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

APR 9 1992

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: CLOMAZONE (COMMAND^R): Request for a permanent tolerance (0.05 ppm) for residues of clomazone in/on cotton

TO: S. Stanton / R. Cool, PM Team 41 ~~S. Stanton / R. Cool, PM Team 41~~
Registration Division (H7505C)

S. Morrill / RD / FHB

FROM: Whang Phang, Ph. D. 4/7/92
Pharmacologist
HFAS / Tox. Branch II / HED (H7509C)

THROUGH: James Rowe, Ph.D. James Rowe 4/7/92
Section Head
and
for Marcia van Gemert, Ph. D. James Rowe 4/7/92
Branch Chief
HFAS / Tox. Branch II / HED (H7509C)

Chemical: Command^R (Dimethasone; clomazone)
2-(2-chlorophenyl)methyl-4,4-dimethyl-3-isoxazolidinone

Caswell No. 463D

HED Proj. No. 2-1654

EPA ID No. 000279-03053

EPA Submission No. S412836

DP Barcode: D175288

Action Requested: The registrant, FMC, is requesting a new use of clomazone on cotton and is proposing the establishment of a tolerance of 0.05 ppm for the residues of clomazone in/on cotton.

Discussion: In evaluating this request the available toxicology data have been reviewed, and relevant toxicity data of Command^R are summarized. In addition, any outstanding data requirements and related issues are listed below:

1). Summaries of the available toxicological data considered for this action:

Study	Results	Tox. Cat.
Acute oral-rats	LD_{50} = 2,077 mg/kg (M) = 1,369 mg/kg (F)	III III
Acute dermal-rabbit	LD_{50} > 2,000 mg/kg	III
Acute Inhalation-rat	LC_{50} = 6.25 mg/L (M) = 4.23 mg/L (F)	III III
3-Month feeding-dog	NOEL not established; insufficient No. of animals sacrificed (2/sex/dose)	
3-Month feeding-mouse	NOEL not established; liver cytomegaly at 20 ppm (LDT)	
3-Month feeding-rat	NOEL not established; report incomplete	
1-Year feeding-dog	NOEL = 500 ppm (12.5 mg/kg/day) LEL = 2500 ppm (62.5 mg/kg/day) (increased absolute & relative liver weights in males and females; increase in cholesterol)	
2-Year feeding-rat*	NOEL = 100 ppm (4.3 mg/kg/day) LEL = 500 ppm (21.5 mg/kg/day) (increases in cholesterol, in absolute & relative liver weights, & in incidence of liver cytomegaly). An increase in tumor incidence was not seen.	
2-Year feeding-mouse	NOEL = 100 ppm (15 mg/kg/day) LEL = 500 ppm (75 mg/kg/day) (increase in white blood cells) An increase in tumor incidence was not seen.	
Teratology-rabbit	Maternal NOEL = 240 mg/kg/dau Maternal LEL = 700 mg/kg/day (decrease in body weights) Develop. tox. NOEL = 240 mg/kg/day Develop. tox. LEL = 700 mg/kg/day (increase in No. of resorptions)	
Teratology-rat	Maternal NOEL = 100 mg/kg/day Maternal LEL = 300 mg/kg/day (decreased locomotion, genital stain, runny eyes)	

	Develop. tox. NOEL = 100 mg/kg/day Develop. tox. LEL = 300 mg/kg/day (increased incidence of delayed ossification)
Mutagenicity Studies:	
a. Reverse mutation (Salmonella 2 studies)	Negative with/without activation
b. Point Mutation (CHO/HGPT)	Weakly positive without activation
c. In vivo cytogenetics (chromosomal aberration)	Negative
d. Unscheduled DNA synthesis	Negative

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*: Reference dose (RfD) was established based on the results of this study.

2. Reference dose(RfD) or acceptable daily intake (ADI): The RfD for command^{R} is derived from the 2-year feeding study in rats with a NOEL of 4.3 mg/kg/day. Applying a safety factor of 100, the RfD is calculated to be 0.043 mg/kg/day.

3. Summary for toxicology data considered desirable but currently lacking: None

Discussion and Conclusion

Currently the TAS analysis is performed by Dietary Risk Evaluation System (DRES) of the Science Analysis and Coordination Branch (SACB). Tox. Branch II will have no objection to granting this request if granting it will not result in the tolerances exceeding a 100% of the RfD, and the supporting residue chemistry data are acceptable to the Dietary Exposure Branch.