UNDATED

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Eight-Point Toxicology Summary for Use of COMMAND In/On Soybeans

FROM: Clint Skinner, Ph.D., Section Head
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Hazard Evaulation Division (TS-769C)

TO: Robert J. Taylor, PM 25
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Registration Division (TS-767C)

Chemical: COMMAND (FMC 57020, Dimethazone)
2-(2-chlorophenyl) methyl-4,4-dimethyl-3-isoxazolidinone

Caswell No.: 463D

Petitioner: FMC Corporation

ID Nos.: PP#4F3128; 279-GNLU/-GNLG/-GNLE; 279-3052/-3053/-3054

Accession Nos.: 072818; 072814; 072797 thru 072812; 072824 thru 072827; 072829; 072815; 072067; 072771; 072813; 072821 thru 072823; 072830 thru 072832.

Command - 8-Point Toxicology Summary for Permanent Tolerances on Soybeans

ID Nos.: PP#4F3128; 279-GNLU/-GNLG/-GNLE; 279-3052/-3053/-3054

ACUTE TOXICITY DATA REVIEW

Study Type	Technical	4EC	6EC
Oral LD_{50}, rat	2077 mg/kg (M) 1369 mg/kg (F)	2343 mg/kg (M) 1406 mg/kg (F)	2388 mg/kg (M) 2235 mg/kg (F)
Dermal LD_{50}, rabbit	Greater than 2000 mg/kg	Greater than 2000 mg/kg	Greater than 2000 mg/kg
Inhalation LC_{50}, rat	6.25 mg/L (M) 4.23 mg/L (F)	4.47 mg/L (M) 4.70 mg/L (F)	3.06 mg/L (M) 2.48 mg/L (F)
Eye Irritation, rabbit	Slight	Moderate to severe	SEVERE
Dermal Irritation, rabbit	Slight	Moderate to severe	Moderate to severe
Skin Sensitization, guinea pigs	Non-sensitizer	Non-sensitizer	Non-sensitizer

COMMAND TECHNICAL (FMC 57020) CHRONIC TOXICITY DATA SUMMARY

Study	Results
3-Month Feeding-dog	NOEL not established; insufficient animals sacrificed (2/sex/dose).
3-Month Feeding-mice	NOEL not established; liver cytomegaly seen at lowest dose tested (20 ppm).
3-Month Feeding-rat	NOEL not established; report incomplete.
1-Year Feeding-dog [doses: 0, 100, 500, 2500, 5000 ppm for 1 year]	NOEL = 500 ppm (12.5 mg/kg/day) LEL = 2500 ppm (62.5 mg/kg/day) [Increased liver weights, absolute and relative to body weight in males and females; increase in cholesterol.]

2-Year Feeding-rat [doses: 0, 20, 100, 500, 1000, 2000 ppm for 2 years; 4000 and 8000 ppm for 3 months]	NOEL = 100 ppm (4.3 mg/kg/day) LEL = 500 ppm (21.5 mg/kg/day) [Lower body weight in 1000 and 2000 ppm males, 2000 ppm females; cholesterol increased in 500, 1000, and 2000 ppm females; SGOT decreased in 1000 and 2000 ppm females; increased liver weights, absolute and relative to body and liver weights in 500, 1000, 2000 ppm females; increased incidence of liver cytomegaly in 500, 1000, 2000 ppm males.]
2-Year Feeding-mice [doses: 0, 20, 100, 500, 1000, 2000 ppm for 2 years; 4000 and 8000 ppm for 3 months]	NOEL 100 ppm (14.3 mg/kg/day) LEL = 500 ppm (71.4 mg/kg/day) [Increase in white blood cells in 500, 1000, 2000 ppm males; increase in SGOT and SGPT in 1000 ppm males at 24 months; increase in absolute liver weights at 1000 and 2000 ppm males; increase in liver cytomegaly in 1000 and 2000 ppm males; increase in lymphoid hyperplasia in 1000 and 2000 ppm females.]
Teratology-rabbit [doses: 0, 30, 240, 1000 (reduced to 700 mg/kg/day from gestation days 13 thru 18) mg/kg/day]	Negative for teratogenicity at Highest Dose Tested, 700 mg/kg/day. Maternal NOEL = 240 mg/kg/day Maternal LEL = 740 mg/kg/day [Decreased body weight.] Fetotoxic NOEL = 240 mg/kg/day Fetotoxic LEL = 700 mg/kg/day [Increased number of resorptions.]
Teratology-rat [doses: 0, 100, 300, 600 mg/kg/day]	Maternal NOEL = 100 mg/kg/day Maternal LEL = 300 mg/kg/day [Decreased locomotion, genital staining, runny eyes.] Fetotoxic NOEL = 100 mg/kg/day Fetotoxic LEL = 300 mg/kg/day [Increased incidence of delayed ossification of 4 sternebrae; increased incidence of hydroureter and hydronephrosis.]

Mutagenicity-Reverse Mutation (Salmonella) [2 studies]	Negative with/without activation.
Mutagenicity-Point Mutation (CHO/HGPT)	Positive without activation [Positive control: Benzopyrene; Command 3X background; "weakly positive".]
Mutagenicity-In Vivo Cytogenetics (chromosomal aberrations)	Negative
Mutagenicity-Unscheduled DNA Synthesis	Negative

Acceptable Daily Intake - Soybeans

A printout of the ADI, MPI, and TMRC based on the NOEL for the rat chronic study (4.3 mg/kg/day) is attached.

The TMRC is equal to 1.5 kg of the tolerance of 0.05 ppm = 0.007 mg/kg/day. The ADI is 1/100 of the NOEL or 0.043 mg/kg/day pending an MPI for 60-kg man of 2.58 mg/kg/day so the TMRC 0.007 is 0.03 percent of the ADI.

Conclusion:

The toxicology data package is complete and supports the accceptance of the use of Command in soybeans to .05 ppm.

Attachment