CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Prohydrojasmon

Chemical Code # 6133, **Document Processing Number (DPN) #** 53229
SB 950 # NA

Original: 3/18/14
Revised: 9/23/15

DATA GAP STATUS

Chronic toxicity, rat:	No study on file*
Chronic toxicity, dog:	No study on file*
Oncogenicity, rat:	No study on file*
Oncogenicity, mouse:	No study on file*
Reproduction, rat:	No data gap, no adverse effect
Developmental toxicity, rat:	No data gap, possible adverse effect.
Developmental toxicity, rabbit:	Data gap, no study on file
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No study on file*
Neurotoxicity:	No study on file*

Toxicology one-liners are attached.
*The active ingredient is a biochemical and is used as a plant growth regulator. The studies identified with an asterisk are not required at this time for the registration of this active ingredient (see 40 CFR, section 158.2050 (2013)).

All record numbers for the above study types through 286461 (Document No. 53229-0009) were examined. This includes all relevant studies indexed by DPR as of 9/23/15.

In the 1-liners below:
indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.
File name: T150923
Revised by T. Moore, 9/23/15
NOTE: The following symbols may be used in the Table of Contents which follows:
* = data adequately address FIFRA requirement
† = study(ies) flagged as “possible adverse effect”
N/A = study type not currently required

This record contains summaries of studies. Individual worksheets may be useful for detailed assessment.

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METABOLISM AND PHARMACOKINETICS

No study submitted.

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute oral toxicity, rat

53229-0002; 275280; "Acute Oral Toxicity Study of PDJ in Rats"; (K. Yamashita; Kashima Laboratory, Mitisubishi Chemical Safety Institute Ltd, , Kashima Gun, Ibaraki, Japan; Study No. 6L043; 6/28/96); Five Sprague-Dawley rats/sex were dosed orally by gavage with 5000 mg/kg of PDJ technical (lot no. SCS-010; purity: 98.50%). No deaths resulted from the treatment. No treatment-related clinical signs were noted. No treatment-related lesions were evident in the necropsy examination. Rat Oral LD50: > 5000 mg/kg; Toxicity Category IV; **Study acceptable.** (Moore, 1/31/14)

Acute dermal toxicity

53229-0002; 275281; "Acute Dermal Toxicity Study of PDJ in Rats"; (K. Yamashita; Kashima Laboratory, Mitisubishi Chemical Safety Institute Ltd, , Kashima Gun, Ibaraki, Japan; Study No. 6L329; 9/18/96); The skin of 5 Sprague-Dawley rats/sex was exposed to 2000 mg/kg of PDJ technical (lot no. SCS-010; purity: 98.50%) for 24 hours under an occlusive wrap. No deaths resulted from the treatment. No treatment-related clinical signs were noted. No treatment-related lesions were evident in the necropsy examination. Rat Acute Dermal LD50: > 2000 mg/kg; Toxicity Category III; **Study acceptable.** (Moore, 1/31/14)

Acute inhalation toxicity, rat

53229-0002; 275282; "Acute Toxicity Study of PDJ by Whole-body Inhalation Exposure in Rats"; (K. Wako; Kashima Laboratory, Mitisubishi Chemical Safety Institute Ltd, , Kashima Gun, Ibaraki, Japan; Study No. 6L330; 1/7/97); Five Sprague-Dawley rats/sex were exposed whole-body to 2.8 mg/l (gravimetric) of PDJ technical (lot no. SCS-010; purity: 98.50%) for 4 hours. The MMAD (GSD) was 2.3 (2.4) µm. No deaths resulted from the exposure. Clinical signs included salivation and nasal discharge which were resolved by 1 hour post-exposure. No treatment-related lesions were evident in the necropsy examination. Rat Acute Inhalation LC50: > 2.8 mg/l; Toxicity Category IV; **Study acceptable.** (Moore, 1/31/14)

Primary eye irritation, rabbit

53229-0002; 275283; "Primary Eye Irritation Study of PDJ in Rabbits"; (J. Oigawa; Kashima Laboratory, Mitisubishi Chemical Safety Institute Ltd, , Kashima Gun, Ibaraki, Japan; Study No. 6L332; 9/13/96); The eyes of 9 Japanese White rabbits were treated by ocular instillation with 0.1 ml/eye of PDJ technical (lot no. SCS-010; purity: 98.50%). The eyes of 3 animals were washed at 2 minutes post-dose. **Non-washed eyes:** corneal opacity, grade 1 (2/6), was evident at 24 hours post-dose, clearing by 48 hours. No iritis was noted during the 72-hour observation period. No conjunctival redness, chemosis or discharge was evident at 24 hours post dose. **Washed eyes:** corneal opacity, grade 1 (2/3), was noted at 1 hour post-dose, diminishing to grades 1 (1/3) at 24 hours and clearing by 48 hours. No iritis was evident for the 72-hour observation period. No conjunctival redness, chemosis or discharge was evident at 24 hours post dose. Toxicity Category III; **Study acceptable.** (Moore, 2/3/14)

Primary dermal irritation

53229-0002; 275284; "Primary Dermal Irritation Study of PDJ in Rabbits"; (J. Oigawa; Kashima Laboratory, Mitisubishi Chemical Safety Institute Ltd, , Kashima Gun, Ibaraki, Japan; Study No. 6L333; 9/13/96); The skin of 6 Japanese White rabbits was exposed to 0.5 ml/site, one site/animal, of PDJ technical (lot no. SCS-010; purity: 98.50%) under a semi-occlusive wrap

for 4 hours. No dermal irritation was evident throughout the 72-hour observation period. Toxicity Category IV; **Study acceptable.** (Moore, 2/6/14)

Dermal sensitization

53229-0002; 275285; "Dermal Sensitization Study of PDJ in Guinea Pigs (Maximization Test)"; (S. Otake; **:** Kashima Laboratory, Mitisubishi Chemical Safety Institute Ltd, , Kashima Gun, Ibaraki, Japan; Study No. 6L334; 9/17/96); Twenty Hartley guinea pigs received a total of 6 intradermal injections of 0.05 ml each, 2 each of Freund's Complete Adjuvant: water (1:1), undiluted PDJ technical (lot no. SCS-010; purity: 98.50%), and the test material in a 50:50 preparation of Freund's Complete Adjuvant and olive oil further mixed 1:1 with water on day 0 of induction. Seven days later, the skin of these animals was exposed to 0.4 ml of undiluted test material for 48 hours under an occlusive wrap as the second induction treatment. The skin of these animals had been pretreated with 10% (w/w) sodium lauryl sulfate in petrolatum 24 hours earlier. Twenty control animals were treated in the same manner except that the test material was not included in the dosing regimen. Twenty one days after the initial induction treatment, the skin of each of the animals was exposed to 0.4 ml of the undiluted test material for 24 hours under an occlusive wrap. In the challenge treatment, none of the twenty treated animals exhibited a positive response through 72 hours post-exposure. No response was noted for the control animals as well. The test material is not a dermal sensitizer in accordance with the Guinea Pig Maximization Test. The positive control was functional. **Study acceptable.** (Moore, 2/7/14)

SUBCHRONIC STUDIES (units of mg/kg/day unless specified)

Oral toxicity, rat:

53229-0003; 275286; "A 13-Week Oral Toxicity Study of PDJ in Rats"; (T. Chida; Kashima Laboratory, Mitisubishi Chemical Safety Institute Ltd., Kashima Gun, Ibaraki, Japan; Study No. 6L303; 4/1/97); Ten F344/DuCrj rats/sex/group received 0, 1000, 3000 or 10000 ppm of PDJ technical (lot no. SCS-010; purity: 98.50%) in the diet for 13 weeks ((M) 0, 56.9, 168, 566 mg/kg/day, (F) 0, 58.5, 176, 587 mg/kg/day). No deaths resulted from the treatment. The mean body weight gains of both sexes in the 10000 ppm group were less than those of the control group over the course of the study ($p<0.05$ or 0.01). The mean food consumption of both sexes in the 10000 ppm group was slightly less than that of the control group, especially at the initiation of the study. No treatment-related effect noted in the hematology. No treatment-related ophthalmological findings were reported. In the clinical chemistry evaluation, the serum urea nitrogen levels of the females in the 3000 and 10000 ppm groups were greater than that of the control group ($p<0.05$ or 0.01). The serum chloride levels for both sexes in the 10000 ppm group and the males in the 3000 ppm group were less than the control levels ($p<0.05$ or 0.01). The total protein level in the serum of the males in the 10000 ppm group was less than the control level ($p<0.01$). Correspondingly, the albumin/globulin ratio was increased for the 10000 ppm males ($p<0.01$). In the urinalysis, the presence of red blood cells in the urine was increased for the 10000 ppm males (NS). For the females, the increased presence of white blood cells and hyaline casts in the urine of the10000 ppm group was noted ($p<0.05$ or 0.01). In the necropsy examination, the mean absolute liver weight of the 10000 ppm males and the mean relative liver weights of both sexes in the 10000 ppm group were greater than the control values ($p<0.01$). The mean relative kidney weight of the 10000 ppm males was greater than the control group ($p<0.01$). The mean relative adrenal weights of both sexes in the 10000 ppm group were greater than the control group values ($p<0.01$). The histopathological examination did not reveal any treatment-related lesions. **No adverse effect indicated. Rat Subchronic Dietary NOEL:** 1000 ppm ((M) 56.9 mg/kg/day, (F) 58.5 mg/kg/day) (based upon treatment-related effects upon clinical chemistry parameters of both sexes in the 3000 ppm treatment group); **Study acceptable.** (Moore, 2/11/14)

Oral toxicity, non-rodent:
Study not submitted.

Dermal toxicity, 21/28-day or 90-day:
Study not submitted.

CHRONIC STUDIES

Chronic, rat
Study not submitted.

Chronic, dog
Study not submitted.

Oncogenicity, rat
Study not submitted.

Oncogenicity, mouse
Study not submitted.

GENOTOXICITY

Gene mutation
** 53229-0003; 275288; "Bacterial Reverse Mutation Study of PDJ"; (F. Mizuno; Kashima Laboratory, Mitsubishi Chemical Safety Institute Ltd., Kashima-gun, Ibaraki, Japan; Study No. 6L045; 10/4/96); *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 and *E.* coli strains WP2 uvrA were exposed to PDJ technical (lot no. SCS-010; purity: 98.50%) at concentrations ranging from 2.44 to 156 ug/plate w/o activation and from 9.77 to 2500 ug/plate with activation, using a pre-incubation procedure in which cells were exposed to the test material for 20 minutes prior to plating and then incubated for another 48 hours. Two assays were performed and each treatment level was plated in triplicate. A phenobarbital and beta-naphthoflavone- induced rat liver S9 fraction was used to metabolize the test material. There was no treatment-related increase in reverse mutations with or w/o activation. No adverse effect indicated. The positive controls were functional. Study acceptable. (Moore, 2/13/14)

Chromosome damage
** 53229-0003; 275289; "Chromosomal Aberration Study of PDJ in Cultured Mammalian Cells"; (T. Nishitomi; Kashima Laboratory, Mitsubishi Chemical Safety Institute Ltd., Kashima-gun, Ibaraki, Japan; Study No. 6L336; 9/25/96); Chinese Hamster Lung cells (CHL/IU) were incubated with PDJ technical (lot no. SCS-010; purity: 98.50%) at concentrations ranging from 10 to 80 ug/ml, non-activated, 24 and 48 hours of treatment and 1250 to 5000 ug/ml, activated, 6 hours of treatment, 18 hours of incubation, at 37° C. In all of the assays, the cells were incubated the last 2 hours with Colcemid prior to fixation. All of the incubations were performed with duplicate cultures. A phenobarbital and 5,6-benzoflavone-induced rat liver S9 fraction was used to metabolize the test material. There was no treatment-related increase in the incidence of cells with chromosomal aberrations under conditions of activation or non-activation. **No adverse effect indicated**. The positive controls were functional. **Study acceptable.** (Moore, 2/18/14)

DNA damage or miscellaneous effects
Study not submitted.

REPRODUCTIVE TOXICITY, RAT

** 53229-0009; 286461; "Two-Generation Reproductive Toxicity Study of PDJ in Rats"; (N. Hoshino; **:** Kashima Laboratory, Mitsubishi Chemical Safety Institute, Ltd., Kashima-gun, Ibaraki Prefecture, Japan; Study No. 7L279; 1/29/99); Thirty Sprague-Dawley rats/sex/group received 0, 400, 2000 or 10000 ppm of PDJ (n-propyl dihydrojasmonate); (lot no. SCS-010; purity: 98.50%) in the diet for a 14-week premating period, mating, 3 weeks of gestation and 3 weeks of lactation. At the time of weaning, 24 F1 generation offspring/sex/group received the test material at the same treatment levels for a 14-week premating period (beginning post-weaning), mating, 3 weeks of gestation and 3 weeks of lactation. In the F0 generation, one male in the 400 ppm group died on study day 105 after having successfully mated. One female in the 400 ppm group died during parturition on gestation day 23. Another female in the control group died on day 7 of lactation. In the F1 generation, one dam in the 10000 ppm group died on gestation day 23 at the completion of parturition. The mean body weight gains of both sexes in the 10000 ppm parental groups of both generations were less than that of the control group over the course of the study ($p<0.01$). The mean food consumption of these animals was likewise less than that of the control group. Atrophy was noted in the uterus and vagina of the 10000 ppm dams of both generations. The fertility indices for the 10000 ppm dams of both generations were less than those of the control group (NS). The litter size of the 10000 ppm treatment group of the F1 generation was less than that of the control group ($p<0.01$). The mean 10000 ppm pup weights of the F1 and F2 generations during the lactation period were less than those of the control group ($p<0.01$). **No adverse effect indicated. Parental NOEL:** (M/F) 2000 ppm ((M) 94.4 mg/kg/day, (F) 103.6 mg/kg/day) (based upon the lower body weight gain and food consumption noted for the parents in the 10000 ppm group of both generations and the incidence of atrophy in the uterus and vagina of the females in the 10000 ppm group of both generations); **Reproductive NOEL:** (M/F) 2000 ppm ((M) 94.4 mg/kg/day, (F) 103.6 mg/kg/day) (based upon the lower fertility index of both generations and smaller mean litter size noted for the dams in the 10000 ppm group of the F1 generation); **Developmental NOEL:** (F) 2000 ppm ((F) 104.8 mg/kg/day (based upon the lower mean body weights of the 10000 ppm pups on post-natal day 0 in the F0 generation). **Study acceptable.** (Moore, 9/9/15)

DEVELOPMENTAL TOXICITY

Rat

**** 53229-0003; 275287**; "Teratogenicity Study of PDJ in Rats by Oral Gavage"; (M. Takahashi; Nippon Experimental Medical Research Institute Company, Ltd., Haruna Laboratory, Agatasuma-gun, Gunma, Japan; Project No. H-96120; 6/24/97); Twenty four mated female Crj:CD rats/group were dosed orally by gavage with 0, 30, 120 or 500 mg/kg/day of PDJ technical (lot no. SCS-010; purity: 98.50%) from gestation day 6 through gestation day 15. No test material-related deaths occurred during the study. The mean body weight gain and mean food consumption of the dams in the 500 mg/kg group were less than the control group values over the course of the treatment period ($p<0.01$). There was an increased incidence in the presence of thymic remnants for the fetuses in the 120 and 500 mg/kg treatment groups. Although the incidence was noted to be within the historical control data range, the effect demonstrated a treatment-related incidence based on litter numbers (0: 3/21 vs. 120: 7/22, 500: 8/20). There was an increase in the incidence of a 14th rib for the fetuses in the 500 mg/kg group (0: 8.3% vs 500: 29.1%). However, the incidence on a litter basis was less significant (0: 8/21 vs. 500: 13/20). **Possible adverse effect:** incidence of thymic remnants in the fetuses; **Maternal NOEL:** 120 mg/kg/day (based on lower mean body weight gain and reduced food consumption of the dams in the 500 mg/kg treatment group); **Developmental NOEL:** 30 mg/kg/day (based upon the increased incidence of thymic remnants in the fetuses of the 120 mg/kg treatment group); **Study acceptable** (Moore, 2/13/14)

Rabbit
Study not submitted.

NEUROTOXICITY

Acute, rat
Study not submitted.

90-day, rat
Study not submitted.

Developmental neurotoxicity, rat
Study not submitted.

Delayed neurotoxicity, hen
Study not submitted.

IMMUNOTOXICITY
Study not submitted.

ENDOCRINE DISRUPTOR STUDIES
Study not submitted.

SUPPLEMENTAL STUDIES
Study not submitted.