

0.555 lb. of indoxacarb per acre, 5X the labeled rate. Samples were collected from control and treated plots 7 days after the last application. The *grape* samples were then processed using standard *grape* processing procedures.

Samples collected at the processing facility were whole fruit, raisins and *grape* juice. The mean KN128/KN127 residues in whole fruit, raisins and *grape* juice treated with the exaggerated

rate were 1.34 ppm, 3.66 ppm and <0.01 ppm, respectively.

B. Toxicological Profile

1. *Acute toxicity*. Based on EPA criteria, indoxacarb is classified as follows for toxicity categories:

Guideline	Title	Results	Category
81-1	Acute oral toxicity	LD ₅₀ : 1,730 milligrams/kilogram (mg/kg) (M Rat) LD ₅₀ : 268 mg/kg (F Rat)	Category II
81-2	Acute dermal toxicity	LD ₅₀ : >5,000 mg/kg (Rat)	Category IV
81-3	Acute inhalation toxicity	LC ₅₀ : >5.5 (milligrams/per Liter (mg/L) (M Rat) (70% MUP)	Category IV
81-4	Primary eye irritation	Effects reversed within 72 hours (Rabbit)	Category III
81-5	Primary dermal irritation	No irritation (Rabbit)	Category IV
81-6	Skin sensitization	Sensitizer (Guinea Pig)	

Formulated products are slightly less acutely toxic than indoxacarb.

In an acute neurotoxicity study, indoxacarb exhibited decreased forelimb grip strength, decreased foot splay, and some evidence of slightly reduced motor activity, but only at the highest doses tested. The no adverse effects level (NOAEL) was 100 mg/kg for males and 12.5 mg/kg for females based on body weight effects in females >50 mg/kg.

2. *Genotoxicity*. Indoxacarb has shown no genotoxic activity in the following listed *in-vitro* and *in-vivo* tests:

- i. Ames—Negative
- ii. *In-vitro* mammalian gene mutation (CHO/HGPRT)—Negative
- iii. *In-vitro* unscheduled DNA synthesis—Negative
- iv. *In-vitro* chromosomal aberration—Negative
- v. *In-vivo* mouse micronucleus—Negative

3. *Reproductive and developmental toxicity*. The results of a series of studies indicated that there were no reproductive, developmental or teratogenic hazards associated with the use of indoxacarb. In a 2-generation rat reproduction study, the parental NOAEL was 1.5 mg/kg/day. The parental NOAEL was based on observations of reduced weight gain and food consumption for the higher concentration groups of the F0 generation, and potential treatment-related changes in spleen weights for the higher groups of the F1 generation. There was no effect on mating or fertility. The NOAEL for fertility and reproduction was 6.4 mg/kg/day. The offspring NOAEL was 1.5 mg/kg/day, and was based on the reduced mean

pup weights noted for the F1 litters of the higher concentration groups. The effects on pup weights occurred only at a maternal effect level and may have been due to altered growth and nutrition in the dams. In studies conducted to evaluate developmental toxicity potential, indoxacarb was neither teratogenic nor uniquely toxic to the conceptus (i.e., not considered a developmental toxin). Developmental studies conducted in rats and rabbits demonstrated that the rat was more susceptible than the rabbit to the maternal and fetal effects of DPX-MP062. Developmental toxicity was observed only in the presence of maternal toxicity. The NOAEL for maternal and fetal effects in rats was 2 mg/kg/day based on body weight effects and decreased food consumption at 4 mg/kg/day. The NOAEL for developmental effects in fetuses was >4 mg/kg/day. In rabbits, the maternal and fetal NOAELs were 500 mg/kg/day based on body weight effects, decreased food consumption in dams and decreased weight and delayed ossification in fetuses at 1,000 mg/kg/day.

4. *Subchronic toxicity*. Subchronic (90-day) feeding studies were conducted with rats, mice, and dogs. In a 90-day feeding study in rats, the NOAEL was 3.1 and 2.1 mg/kg/day for males and females, respectively. In male rats, the NOAEL was based on decreased body weight and nutritional parameters, mild hemolytic anemia and decreased total protein and globulin concentration. In female rats, the NOAEL was based on decreased body weight and food efficiency.

In a subchronic neurotoxicity study in rats, there was no evidence of neurotoxicity at 11.9 and 6.09 mg/kg/day, the highest dose tested for males and females, respectively. The subchronic NOAEL in dogs (5.0 mg/kg/day, M/F) was based on hemolytic anemia. Erythrocyte values for most dogs were within a range that would be considered normal for dogs in a clinical setting. Mice were less sensitive to indoxacarb than the rats or dogs. NOAELs (23 mg/kg/day, males, 16 mg/kg/day, females) were based on mortality (males only); increased reticulocytes and Heinz bodies and decreased body weight, weight gain, food consumption, food efficiency; and increased clinical signs (leaning to one side and/or with abnormal gait or mobility) (females only). In a 28-day repeated dose dermal study, the NOAEL was 50 mg/kg/day based on decreased body weights, body weight gains, food consumption, and food efficiency in females, and changes in hematology parameters, the spleen and clinical signs of toxicity in both sexes in rats.

5. *Chronic toxicity*. Chronic studies with indoxacarb were conducted on rats, mice, and dogs to determine oncogenic potential and/or chronic toxicity of the compound. Effects generally similar to those observed in the 90-day studies were seen in the chronic studies. Indoxacarb was not oncogenic in rats or mice. The chronic NOAEL in male rats was 5 mg/kg/day based on body weight and nutritional effects. In females, the NOAEL of 2.1 mg/kg/day was based on body weight and nutritional changes, as well as biologically significant hematologic changes at 3.6 mg/kg/day and above.