Memorandum

Date: 7 December 1983

Subject: CARBARYL ACUTE TOXICITY STUDIES; EPA Reg. No. 264-324
Caswell #160
In 11-04-83; record no. 109134.

From: B. T. Backus
IRB/TSS

To: Mr. Jay Ellenberger
Product Manager 12

Registrant: Union Carbide Agricultural Products Co. Inc.
P.O. Box 12014
T.W. Alexander Drive
Research Triangle Park, NC 27709

Active Ingredient:
Carbaryl.....99%
Inert Ingredients:.....1%

Background:

The registrant has sent in a number of studies (primarily acute) which have been conducted on technical Carbaryl or similar formulations. The question is whether these studies are adequate to meet the Carbaryl registration standard requirements, and whether, based upon these studies, what labeling revisions may be appropriate.

Comments and Recommendations:

1. The two "best" oral LD_{50} studies indicate oral LD_{50}'s (combined M+F) of 255 and 264 mg/kg. This suggests that products containing 50% or more Carbaryl are in toxicity category II (signal word WARNING) on the basis of potential oral hazard.

2. The acute dermal LD_{50}, and primary eye and dermal irritation studies conducted at the Bushy Run Research Center under Project Report 46-71, dated July 12, 1983 are acceptable as indicating the 99% technical material is no worse than toxicity category III by dermal toxicity hazard, is in toxicity category III by eye irritation potential, and is in toxicity category IV by the dermal irritation hazard potential.

3. There is no adequate inhalation LC_{50} study in this submission. The material dated June 6, 1974 from Carnegie-Mellon University gives no information as to the sex(es) of exposed rats, and there is no indication that actual analytical measurements were made on the atmosphere to which subjects were exposed. There are similar inadequacies for the studies from the Mellon Institute dated 1-27-64 (Report 27-11), and additionally these utilized formulations which contained no more than 5% Carbaryl.

The following are among the studies in Acc. 251719. Several criteria were used in selection of these particular studies as being most likely to be applicable to adequacy, including how recently studies were conducted, whether animals were identified as to sex, whether the material tested was formulated within this country etc.

1. Acute oral LD_{50} - rat. Mellon Institute, Carnegie Mellon University, Special Report 34-71; dated 9-1-71.

   Procedure: Two groups of 5F rats received oral doses of 0.2 and 0.4 g/kg, administered in a corn oil suspension at 0.05 g/ml.

   Results:

Dosage Level (g/kg)	Mortality/Animals Dosed (F only)
0.20	2/5
0.40	5/5

   Oral LD_{50}(F) reported as 0.224 (0.117-0.432) g/kg
   Symptoms reported as: bulging eyes, tremors, salivation. Deaths occurred days 0-4.

   Study Classification: Core Supplementary Data (suggests toxicity category II)

2. Acute oral LD_{50} - rat. Carnegie-Mellon University, 4400 Fifth Ave., Pittsburgh, PA 15213. Special Report 36-19; dated March 13, 1973.

   Procedure: Groups of 5M rats received 0.125, 0.25, 0.5 or 1.0 g/kg of material either identified as "Sevin NCF" or "Sevin MIC." Material was administered by stomach intubation, as 0.05 g/ml suspension in 0.25% agar.

   Results:

Dosage (mg/kg)	Mortalities/Animals Dosed (males only) SEVIN NCF	SEVEN MIC
125	0/5	-
250	3/5	1/5
500	4/5	3/5
1000	4/5	5/5

   Oral LD_{50}(M) for Sevin NCF = 273 (150-496) mg/kg
   Oral LD_{50}(M) for Sevin MIC = 420 (237-746) mg/kg

   Reported symptoms: tremors, salivation and prostration.

   Study Classification: Core Supplementary Data

3. Acute oral LD_{50} - rat. CDC Research Inc; Study No. CDC-UC-046-79; dated 1-03-80.

   Procedure: Groups of 5M, 5F Charles River CD rats received oral dosages of 200, 320, 400, 500 and 630 mg/kg technical grade Carbaryl, administered as a suspension in 0.25% methyl cellulose, with subsequent 14-day observation.

Results:

Dosage Level (mg/kg)	Mortalities/Animals Dosed M	F
200	0/5	2/5
320	1/5	4/5
400	4/5	5/5
500	2/5	3/5
630	4/5	5/5

(Results from dosage level of 500 mg/kg were not used in LD_{50} calculations).

Oral LD_{50} (combined) = 255 (202-321) mg/kg.

Symptoms: reported as salivation, body tremors, depression, lacrimation, muscle fibrillation, hyperpnea, chromodacryorrhea, loss of righting reflex.

Necropsy findings reported for some animals which died included erosion of gastric mucosa, gastrointestinal hemorrhages, bile-filled intestines, pale liver, distended stomach and intestines. However, some mortalities reported as showing no gross lesions.

Study Classification: Core Minimum Data

Product Classification: Tox. Cat. II

4. Acute oral LD_{50} - rat. Union Carbide Bushy Run Research Center, R.D. 4, Mellon Rd, Export PA 15632. Project Report 46-71; dated July 12, 1983.

Procedure: Groups of 5M, 5F Hilltop-Wistar albino rats received dosage levels of 100, 200, 400 or 800 mg/kg, mixed with 0.25% methyl cellulose solution. Subjects were subsequently observed for 14 days.

Results:

Dosage level (mg/kg)	Mortality/Animals Dosed M	F
100	0/5	0/5
200	2/5	1/5
400	3/5	5/5
800	5/5	5/5

Oral LD_{50}(M) = 283 (168-477) mg/kg
Oral LD_{50}(F) = 246 (182-333) mg/kg.
Oral LD_{50}(combined) = 264 (198-352) mg/kg.

Reported symptoms: tremors, sluggishness, salivation, lacrimation, piloerection. Necropsies of animals which died reported as showing mottled and red lungs. liquid-filled stomachs, red and yellow intestines. Post-sacrifice necropsies of survivors reported as showing nothing remarkable.

Study Classification: Core Minimum Data

Product Classification: Tox. Cat. II

5. Acute dermal LD_{50} - rabbit. Union Carbide Research Center, Project Report 46-71; dated July 12, 1983.

   Procedure: A group of 5M, 5F NZ white rabbits received 24-hr occluded dermal exposure to a dosage level of 2 g/kg, with subsequent 14-day observation.

   Results: 1M died at 14 days. Most animals (including mortality) reported as showing nothing remarkable on necropsy. Dermal $LD_{50} > 2$ g/kg.

   Study Classification: Core Minimum Data

   Product Classification: Tox. Cat. III

6. Primary dermal irritation - rabbit. Union Carbide Research Center, Project Report 46-71; dated July 12, 1983.

   Procedure: 6 rabbits received a 4-hr occluded dermal exposure to 500 mg of moistened test material. Application was made at an intact skin site.

   Results: No irritation noted at 5 hrs, 1, 2, 3 or 7 days.

   Study Classification: Core Minimum Data

   Product Classification: Tox. Cat. IV

7. Primary eye irritation - rabbit. Union Carbide Research Center, Project Report 46-71; dated July 12, 1983.

   Procedure: 0.1 ml was applied to one eye of each of 6 rabbits, with no subsequent wash.

   Results: 3/6 eyes showed minor conjunctival irritation at 24 hrs. All eyes clear by 48 hrs.

   Study Classification: Core Minimum Data

   Report Classification: Tox. Cat. III

Byron T. Backus 12-07-83

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