



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 Evaluation 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

<u>Study Type</u>	<u>Technical</u>	<u>4EC</u>	<u>6EC</u>
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 Irrit- ation, rabbit	Slight	Moderate to severe	Moderate to severe
Skin Sensitiza- tion, guinea pigs	Non- sensitizer	Non- sensitizer	Non- sensitizer

COMMAND TECHNICAL (FMC 57020) CHRONIC TOXICITY
DATA SUMMARY

<u>Study</u>	<u>Results</u>
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.]

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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 hydronephrosis
 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 acceptance of the use of Command in soybeans to .05 ppm.

Attachment