9/2/92

D172675
DPBARCODE (RECORD)
111401
SHAUGHNESSY NO

REVIEW NO.

EEB REVIEW

DATE IN: 01-13-92 OUT:

CASE # : 816375 REREG CASE #: 2540
SUBMISSION # : S409050 LIST B
ID # : 111401-000100

DATE OF SUBMISSION 12-18-91

DATE RECEIVED BY EFED 01-07-92

SRRD/RD REQUESTED COMPLETION DATE 02-29-92

EEB ESTIMATED COMPLETION DATE 02-29-92

SRRD/RD **ACTION** CODE/TYPE OF REVIEW 620 - 3(C)2(B) resp.

MRID #(S)

DP TYPE 999 - Miscellaneous Data Package

PRODUCT MANAGER, NO. C. Rice (52)

PRODUCT NAME(S) Curacron

TYPE PRODUCT F R I N H D Insecticide

COMPANY NAME Ciba-Geigy Corp.

SUBMISSION PURPOSE Review registrant rebuttal to EEB

INCLUDE USE(S) review of avian dietary studies

COMMON CHEMICAL NAME Profenofos

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ECOLOGICAL EFFECTS BRANCH

Chemical: Profenofos, Curacron

100.0 Purpose of Submission

The Registrant (Ciba-Geigy) has requested that the EEB reconsider its' evaluation of two avian dietary studies (MRID#s 41627303 and 41627302) which were classified as Invalid because nominal rather than measured concentrations were used to calculate the LC50 values. Ciba-Geigy argues that, because (1) the test material is stable in diets and readily mixes, (2) EPA guidelines do not require dietary analysis, (3) food analysis is only supplemental information and, (4) EEB policy has traditionally allowed avian dietary studies to be accepted with nominal concentrations, the studies should be upgraded to "Core" status.

101.0 Discussion

The EEB has previously reviewed the two studies in question (See DER by R. Felthousen dated 6/14/91) and found the studies to be "Invalid" because it was learned, from reviewing a dietary study for another chemical that the test rations prepared by Bio-Life Associates, Ltd. (BLAL-the testing facility that conducted the tests for Ciba-Geigy) could have so much variability between the measured concentrations (as determined from grab samples) that it is impossible to determine the actual treatment levels used to determine the LC50 value (See attached telephone conversation sheet detailing a discussion between the EEB and an analytical chemist with the Denver Wildlife Research Center).

As a result of further investigation, the EEB learned that one of the reasons for this variation was that BLAL did not routinely sift the fine from the coarse materials in the rations. This lead to very high concentrations of the toxicant being found in the fines and lower concentrations in the coarser material. Therefore, even though Curacron may be stable and readily mix in the diet, there is no way of knowing what were the actual dietary concentrations used in the study.

The BLAL was notified of this problem and has agreed to correct it in the future by sifting the dietary ration prior to using it in an avian dietary test. The EEB is satisfied that this added procedure will greatly reduce the variability in the test ration.

102.0 Conclusions

The EEB has reviewed Ciba-Geigy's request that the avian dietary LC50 tests for the bobwhite quail and mallard duck be reclassified as "Core" data. Based upon information that was made available to the EEB relative to preparation of the diets as well as analytical data for the test concentrations prepared by BLAL, which shows tremendous variation between residues for the coarse, median and fine materials, the EEB must still conclude that the two studies in question are invalid and that the guideline requirements 71-2(a) and 71-2(b) have not been satisfied.

Richard W. Felthousen 9/1/92
Richard W. Felthousen, Wildlife Biologist
EFED/EEB

Allan W. Vaughan 9.2.92
Allan Vaughan, Acting Head, Section 2
EFED/EEB

Douglas J. Urban 9/2/92
Doug Urban, Acting Chief
EFED/EEB

TELEPHONE RECORDS: JUNE 26, 1990

TELE. NO: (303) 236-7872

Beth Michalanie Analytical Chemist

Research Chemist -

Preliminary batches of feed from Bio-Life showed tremendous variation in residues in feed.

—— 10 — 40% Coefficient of variation.

Feed - 6000 feed assayed:

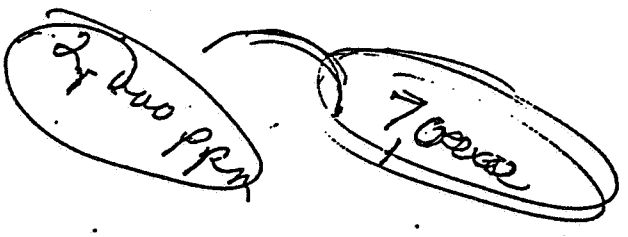
	Actual Values	
Coarse grain	3,500 ppm	Strychnine
Medium grain	4,000 ppm	"
Fine	11,000 ppm	"
	10 — 12 ppm	

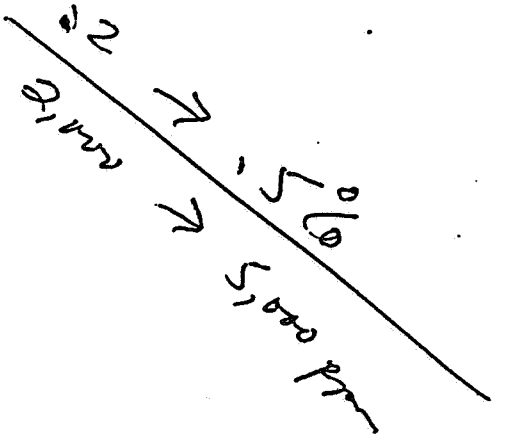
~~3~~ preliminary batches.

Precision -

Biological variability too large

* Don't know how to analyze the material





REREGISTRATION PHASE 4
PROFENOFOS
CHEMICAL NO. 111401, CASE NO. 2540

CORRESPONDENCE
PAGE 1 OF 6

PHASE 4 RESPONSES:

Guideline	Description	Phase 4 Response
71-2(a)	Acute avian diet. quail	Upgrade

Dietary residue measurements were requested for the avian dietary study with Bobwhite Quail (MRID 41627303) to upgrade the study to acceptable status. The study did not include dietary analysis because the test material is stable in diets and readily mixes. We request that the status of this study be reconsidered given the following: EPA guidelines (EPA-540/9-82-024) do not require analyses, EPA Subdivision E acceptance criteria (Nov. 7, 1989) list food analyses as supplemental information and it is known that EEB branch policy has traditionally allowed avian dietary studies to be accepted with nominal test concentrations.

71-2(b)	Acute avian diet. duck	Upgrade

See comment for guideline 71-2(a). This applies to MRID 41627302 as well.

71-5(b)	Actual field study	Developing Data

We note that no protocol review is required by the DCI. We will be requesting a meeting in the first quarter of 1992 to discuss the siting of these studies.

72-4(a)	Early life stage fish	Citing a Study.

EG & G Bionomics Study No. BW-79-6-490 (MRID 85958) was submitted on 11/5/81, but was not included in the bibliography enclosed with the Phase 2 package. As a result, we erroneously used response code 6 for this guideline in our Phase 2 response. This study was summarized in Phase 3, but was denied based on the fact that the species used was the fathead minnow rather than the brook trout. We have requested a DER for this study.

Ciba-Geigy notes that EPA Subdivision E Guidelines suggest fathead minnow as a test species (p. 78). Moreover, a recent telephone discussion with personnel in

the Ecological Effects Branch (12/6/91) indicates that fathead minnow are an acceptable test species.

We request that this study be reevaluated. In order to facilitate this reevaluation, we are resubmitting the study today. Enclosed you will find three copies of a transmittal document and of the study. A new statistical analysis of the results is included.

72-7(b) Actual field-aquatic organisms Developing Data

We note that no protocol review is required by the DCI. We will be requesting a meeting in the first quarter of 1992 to discuss these studies.

85-4-SS 6-Months ocular toxicity - dog Citing a Study

CIBA-GEIGY believes the ocular toxicity of profenofos has been adequately assessed in studies previously submitted to the Agency: a Neurotoxicity Study with CGA-15324 38% E.C. in Chickens (MRID 45032 and related MRIDs 82084 and 126493); a 90-Day Subacute Oral Toxicity Study with CGA-15324 Technical in Beagle Dogs (MRID 108016); a Six-Month Toxicity Study with Dogs (MRID 81687 and related MRID 102939); a Two-Year Chronic Oral Toxicity Study in Albino Rats (MRID 81685 and related MRID 83436); and a Twenty-Four Month Carcinogenicity Study in Mice (MRID 81686 and related MRIDs 82901 and 83435). None of the above rodent or dog studies presented an indication of neurologic problems resulting from exposure to profenofos for up to two years.

Opthalmologic examinations, when performed, did not detect any ocular and/or neurologic dysfunction or degenerative changes after short or long term exposure to profenofos in several species. Further, histologic examinations of eyes from those species showed no architectural changes in any ocular structure to indicate that the eye is a target organ. Examination of peripheral nerves and other nervous system tissue showed no treatment-related effects. No signs of delayed neurotoxicity were observed in chickens dosed with profenofos. There were no treatment-related clinical signs indicative of neurotoxicity noted in subchronic or chronic dietary exposure studies with rats, mice, or dogs, even at levels which significantly affected cholinesterase activity.

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