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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 27 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

Subject: EPA ID # 10182-145: Captan Technical - Response to 24
(C) registration of captan for control of diseases in
raspberries and blackberries (caneberries)

Tox. Chem. Number: 159
Project Number: 2-0507
Submission Number: S313030

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Registrant: ICI Americas, Inc.

CONCLUSIONS:

The application rate of proposed label is lower than that of the previous label. Therefore, the oncogenic risk to applicators and mixer/loaders to captan is expected to be lower than 10^{-6} which was published in Captan Special Review Position Document 2/3 (Office of Pesticides and Toxic Substances, EPA, June 1985). This estimate reflects the upper limit of excess cancer risk which is not likely to be exceeded if this application is approved.

REQUESTED ACTION:

The Registration Division requested that the Toxicology Branch review the 24 (C) registration of captan by the State of Oregon.

BACKGROUND:

The oncogenic risk to applicators and mixer/loaders (for raspberry and blackberry from dermal and inhalation exposure) to captan is 2.2×10^{-6} and 4.4×10^{-7} based on the lifetime average daily exposure (LADD) x cancer potency (Q_1^*) (SEE calculations below). The LADD of applicator and mixer/loaders are 0.092 mg/kg/day (PD 2/3, Table 21) and 0.018 mg/kg/day (derived from PD 2/3, Table 10), respectively and the cancer potency is 3.6×10^{-3} (mg/kg/day)⁻¹. The PD 2/3 assumed applicators and mixer/loaders wearing no gloves or protective clothing. These exposure estimates were derived from the application rate of 4 lbs ai/acre and 5 applications/season. The proposed label (by the State of Oregon) is for the application of 2.5 lbs ai/acre and 3 applications/season. Based on this, the exposure is estimated to be reduced to 37.5% of the estimated exposure. Consequently, if this application is approved the lifetime cancer risk would be 0.83×10^{-6} and 1.65×10^{-7} to applicators and mixer/loaders, respectively.

THE EXPOSURE AND RISK CALCULATIONS

Calculate the lifetime average daily dose (LADD) using the following formula:

$$\begin{aligned} \text{LADD} = & (\text{average daily dose in mg/kg/day}) \\ & \times (\text{no. of days exposed per year} / 365) \\ & \times (35 \text{ years of working}) / (70 \text{ years lifetime}) \end{aligned}$$

Calculate the LADD risk using the following formula:

$$\begin{aligned} \text{LADD Risk} = & \text{LADD} \times Q_1^* ; \\ \text{where } Q_1^* = & 3.6 \times 10^{-3} \text{ (mg/kg/day)}^{-1} \\ \text{applicator LADD} = & 0.092 \text{ mg/kg/day} \\ \text{loader/mixer LADD} = & 465 \text{ (mg/year)} / 365 \text{ (days/70} \\ & \text{(kg))} = 0.018 \text{ mg/kg/day} \end{aligned}$$

$$\begin{aligned} \text{Therefore, Applicator LADD Risk} = & 0.092 \text{ mg/kg/day} \times 5/365 \times \\ & 35/70 = 2.2 \times 10^{-6} \text{ and} \end{aligned}$$

$$\begin{aligned} \text{L/M LADD Risk} = & 0.018 \text{ mg/kg/day} \times 5/365 \times \\ & 35/70 = 4.4 \times 10^{-7} \end{aligned}$$

EIGHT POINT SUMMARY:

1. Summary of selected Toxicology Data considered in setting the Tolerance of Captan

Citation	ACC/MR ID NO.	RESULTS	CORE CLASS.
Feeding/oncogenicity-lifetime; rat	252722 to 252725 260078	systemic NOEL = >2000 ppm (HDT) oncogenic NOEL = 500 ppm oncogenic LEL = 2000 ppm (weakly oncogenic for uterine sarcomas)	minimum
Feeding - 1 yr; dog	408936 -04	NOEL = 60 mg/kg LEL = 300 mg/kg (emesis and soft mucoid stools)	minimum
Oncogenicity-113 wk; mice	244220 000680 76	Oncogenic NOEL < 6000 ppm (LDT) (significantly increased incidence duodenal adenomas & adenocarcinomas; decreased wt. gain & food consumption)	guideline
Develop. Tox; hamster	000878 03	develop. toxicity NOEL > 400 mg/kg (HDT) maternal NOEL = 50 mg/kg/day maternal LEL = 200 mg/kg/day (body wt. loss, mortality) fetotoxic NOEL = 200 mg/kg/day fetotoxic LEL = 400 mg/kg/day (reduced ossific., incr. resorptions, decr. body wt.)	minimum
Develop. Tox; rabbit	246624 000938 83	develop. toxicity NOEL > 60 mg/kg/day (HDT) maternal NOEL = 25 mg/kg/day maternal LEL = 60 mg/kg/day (wt. loss) fetotoxic NOEL > 60 mg/kg/day	minimum
Reproduction-3 generation; rat	249334 001252 93	NOEL = 12.5 mg/kg/day LEL = 25 mg/kg/day (decr. mean litter wt)	minimum

2. Summary of toxicological Data considered desirable but currently lacking
 - The data base supporting this registration is complete.
3. Action taken to obtain lacking information
 - No action is necessary.
4. Summary of tolerances granted
 - Tolerances for captan are listed in 40 CFR, Part 180.103. A tolerance of 25 ppm is currently exists for residues of captan on raspberries.
5. Effect of action on the theoretical maximum residue concentration (TMRC) and RfD
 - SACB will make this determination.
6. RfD
 - The RfD is 0.125 mg/kg/day based on the results of a three generation rat study in which the NOEL was 12.5 mg/kg/day (Federal Register Vol. 54, No. 36, February 24, 1989). An uncertainty factor of 100 was used in determining the RfD.
7. Pending regulatory action against registration
 - None
8. Other relevant considerations in setting tolerance
 - Captan is classified as a probable human carcinogen (Group B2) (Federal Register Vol. 54, No. 36, February 24, 1989). The estimated potency or Q_1^* for captan is 3.6×10^{-3} (mg/kg/day)⁻¹.