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CASWELL FILE

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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA ID 0120: Captan 90-day rat inhalation study and request for waiver on the 90-day rat dermal inhalation study.

TO: L. Schnaubelt/K. Samek (PM74)
Special Review & Reregistration Division (H-7508C)

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2/13/90

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1) A new 90-day inhalation study has been submitted to the Agency in response to the Registration Standard for Captan.
2) In addition the Agency has been requested to waive the data requirement for a 90-day dermal rat study based on the results of this study.

CONCLUSIONS:

A critical review of the final report of the new 90-day inhalation study will be submitted in a separate memorandum, however the following conclusions can be made:

1) The 90-day inhalation study satisfies the guideline requirements for a 90-day inhalation study.
2) There are no indications of the renal effect that was observed in a previous study. Therefore, a subchronic dermal toxicity study should not be required.
3) Toxicology Branch 1 (TB1) has no objections to the waiver request for the 90-day dermal rat study with Captan.

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BACKGROUND:

The Agency has currently completed a Special Review on Captan. Position Document (PD) 2/3 was completed (June, 1985). The PD4 was published in the Federal Register on 2/24/89. The Health Effects Division Peer Review Committee determined that Captan is a B_2 oncogen (12/29/86 and 4/13/88). The following data gaps identified in the Registration Standard for Captan (March 1986) still remain:

° Chronic (oral) - non-rodent
° Metabolism
(either supplementary or not submitted)

A 90-day inhalation study (#86-7951) was submitted using doses between 5 and 50 mg/m^3. This study was determined to be supplementary since signs of renal and upper respiratory tract alterations occurred at all doses. A 90-day dermal study was required by DCI in order to determine if dermal and inhalation exposures should be combined. If combined, there were inadequate margins-of-exposure (MOE) when compared to an estimated NOEL of 0.5 mg/m^3 (this was 0.1 of the LEL from the flawed study). Following this determination, ICI reevaluated the exposure methods of the earlier inhalation study and determined (TB1 agreed) that they were seriously flawed (see memorandum from M. Copley to R. Mountford dated 10/20/88) and should not be used to regulate captan. As a result, a second 90-day inhalation study was conducted using doses between 0.13 and 12.98 mg/m^3. Preliminary data indicated that the renal lesion was not present in the new study. Therefore an extension was granted to the registrant for the 90-day dermal study until the new 90-day study could be submitted and evaluated by the Agency.

CURRENT ACTION

ICI has submitted the final 90-day inhalation study (MRID 412344-01, study # PR0735) and a 3 week range-finding study (MRID 412344-02). Results of this well conducted study confirm the preliminary data submitted previously.

1) Exposure data indicates that rats received up to 13 ug/l captan. These concentrations were numerically greater than those supposedly obtained at the lowest dose in the flawed study. Particle sizes were within the required range.

2) Histologic data indicates that renal lesions, observed in the flawed study at all doses, were not present at any dose. This suggests that the earlier study may have markedly under-estimated the actual exposure.

Special stains were used to confirm the absence of the previously observed renal tubular lesions.

3) In addition, a 21-day range finding study (MR0113), testing to 25 ug/l did not result in renal lesions at any dose. The type of lesion observed in the flawed study would be expected to be present during this time frame.

Based on the above studies, it is unlikely that exposure to Captan, by the inhalation route, would result in inadequate MOS for renal changes. The NOEL for renal effects is at least 25 ug/l or 3.365 mg/kg/day. MOS for the combined exposure, when dermal exposure and protective clothing is considered are greater than 100 (worst case applicator exposure for mangos, nectarines, peaches = 0.154 mg/kg/day, times 0.2 for protective clothing). This diminishes significantly, our concern for dermally induced renal toxicity.

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