

US EPA ARCHIVE DOCUMENT

Shaughnessy Number: 110201

Date out of EFGWB: 8/30/90

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Product Manager
Registration Division (H7505C)

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Thru: Hank Jacoby, Chief *Hank Jacoby*
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Attached, please find the EFGWB review of...

Reg./File #: 55947-UR

Chemical Name: Prodiamine

Type Product: herbicide

Product Name: Technical Prodiamine

Company Name: Sandoz Crop Protection

Purpose: submission of preliminary co-solvent test results and protocol for
fish bioaccumulation study

Date Received: 4/20/90

Action Code: 115

EFGWB#(s): 90-0528

Total Reviewing Time (decimal days): _____

Deferrals to: Ecological Effects Branch, EFED

Science Integration and Policy Staff, EFED

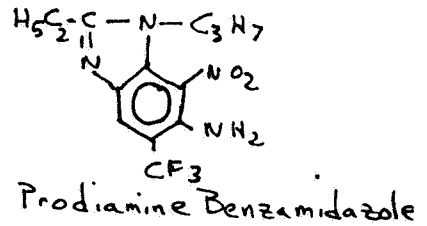
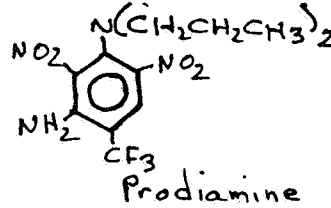
Non-Dietary Exposure Branch, HED

Dietary Exposure Branch, HED

Toxicology Branch

1. CHEMICAL:

chemical name: N³,N³-Di-n-propyl-2,4-dinitro-6-(trifluoromethyl)-m-phenylenediamine
common name: prodiamine
trade name: Endurance
structure:
CAS #: 29091-21-2
Shaughnessy #: 110201



PHYSICAL/CHEMICAL CHARACTERISTICS are as follows:

physical state -- crystalline powder
color -- dark yellow
odor -- odorless
m.p. -- 124-125° C
vapor pressure -- 2.5×10^{-7} mm Hg at 25° C
water solubility -- 0.05 ppm
octanol/water coefficient (k_{ow}) -- 3.3×10^4

2. TEST MATERIAL: as described below

3. STUDY/ACTION TYPE: submission of two items:

- 1) preliminary study on efficacy of various co-solvents which might enhance solubility of prodiamine in the fish study
- 2) study protocol for fish bioaccumulation

4. STUDY IDENTIFICATION: n.a.

5. REVIEWED BY:

Typed Name: E. Brinson Conerly
Title: Chemist, Review Section 2
Organization: EFGWB/EFED/OPP

E. B. Conerly 8/21/90

6. APPROVED BY:

Typed Name: Henry Nelson
Title: Section Head, Review Section 3
Organization: EFGWB/EFED/OPP

H. Nelson
8/29/90

7. CONCLUSIONS:

- 1) Polyethylene glycol (PEG) appears to be effective at lower concentrations than the other cosolvents tested.
- 2) The lowest concentration of PEG tested (0.01%) appears to be at least as effective as the maximum tested, and may even be slightly better. It is always desirable to use minimal co-solvent or other potential toxicant.
- 3) EFGWB does not have information on the toxicity of PEG. Unless the applicant can document that PEG has no effect on the fish, the investigator must choose a different cosolvent, or perform an additional control using no PEG or pesticide in the bioaccumulation study.

8. RECOMMENDATIONS:

- 1) The applicant should proceed with the fish bioaccumulation study with the following modifications:
 - a) Minimize direct light exposure of the aquaria, to reduce, if possible, the amount of photodegradation taking place.
 - b) Analyze the water in the exposure tank at frequent intervals to determine the composition of material (parent and degradates) that actually is present at any given time. Appropriate time intervals can be established during the preliminary study. If an apparent steady state is reached, subsequent analyses may be done less often.
 - c) If the amount of PEG to be used is known to have little or no adverse effect on the fish, then a single control with co-solvent and without pesticide, as described in the protocol, is satisfactory. The applicant must provide data to support this claim of non-toxicity.

If the toxicity of PEG is known to be significant, then an alternative, less toxic, cosolvent should be chosen if possible.

If PEG is known to be toxic or if data on its toxic properties are not available, but its use is deemed to be essential, the applicant should perform the test with an exposed group of fish and two control groups, one with test water only and one with water and PEG.
 - d) Use the minimum effective concentration of PEG (apparently 0.01%).
- 2) The applicant should note that acceptance of a protocol does not necessarily indicate that the resulting study will also be accepted.

9. BACKGROUND:

Prodamine is a not-yet-registered herbicide used to control the germination of grasses and broadleaf weeds in ornamentals and turf. Label directions indicate that it may be applied either to a cover crop (established turf) or to bare soil (around ornamental plants and in non-crop areas). The recommended label rate is up to 3.9 lb ai./A (3.9 ppm, 3" soil layer) per single application or 7.8 lb a.i./A/yr.

Available data indicate a compound which

- 1) is stable to hydrolysis (no degradation after 30 days -- all pHs).
- 2) is highly susceptible to photolysis in aqueous solution. Because of its extreme lability to photolysis in solution, it would also be expected to photolyze rapidly on leaf surfaces exposed to light, although there are no specific leaf-surface photolysis data in EFGWB files.
- 3) metabolizes slowly under aerobic conditions (half-life ca. 2 months, one major degradate).
- 4) is not mobile in laboratory studies, nor, apparently, is the major degradate.
- 5) is not mobile based on a field study on turf.
- 6) accumulated in both confined rotational crops and fish.

Because of its extremely short photolytic half life and lack of mobility, prodiamine does not appear likely to reach ground water. Though it is improbable that it would reach ground water, if somehow it did, it would persist there, since photolysis, the major mode of disappearance, would not occur.

Prodiamine does not appear to be a major threat to surface water since it photolyzes rapidly. Although the probability seems very low, any prodiamine which is present on soil affected by a runoff event could be carried on suspended particles to adjacent bodies of surface water. Once there, it would be expected to remain in the sediment and degrade/dissipate very slowly.

The status of data requirements is as follows:

hydrolysis -- **FULFILLED** 6/22/90 [*Bowman and Fenessey*, MRID #'s 406091-01 and 413594-01 -- $t_{1/2} > 6$ months is indicated at all three pHs

photolysis in water -- **FULFILLED** 5/13/80 [reference not indicated in that review] -- not done under current Guidelines. A short half life (ca. 20 min.) is indicated

soil photodegradation -- submitted study [reference not indicated in that review] unacceptable as of 5/13/80, not required for this use

aerobic soil metabolism -- **FULFILLED** 6/22/90 [*Krueger and Butz*, MRID #'s 405934-24 and 413594-02]-- half-life ca. 2 mos, one major product

anaerobic soil metabolism -- submitted study unacceptable as of 5/14/80, not required for this use

leaching/adsorption/desorption -- **FULFILLED** 5/13/80 for parent [reference not indicated in that review-- **NEW STUDY REQUIRED ON AGED MATERIAL** [as of 6/22/90 -- *Daly*, MRID #'s 405934-26 and 413594-03 are not acceptable]. The mobility of primary degradate has not been satisfactorily defined at this time, although it is apparently also relatively immobile.

turf terrestrial field dissipation -- **FULFILLED** 6/22/90 [*Bade and Rosas*, MRID MRID # 413594-05] -- no leaching or significant dissipation noted.

confined accumulation on rotational crops -- **FULFILLED** 5/14/80 [reference not indicated in that review] -- not done under current Guidelines -- not required for this use -- no significant accumulation except in root crops

fish bioaccumulation -- study submitted [Acc.# 243135] but not acceptable [static system], not done under current Guidelines -- significant accumulation and slow depuration

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

There are no actual studies in the submission. The applicant has submitted results of tests with different co-solvents, and also a protocol for a fish bioaccumulation study in which they propose to use a co-solvent to enhance solubility of prodiamine.

CO-SOLVENT TEST -- summarizing the results, polyethylene glycol (PEG, average m.w. 200) in concentrations of 0.05 - 1% enhances solubility by approximately a factor of 10. Other solvents tested were

tetrahydrofuran (THF), dimethylformamide (DMF), methanol, and acetone, which are somewhat less effective. Available LC₅₀s were as follows:

THF -	2.160 gm/l (90 hr)	= 2160 ppm
acetone -	6 - 8 gm/l (96 hr), results of three tests	= 6000 ppm (minimum)
methanol -	29.4 gm/l (96 hr)	= 29400 ppm

The lowest concentration of PEG is the equivalent of 100 ppm. The toxicity of PEG is not known to EFGWB, but 100 ppm is clearly lower than the LC₅₀s of those that are known.

PROTOCOL FOR FISH BIOACCUMULATION STUDY -- provided by the intended testing laboratory, and not tailored to the specific test compound, prodiamine. It takes into account the general points which must be covered in the study, but prodiamine has some specific characteristics which must also be considered [see comments].

materials and methods

test material -- description is not specific to prodiamine

test fish -- *Lepomis macrochirus*, 2 -10 gm, same year class, fed commercial food tested for contaminants

test conditions -- 14 day pre-study fish observation period, minimum of 24 hours acclimation prior to initiation of exposure, 16 hour photoperiod

test system for adding pesticide -- proportional diluter

test aquaria -- 100 l size containing 70 l solution; solution replaced 5 x in 24 hr period; temperature to be maintained by immersion in a water bath controlled at 22± 2 C

test procedure

preliminary -- 4 - 14 day exposure to establish one of the following:

- 1) an LC₅₀ level under flow-through conditions
- 2) a no-effect level based on mortality and behavioral effects
- 3) a no-effect level at the maximum practical exposure

definitive -- based on the preliminary experiment. The exposure concentration will be established at 1/10 to 1/100 of the acute toxicity or no-effect level of the test compound. [Note that this is *verbatim* from the submission. See the comment below.] Exposure will continue for 28 days, or longer if necessary, until the fish demonstrably have reached a plateau (steady state) of uptake. Fish will be observed twice daily for behavioral aberrations and mortality. At the end of the exposure phase, addition of test

material will be discontinued. To remove test material from the aquarium, the water will be twice siphoned off to approximately an 8 cm level (20 l) and replaced with fresh water. [Approximately 20/70 = 28.6% of the test material will remain after the 1st draining, and 8.1% after the 2nd.] This will be the starting point (day zero) for depuration.

sampling procedure -- fish and aquarium water sampled at 0, 1, 3, 7, 14, 21, and 28 days. Fish will be dissected into edible and non-edible tissues or kept whole. Samples will be homogenized with dry ice and the CO₂ allowed to sublime before storage or combustion. Length and weight of fish will be measured on a representative group at the beginning and end of the study.

analyses and measurements

pH and temperature -- aquarium water

total radioactivity -- whole fish, fillet (edible), viscera (non-edible -- fins, head, internal organs)

metabolite identification -- samples from days 21 and 28 (specific technique not given)

REVIEWER'S COMMENTS

Based on an unacceptable study, prodiamine has an extremely short photolytic half-life in water. This means that the fish will probably be exposed to the photolytic degradates much more than to parent compound. Two actions may mitigate the effect of this complication without keeping the fish [or investigators] in darkness for 28 days. First, direct light impinging on the aquaria should be minimized. Second, the water should be analyzed frequently for parent and degradates, to determine the composition of the exposure solution throughout the experiment. If this were done during the preliminary study, any technical difficulties with analyses or sampling could be worked out before committing to the longer study. Further, since some photolysis almost certainly will occur and the fish will be exposed to a mixture of compounds, interpretation of the data will be somewhat difficult. EFGWB can make this interpretation with more confidence if the actual composition of the solution is defined.

The description of the exposure concentration to be used in the definitive experiment is somewhat unclear. This point should be clarified. This reviewer believes that the concentration will be established either

- a) at some no-effect level if one can be determined
- b) or at 1/10 to 1/100 of the LC₅₀ if one is defined in the preliminary experiment.

The recharge rate of the aquarium during depuration has not been specified. This reviewer assumes that it will be the same (complete replacement 5 x every 24 hours) as in the exposure phase.

11. COMPLETION OF ONE-LINER: no information added

12. CBI APPENDIX: protocol and co-solvent data attached