Supplement to HED Document No. 010242 - DER for MRID No. 42415701: CGA 64250 Technical - Dermal Absorption in Rats. This supplement provides an Executive Summary to upgrade the original DER.

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DATA EVALUATION RECORD

STUDY TYPE: Dermal Absorption - Rat; OPPTS 870.7600 [§85-3]

DP BARCODE: D272339, D273491 SUBMISSION CODE:S591835, S594147
P.C. CODE:122101 TOX. CHEM. NO.:323EE

TEST MATERIAL (PURITY): CGA-64250, Propiconazole

SYNONYMS: 1-[[2-(2',4'-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]-methyl]-1H-1,2,4-triazole

CITATION: Murphy T. 1986. Dermal Absorption of ^{14}C-Propiconazole: Addendum to ABR-86053. Study number 86064, Ciba-Geigy Corp, Greensboro, NC. September 30, 1986. MRID 42415701. Unpublished.

Murphy, T.; Brown, K.; Doornheim, D.; *et al.* 1986 Dermal Absorption of Carbon 14-Propiconazole in Rats after a Ten-Hour Exposure Period: Report No. ABR-86053. Unpublished study prepared by Ciba-Geigy Corp. 76 p., MRID 00164469

Murphy, T. 2001. Dermal Absorption of ^{14}C-Propiconazole: Addendum to ABR-86053, MRID 42415701. Study number 1596-01, Syngenta Crop Protection, Inc., Greensboro, NC. March 2, 2001. MRID 45345901. Unpublished.

SPONSOR: Ciba-Geigy Corporation

EXECUTIVE SUMMARY: In a dermal absorption study (MRID's 42415701, 45345901), groups (4/group) of young adult male, Harlan Sprague-Dawley rats (age not given) were exposed to triazole-[3,5-]^{14}C-

CGA-64250 (95% radiochemical purity, specific activity 28.2 µCi/mg for low and mid-dose levels and 2.01 µCi/mg for the high-dose level) at doses of 0.1, 1.0 or 10 mg/rat (0.01, 0.1 or 1 mg/cm², respectively) to a 10 cm² shaven dorso-lumbar area. The radioactive test compound was added to the 3.6EC formulated product (45.8% active ingredient and 54.2% inert substances) and applied as an aqueous suspension. One group of four rats/dose were exposed for 24 hours, while two other groups of four rats each/dose were exposed for 10 or 24 hours followed by a 72-hour depletion phase. This study is an addendum to an earlier study where groups of four male rats each were treated similarly but exposed for 2, 4 or 10 hours (MRID 00164469). In both studies, following the exposure period, the test compound remaining on the skin was removed with a soap rinse. Fecal and urinary samples were collected at the end of the exposure periods and at 24 hour intervals (for the depletion groups) following the exposure.

At sacrifice time rats were anesthetized and blood colleted. The radioactivity present in excreta, blood, carcass, skin, skin washes and patch components were determined. The applied radioactivity was accounted for, with recoveries ranging from 82.8 to 108 % for MRID 42415701 and 86.6 to 112.6% for MRID 00164469.

The amount of test compound absorbed was directly proportional to the applied dose. The rate of absorption appeared to be saturated at the highest dose level; at the low dose level, there was a time dependent increase in the amount of compound absorbed. After 24 hours, 57.1, 271 and 3010 µg/cm² (57.13, 27.14 and 30.10% of total dose were absorbed at the low, mid and high dose levels, respectively). During the 72-hour depletion phase essentially all of the compound was eliminated in the urine and feces; urinary elimination predominated at the mid and high dose levels. At the end of the 72 hour depletion phase, less than 2% of the test compound was still present in the carcass. The results of the earlier study (MRID 00164469) demonstrated that 26-35% of the applied radioactivity (at all dose levels) is absorbed within the first two hours and remained fairly constant for the longer exposure periods of 4 and 8 hours except for the low dose of 0.01 mg/cm² where it increased to 54%. The average dermal absorption of propiconazole over a 10 hour period at an exposure level of 0.01 mg/cm² is approximately 40%. The attached appendix provides a summary of both studies.

The two studies were classified **Acceptable/guideline** and both satisfy the guideline requirement (870.7600; 85-3) for a dermal absorption study.

COMPLIANCE: Signed and dated GLP and Quality Assurance statements were provided. Data Confidentiality and Flagging statements were not provided for MRID 00164469 and 42415701.

APPENDIX

SUMMARY TABLE OF DERMAL ABSORPTION OF ^{14}C-PROPICONAZOLE IN RATS

Fraction	Percent of the applied dose at the application rates of[4]		
	0.01 mg/cm^2	0.1 mg/cm^2	1.0 mg/cm^2
24-hr exposure*			
Absorbed[1]	47.44	10.22	8.46***
Absorbed including skin[2]	57.13	27.14	39.47***
Unabsorbed[3]	48.17	55.70	57.11***
10-hr exposure + 72 hr depuration*			
Absorbed[1]	42.37	21.46	30.97
Absorbed including skin[2]	48.25	25.16	37.02
Unabsorbed[3]	59.79	61.49	58.37
24-hr exposure + 72 hr depuration*			
Absorbed[1]	54.71	29.83	29.83
Absorbed including skin[2]	59.41	35.36	42.39
Unabsorbed[3]	42.33	59.92	48.49
2-hr exposure**			
Absorbed[1]	14.68	2.70	1.42
Absorbed including skin[2]	34.74	26.15	30.10
Unabsorbed[3]	77.87	79.07	72.88
4-hr exposure**			
Absorbed[1]	12.79	20.65	1.34
Absorbed including skin[2]	36.73	36.12	31.07
Unabsorbed[3]	58.02	69.22	64.76
10-hr exposure**			
Absorbed[1]	39.67	11.20	4.81
Absorbed including skin[2]	53.70	36.19	29.29
Unabsorbed[3]	43.63	62.51	57.32

* Data extracted from Tables I, II and III of MRID 42415701
** Data extracted from Tables I, II AND III of MRID 00164469
*** Data extracted from Appendix Table VII of MRID 45345901
[1] Sum of urine, feces, blood and carcass
[2] Sum of urine, feces, blood, carcass and skin
[3] Sum of soap rinse, water rinse, bridge rinse, paper, paper rinse, bandage rinse, gauze squares, and cage wash
[4] Mean of four rats per time point

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