

US EPA ARCHIVE DOCUMENT

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TXR-5659



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

JAN 12 1987

005659

MEMORANDUM

Subject: Command® : Review of the Data Base of Command®

To: Jim Yowell, PM #25  
Registration Division (TS-767c)

From: Whang Phang, Ph.D.  
Pharmacologist  
Toxicology Branch/HED (TS-769c)

*Whang Phang 1/12/87*

Through: Marcia van Gemert, Ph.D.  
Section Head  
and  
William Burnam, Deputy Branch Chief  
Toxicology Branch/HED (TS-769c)

*M. van Gemert 1/12/87*

*W. Burnam 1/12/87*

Chemical: Command® (FMC 57020, Dimethazone)

Caswell No.: 463D; EPA ID. No.: 4F3128; Project No. 7-0256

Petitioner: FMC Corp.

Action Requested: To review the toxicology data file of Command®, to determine if the issue of maximum tolerated dose (MTD) in a 2-year mouse feeding/oncogenicity study (FMC Study No. A-81-651, July 25, 1984) was resolved, and to consider if the studies would support the use of Command® on additional crops.

Discussion and Conclusion:

- 1). In examining the data file, there is a memorandum concerning the issue of MTD in the 2-year mouse feeding/oncogenicity study (memo, Gregorio to Yowell, April 18, 1986). According to the memorandum, the Toxicology Branch has utilized a decision tier scheme for addressing the adequacy of chronic studies in which the MTD has not been achieved (draft: Toxicology Branch Position Paper on Maximum Tolerated Dose in Oncogenicity Studies). It has been determined that the study is adequate.
- 2). This reviewer has discussed the adequacy of this 2-year mouse feeding/oncogenicity study with Mr. William Burnam, Deputy Branch Chief. He confirmed that the study has been considered as adequate. This study is classified Core Minimum.

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- 3). Based upon the previous ADI printout (Attachment). Granting the tolerance of soybeans (0.05 ppm) had used 0.03% of the ADI. Therefore, the studies could support additional crops provided the residue levels in those crops are acceptable.

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

CASWELL  
C. Y. Gregorio  
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april  
OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

April 18, 1986

DATE:

SUBJECT: Request For "8 Point Summary" For COMMAND

TO: Jim Yowell, PM #25  
Registration Division (TS-767)

FROM: Carolyn Gregorio, Toxicologist  
Toxicology Branch/HED (TS-769) *CGC*  
1-29-86

THRU: Clint Skinner, Ph.D.,  
Section Head,  
and  
Theodore M. Farber, Ph.D.  
Branch Chief,  
Toxicology Branch/HED (TS-769) *TFB*

Chemical: COMMAND (FMC 57020, Dimethazone)

Caswell No.: 463D

Petitioner: FMC Corporation

Petition No.: 4F3128

Background: The Branch had previously recommended that tolerance request for the use of COMMAND on soybeans be denied (Gregorio to Taylor, August 20, 1985). This recommendation was based on an insufficient toxicology data base:

- 1.) The rat teratology study (FMC Study No. A83-1142, June 29, 1984) was classified as Supplementary and additional information was requested in concert with a request for a lab/data audit. The Branch's concern has been adequately satisfied (memo, Gregorio to Taylor, January 17, 1986 and January 21, 1986). Therefore, the rat teratology studied has been reclassified as Minimum.

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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 800 ppm for 3-months]

NOEL = 100 ppm (15 mg/kg/day)  
LEL = 500 ppm (75 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 = 700 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]

Negative for teratogenesis

Mutagenicity-Reverse Mutation  
(Salmonella) [2 studies]

Negative with/without activation

Mutagenicity-Point Mutation  
(CHO/HGPT)

Weakly positive without activation  
[Positive control: Benzopyrene;

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Command 3x background; "weakly positive"]

Mutagenicity-In Vivo -  
Cytogenetics (chromosomal  
aberrations)

Negative

Mutagenicity- Unscheduled  
Dna Synthesis

Negative

2.) Summary of Toxicology Data Considered Desirable But  
Currently Lacking:

NONE

3.) Action Being Taken To Obtain Lacking Data:

NONE

4.) Summary of Temporary Tolerances Granted:

soybeans ---- 0.5 ppm residue

5.) Summary of How Total Tolerances Would Affect The MPI:

The ADI that would be used by granting the soybean tolerance is 0.03. The TMRC is 0.0007 mg/kg/1.5 kg and the MPI is 2.5800 mg/day (60 kg).

6.) Acceptable Daily Intake Data:

The ADI (0.0430 mg/kg/day) is based on the 2 year feeding/oncogenicity rat study (NOEL = 4.3 mg/kg/day; safety factor = 100).

7.) Pending Regulatory Action Against Registration:

NONE

8.) Other Considerations:

NONE

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NO CER Number

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ACCEPTABLE DAILY INTAKE, DA

**DRAFT**

*NOEL change  
not  
recorded  
ssr*

RAT, Older	NOEL	S.F.	ADI	IPI
mg/kg	ppm		mg/kg/day	mg/day (60kg)
4.300	40,000	100	0.0430	2.5800

unpublished, not Approved 132937

SKC	Tolerance	Food Factor	mg/day (1.5kg)
soybeans (oil) (14)	0.050	0.92	0.00069

IPI	PIRC	ADI
2.5800 mg/day (60kg)	0.0007 mg/day (1.5kg)	1.03

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