UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 069200

DATE: October 17, 1979 003690

SUBJECT: EPA Reg.#3125-121, 122, 146, 214, GNA; PP#2F1244; Baygon for use in/on alfalfa, pasture grass, meat, fat and meat by-products of cattle, goats, hogs, horses, poultry and sheep, eggs, milk. CASWELL #508, Acc.#0975494

FROM: William Dykstra, Ph.D
Toxicology Branch (TS-769) WHD 10/17/79 WSW

TO: Frank Sanders
Product Manager#12 & Residue Chemistry Branch
(TS-769)

Petitioner: Mobay Chemical Corp.
Agricultural Chemicals Div.
Kansas City, Missouri 64120

Recommendations:

1) The requested tolerances are not toxicologically supported. The following toxicity studies are required:

   (a) teratology - 2nd species
   (b) oncogenicity - 2nd species

2) The toxicology studies submitted are acceptable as Core-Minimum Data.

3) The human exposure safety information for ULV nonthermal aerosols is acceptable as supplementary information.

4) In response to Oct. 25, 1978 letter from petitioner to F. Sanders(21) regarding toxicology items from previous EPA memorandum:

   Item A1: Since the mouse oncogenicity study was scheduled to be completed in mid-1979, Toxicology Branch requests that this study be submitted.

   Item A2: Additional mutagenic studies may be required in the future.

   Item A3: This item has been satisfactorily resolved by the petitioner.

   Item A4: This item has been satisfactorily addressed by the petitoner.

   Item B1 and B2: These items have been satisfactorily addressed by the petitoner.

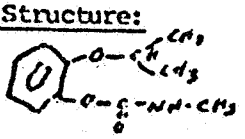
1786

003690

Proposed Tolerances - Section F

Alfalfa (fresh)	10 ppm
Alfalfa (hay)	40 ppm
Pasture grass (green)	10 ppm
Pasture grass (hay)	40 ppm
Meat, fat and meat by-products of cattle, goats, hogs, horses, poultry and sheep	0.2 ppm
Eggs	0.04 ppm
Milk	0.10 ppm

A. Chemical Structure:



B. Chemical Name: 2(1-methylethoxy)phenol methyl carbamate

C. Proposed Uses

A. Control of adult mosquitoes over alfalfa and pasture grass fields. To be applied at the rate of 1.25 - 4 fluid ounces per acre as necessary at 7 to 14 day intervals with no more than 10 applications per crop year.

B. For fly control in livestock and animal barns including dairy barns, milk rooms, horse, sheep and swine barns and dog kennels as an aqueous 1% w/w solution.

D. Confidential Statement of Formulation Baygon 70% Wettable Power.

Active Ingredient	Percent Weight
o-Isopropoxyphenyl methyl carbamate	70
Inerts	[redacted]

Inerts cleared under 40 CFR 180.1001.

INFORMATION WHICH MAY REVEAL AN INERT INGREDIENT IS NOT INCLUDED

2

003690

Review

A. Toxicology Studies Submitted.

1. Supplement No.7, June 26, 1978 to Brochure entitled: Baygon (Bay 39007) Toxicology, March 15, 1973.

(a) The acute oral toxicity of Baygon 70% Wettable Powder at the Use Dilution (Chem Agro, Report#74-144, August 26, 1976).

Baygon 70% Wettable powder was diluted in water (2 oz./gal.) and was administered to rats fasted 20 hours. Dose volumes of this sample ranged from 0.1 to 0.8% body weight to arrive at the desired dose levels on a geometric log scale of 2. Animals (5M & 5F) received 1, 2, 4 and 8 gm/kg doses and were observed for 14 days.

Results: LD_{50} = 4 gm/kg (males) (2-6)
LD_{50} = 2 gm/kg (females) (2-3)

Toxic Signs: Tremors, salivation & muscular fasiculations. Duration of symptoms was dose-related.

Body Weight: Not reported

Necropsy: Females appeared normal. Males had minor lung lesions not attributed to the compound.

Classification: Core-Minimum Data

TOX Category III: CAUTION

(b) Toxicity of Propoxur to Rats by Subacute Inhalation (Gevig Kinnerle and Akihiko Iyatomi) Jap. J. Ind. Health, Vol. 18, 1976.

Three experimental groups of 10 male and 10 female rats were exposed to inhalation of propoxur concentrations averaging 5.7 (3.7-7.0), 18.7 (17.3-20.2) and 31.7 (26.2-36.3) mg/m^3, respectively, for 6 hours daily on 5 days per week over a period of 12 weeks (360 hours total). A control group of 10 male and 10 female rats was exposed only to the solvent mixture (ethanol/poly ethylene glycol, 20 ml/m^3). Hematology, urinanalysis, Clinical Chemistry, plasma and RBC cholinesterase activity were determined on 5M & 5F/group after termination of the 5th, 10th, 20th, 30th, 45th and 60th exposures; brain cholinesterase activity was measured at autopsy. Organ weights and histopathology was performed.

Results: The effects depression of plasma 20 to 30% and of RBC and brain cholinesterase activities which were caused by the highest air concentrations of 31.7 mg/m_3. No compound related effects on organ weight or histopathology were noted.

Conclusion: On the basis of physical, and metabolic behaviors, a maximum allowable concentration of 2.5 mg/m_3 air is suggested. 3

Classification: Core-Minimum Data

C. The Acute Oral Toxicity of Baygon 70% Wettable Powder (Chemagro, 72-252, March 10, 1978).

For each dose level 10M & 10F were used. Dose levels were male: 79, 111, 115 and 218 mg/kg; female: 40, 56, 79, 111, 155 and 218 mg/kg. Observations were for 14 days.

Results: LD_{50} males = 111 mg/kg (99-124)
LD_{50} females = 75 mg/kg (61-92)

Toxic Signs: males: salivation, tremor, decreased activity, convulsions and bloody froth at mouth; females: diarrhea, salivation, lacrimation, exophthalmos, tremors, convlusions and decreased activity.

Body Weight: Body weight gain appeared normal for both males and females.

Necropsy: Congested lungs, dark livers, hemorrahagic enteritis, mottled kidneys.

Classification: Core-Minimum Data

TOX Category II: WARNING

D. The Acute Dermal Toxicity of Baygon 70% Wettable Powder to Rabbnits (Chemagro, 77-252, March 21, 1978).

4M & 4F rabbits received 5000 mg/kg doses on the abraded skin under an occluded patch for 24 hours. Observations for 14 days.

Results: No deaths, LD_{50} > 5000 mg/kg

Toxic Signs: Ataxia, dropping ears, weeping eyes.

Body Weight: Animals gained weight.

Necropsy: Pale kidneys, subcapular hemorrhages.

Classification: Core-Minimum Data

TOX Category III: CAUTION

E. Propoxur; Mutagenicity test on bacterial systems (H. Inukai, A. Iyatomi, Nitokuno, Agricultural Chemicals Institute, Laboratory of Toxicology, Report 103, Feb. 24, 1978).

The test compound used in the experiments was a sample of technical grade propoxur (purity; 98%). Furylfuramide (AF-2), 9-aminoacridine. HCl (9-AA), acetylaminofluorene (AAF), N-methyl-N'-nitro-N-nitrosoguanidine (NTG), dimethylnitrosoamine (DMNA) and mitomycin C (MC) were used as the positive control, Propoxur, AF-2 and AAF were dissolved in DMSO, and NTG, DMNA, 9-AA and MC in distilled water, respectively.

Rec-Assay

The rec-assay was performed on two strains, N1G17 and N1G45 of Bacillus subtilis according to Kada et al. The N1G45 is a recombinational repair deficient stain (rec -) which cannot repair the damages on DNA and N1G17 strain is a wild strain (rec +) which can do it. Both overnight cultures of Bacillus subtilis were streaked on the surface of solid agar broth.The paper disc which was immersed with the tested compound was put on the edges of the streaks. The plates were incubated at 37°C overnight and then the length of growth inhibition were measured.

MC was used as positive control in rec-assay.

Reversion Assay with in vitro metabolic activation.

The reversion assay was performed on four strains, TA1535, TA1537, TA98 and TA100 of Salmonella typhimurium according to Ames et al. The supernatant (S-9) of liver homogenate at 9000 xg centrifugation from rats or mice treated with phenobarbital was used for the metabolic activation. For mutagenicity test with the S-9 fraction, 0.1 ml of overnight culture of each tested strain, 0.3 ml of S-9 mixture, and 0.1 ml of the test compound were spread by a glass spreader. The plates were incubated at 37°C for 48 hours and then revertant colonies on the plate were counted.

NTG in TA1535 strain, 9-AA in TA-1537 and TA98 and AF-2 in TA100 were examined as the positive control in the reversion assay, respectively, and AAF in TA98 was used for in vitro metabolic activation with the rat liver homogenate, and DMNA in TA1535 and TA100 was used with the mouse liver homogenate, respectively.

Results:

1. Rec-Assay - The growth of both strains of B. subtilis was not inhibited at the tested doses (3, 30, 300 ug/disc) of propoxur, while the growth inhibition between N1G17 and N1G45 was significantly different at 0.3 ug/disc of MC.

2. Reversion Assay with in vitro metabolic activation - In the experiments with the S-9 mixture of rats and mice, there was no remarkable difference in the frequency of revertant colonies between plates treated with propoxur and those with no-drug in the TA1535, TA1537, TA98 and TA100, respectively. Therefore, propoxur and its liver metabolites with liver homogenates of either rats or mice are non-mutagenic in S. typhimurium.

Conclusion: Propoxur is non-mutagenic in rec-assay with B. subtilis and and the reversion assay with and without metabolic activation in S. typhimurium.

Classification: Core-Minimum Data

B. Baygon MOS - Human Exposure Safety Information for ULV nonthermal aerosols - 7/26/76.

Purpose:, To submit reports of extent and effects of human exposure to Baygon MOS as a result of efficacy testing, and data on airborne concentrations as a result of ULV nonthermal ground observations.

Conclusion: No adverse effects were noted with applicators exposed to Baygon.

Classification: Supplementary Data

C. Previously Submitted Toxicity Data.

1. Memo of 4/7/69 from M. Quaife; PP#9G0765.

Acute Oral LD50 - Rat - Female - 87-110 mg/kg
Rat - Male - 88-150 mg/kg
Guinea Pig - Male 40 mg/kg
Hen - Female 150 mg/kg
Chick - Male 46.5 mg/kg
28-Day Intubation M-Rats; systemicm NEL = 7.5 mg/kg
16-Week Feeding Study Rats: NEL > 800 ppm; ChE NEL not established.
2-year Feeding Study - Rats; systemic NEL = 250 ppm; ChE NEL not established.
2-year Feeding Study - Dogs; systemic NEL = 250 ppm; ChE NEL not established.

2. Memo of 7/10/72 from D.V. Parkin to Mr. Drew Baker; PP#2F1244.

°pathology report on 2 year dog - no compound related effects
°pathology report on 2 year rat - no compound related effects
°teratology in rats: no terata at 10,000 ppm; fetotoxic NEL = 1000 ppm

3. Memo of 10/26/77 from K. Bailey to F. Sanders (21); PP#2F1244.

°3-generation rat reproduction - NOEL = 250 ppm
°Acute delayed neurotoxicity: no evidence of neurotoxicity to hens after acute oral (100 - 1000 mg/kg), intraperitoneal (25-100 mg/kg) or 30-day feeding (300-4500 ppm). Histopathological examination was performed.

°2-year dog feeding study: NOEL = 250 ppm
°2-year rat feeding study: NOEL = 250 ppm; supplementary data as oncogenic study.
°teratology in rats: supplementary data

4. Memo of 10/19/78 from D.G. Van Ormer to Frank Sanders(21).

Consideration of teratogenicity:

(A) K.S. Khera, Toxicology and Applied Pharmacology, 8, 345, 1966 (abstract) when injected at the middle of embryogenesis into duck and chick embryos, Bayer 39007 (Baygon, technical) induced congential foot deformities at 0.01 to 1.0 mg/egg.