

Memorandum

To : Terry Schmer, Registration Specialist
Pesticide Registration Branch

Date: January 31, 1989
Place: Sacramento

Via : John Ross, Staff Toxicologist
Worker Health and Safety Branch

Phone: 5-8474
**HSM-89001 (# assigned
after original issuance
of memo)**

From : **Department of Food and Agriculture** - Tian Thongsinthusak, Staff Toxicologist
Worker Health and Safety Branch

Subject: PRODUCT NAME: Comite II, Omite 6E, Omite-30W
ACTIVE INGREDIENT: Propargite
COMPANY NAME: Uniroyal Chemical Co.
I.D. NUMBER: 114378-ER (one of 11 memos)
DOCUMENT NUMBER: 259-090
EPA REGISTRATION NUMBER: 400-0-
TITLE: Study on Dermal Absorption of Different ¹⁴C-Omite Formulations by
Male Rats (Draft)

Dermal absorption of propargite in male rats was conducted by Arthur D. Little (for Comite II and Omite-6E formulation) and Ricerca, Inc. (for Omite-30W) on behalf of Uniroyal Chemical Co. The three dose levels used were 0.05, 0.5 and 5 mg/kg. ¹⁴C-Omite was mixed with either Omite or Comite formulation blank prior to administration to approximately 10 cm² of shaved skin.

Four rats were used for each exposure period. The exposure times were 0 hour (5 mg/kg only), 2, 4, 8 and 24 hours for all doses. Rats were properly handled in respect to, acclimatization, preparation of shaved skin, administration of the dose, and collection and handling of the samples. Exposed skin sites were washed off using gauze pads soaked in five percent (w/v) Ivory soap in water.

The rats were killed after anesthesia at the end of 0, 2, or 4 hour exposure, whereas for exposure at 8 and 24 hours, rats were kept for 5-6 days and daily urine and feces samples were collected. At the end of the studies, rats were killed and samples were collected accordingly.

Analysis of radioactivity in samples including urine, feces, carcasses, cage washes, blood, exposed skin, unabsorbed dose and skin cover were accomplished using a liquid scintillation counter.

Dermal absorption of Omite as percent administered dose are calculated as shown in Table I for Comite II, Omite 6E and Omite-30W. Additional percent dermal absorption has been added to figures suggested by the registrant. This is due to the fact that percent residues in the exposed skin are relatively high, especially for Omite-30W (17-34 percent). Furthermore, percent of administered dose in carcasses for Comite II (0.05 and 0.5 mg/kg)

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and Omite 6E (0.05 mg/kg) were not given. Percent recovered doses also varied tremendously from a low of 67.5 percent to a high of 101.9 percent. High percent residue in the exposed skin suggests bioavailability for further absorption. Plots of percent excretion of Omite in urine and feces against time suggested bioavailability of the dose in exposed skin. Adjustment of the percent dermal absorption to take these factors into account is considered essential.

The overall percent dermal absorption of Omite was summarized in Table II. Seventeen percent dermal absorption will be used in the human exposure assessment since the dose ranges of 0.05 to 0.5 mg/kg are comparable to actual worker exposure to propargite.

As a general guideline, a longer study which extends the observation period up to three weeks when high residue in skin was observed should be conducted (per Zendzian, U.S. EPA).

Studies as reported in the draft document are considered well executed. Nevertheless, complete reports on percent residue in carcasses and quality control regarding percent recovery are needed.

Table I. Twenty-four hour dermal absorption of propargite (Comite II, Omite 6E, and Omite-30W in male rats^a

<u>Formulation</u>	<u>Dosage</u> <u>mg/kg</u>	<u>Apparent</u> <u>Absorption^b</u>	<u>Percent Adjustment</u> <u>of Dermal Absorption</u>		<u>Percent</u> <u>Total</u> <u>Absorption</u>
			<u>Total Recovered^d</u>	<u>Curve^e</u>	
Comite 11	0.05	15.8+5.0c	-0.3	+1.8	17
Comite 11	0.5	13.8+2.0c	+0.9	+1.2	16
Comite 11	5.0	11.7+0.8	+1.8	+0.6	14
Omite 6E	0.05	8.0+1.3 ^c	+0.5	+0.0	9
Omite-30W	0.05	8.0+2.1	0.5.	+0.2	9
Omite-30W	0.5	9.1+4.0	+4.4	+1.4	15f
Omite-30W	5.0	2.4+0.2	+0.7	+0.0	3

^aCombined percent administered dose (AD) in urine, feces, cage washes, carcasses, blood; percent adjustment of total dose recovered and potential bioavailability of exposed skin residue (extrapolation from the excretion curve).

^bPercent AD in urine, feces, blood, carcasses and cage washes.

^cPercent residue in carcasses estimated from the proportion of percent AD excreted in urine and feces (U+F) of 5 mg/kg dose and percent AD in carcasses, e.g., percent AD in carcasses of 0.5 mg/kg [Comite II] = 0.5% (AD in carcasses of 5 mg/kg) x 8.8% (U+F of 0.5 mg/kg)/7.5% (U+F of 5 mg/kg) = 0.59%.

^dAssume a proportional gain or loss between percent absorbed and unabsorbed AD. Example: Comite II, dose 0.5 mg/kg, has a total absorption of 13.8% and the total recovered dose (absorbed + unabsorbed) of 94.1%. Percent adjustment for the total mass recovered to 100% is calculated as follows:

$$\text{Percent Adjustment} = \frac{(13.8 \times 100) - 13.8}{94.1} = 0.9\%$$

^eExtrapolation of the excretion curve until it reaches a plateau (see attached figure for adjustment for Comite 11, 0.5 mg/kg). Adjustment for residue in blood and cage washes was not made due to insignificant increase.

^fThis dosage is being repeated at the contract lab.

Table II. Summary: 24-hour dermal absorption ranges of propargite in male rats

<u>Dosage</u> <u>(mg/kg)</u>	<u>Percent Dermal Absorption</u>		<u>Percent Dermal</u> <u>Absorption for</u> <u>Exposure Assessment</u>
	<u>Determined</u> <u>by Uniroyal</u>	<u>Determined</u> <u>by WH&S</u>	
0.05	8-15	9-17	17
0.5	9-13	15-16	17
5.0	2-12	3-14	14

cc: Joshua Johnson (1 original, 5 copies)

Figure. Excretion of Comite II (0.5 mg/kg) in urine and feces of male rats after 24-hr exposure

