days. [Time-averaged dosages for males were: 0, 11.9, 120, 583, or 1165 mg/kg/day, those for females were: 0, 11.6, 112, 563, or 1140 mg/kg/day]. No mortality. Perineal urine soiling was observed in 3 females from 500 and 2 females from 1000 mg/kg/day groups without histopathologic alterations. There were no test substance related effects in body weight, feed consumption, clinical and anatomic pathology examinations. **No observed adverse effect level (NOAEL):** 1000 mg/kg/day for male and female rats for the 28-day dietary toxicity study [Time-averaged dosages 1165 and 1140 mg/kg/day for males and females, respectively.] **Acceptable** (Pan, 11/30/10).

### **Subacute Toxicity Study in Mice**

\*\*53115-0048 253200, "XR-742/BAS 770H: 90-Day Dietary Toxicity Study in CD-1 Mice", 821; mice; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 021106, 4/16/03; Johnson, K., et al. ; XR-742/BAS 770H; 98.0%, Lot# E0952-52-01, groups of 10 mice/sex received diets containing 0, 10,

100 or 1000 mg/kg/day XR-742/BAS 770H for 90 days. [Time-weighted average dosages for males were: 0, 10.3, 102, or 1030 mg/kg/day, those for females were: 0, 10.2, 103, or 1010 mg/kg/day]. No mortality. There were no test substance related clinical signs, body weight changes or feed consumption. Statistically significant increase of cholesterol concentrations were observed in 1000 mg/kg/day females compared with the control females. The increase of cholesterol concentration in males was not statistically significant compared with the control males. Statistically significant increase of absolute and relative liver weight was observed in 1000 mg/kg/day group males. **No observed adverse effect level (NOAEL):** 100 mg/kg/day for male and female mice for the 90-day dietary toxicity study [Time-averaged dosages 102 and 103 mg/kg/day for males and females, respectively.] **Acceptable** (Pan, 12/6/10).

### **13-Week Subchronic Oral Toxicity Study in Beagle Dogs**

\*\*53115-0049 253201, "XR-742/BAS 770H: 90-Day Dietary Toxicity Study in Beagle Dogs", 821; Beagle Dogs; Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan 48674, Laboratory Project ID: 021111, 5/22/03; Stebbins, K., Baker, P. ; XR-742/BAS 770H; 98.0%, Lot# E0952-52-01, groups of 4 Beagle Dogs /sex received diets containing 0, 0.03, 0.3, or 3.0% XR-742/BAS 770H for at least 90 days. [Time-weighted average dosages for males were: 0, 10.9, 91.3, or 884.1 mg/kg/day, those for females were: 0, 10.4, 98.6, or 1142.4 mg/kg/day]. No mortality. There were no test substance related clinical signs. Body weight decrease was observed in high dose male and female groups compared with control animals. Decrease of feed consumption was observed in high dose males only. Statistically significant increase of cholesterol and alkaline phosphatase concentrations were observed in high dose females compared with the control females at 7-week and 13-weeks. Statistically significant increase of absolute and relative liver weight was observed in high dose females. Histopathology examinations showed very slight panlobular hepatocyte hypertrophy in 3 high dose females. **No observed effect level (NOEL):** 0.3% (91.3 and 98.6 mg/kg/day for male and female Beagle Dogs, respectively) for the 90-day dietary toxicity study. **Acceptable** (Pan, 12/14/10).