Cal/EPA

California Environmental Protection Agency

Department of Pesticide Regulation

1020 N Street
Sacramento, CA
95814-5624
(916)445-4300

Branches:

Pesticide Registration

Medical Toxicology

Worker Health and Safety

Environmental Monitoring and Pest Management

Pesticide Enforcement

Information Services

Audits

Resources Management

NOTICE OF COMPLETION OF RISK ASSESSMENT FOR THE PESTICIDE PRODUCT BIFLEX® TC (Bifenthrin)

The Department of Pesticide Regulation (DPR) has completed a human health risk assessment on the use of the active ingredient bifenthrin as a subterranean termiticide (Biflex® TC).

Enclosed are copies of the final Risk Characterization and Exposure Assessment documents. Using current toxicity and exposure data, DPR finds that significant adverse effects could occur as a result of the use of Biflex® TC during postconstruction termiticide treatments. DPR needs to make a determination as to whether the risk can be mitigated.

DPR is considering feasible mitigation measures that would reduce exposure to:

- Postconstruction mixers/loaders and applicators.

If you would like to participate in that process, please submit proposed mitigation measures to DPR. Submit the proposals in writing and within **90** days. Proposals received after 90 days may not receive consideration by DPR before finalization of the risk mitigation document. Please address all proposals to:

Risk Mitigation Proposals - (Biflex® TC)
Pesticide Registration Branch
Department of Pesticide Regulation
1020 N Street, Room 332
Sacramento, California 95814-5624

If requested, DPR will schedule a meeting to discuss submitted mitigation proposals. When completed, DPR intends to send you a copy of the Risk Mitigation document. The document will include mitigation measures that must be taken in order to allow registration of the product.

Please address all requests for additional information to Ms. Ann Prichard, Environmental Research Scientist, Pesticide Registration Branch, at (916) 324-3931.

Barry Cortez, Chief
Pesticide Registration Branch
(916) 445-4377

May 12, 1997
Date

Enclosures

cc: Ms. Ann Prichard

State of California

Memorandum

To Ronald J. Oshima, Assistant Director
Division of Registration and Health Evaluation

Date March 5, 1997

Place

From Department of Pesticide Regulation - 1020 N Street, Room 234
Sacramento, California 95814-5624

Subject

Risk Assessment of Biflex TC (bifenthrin)

Attached, for your acceptance, is the risk characterization document appendix for assessing the use of the registered active ingredient, bifenthrin, as a subterranean termiticide. This risk characterization document contains no new toxicological study reviews since our initial review of bifenthrin (1991). This document indicates that the acute risk margins of exposure (MOE) for mixer/loaders and applicators range from 30 to 40. The potential lifetime oncogenic risk for mixer/loaders and applicators range from 5×10^{-5} to 13×10^{-5}.

Gary T. Patterson, Chief
Medical Toxicology Branch
(916) 445-4233

Signature for Approval: Ronald J. Oshima, Assistant Director

SURNAME

RISK ASSESSMENT OF BIFLEX® TC

BIFENTHRIN RISK CHARACTERIZATION DOCUMENT C:

SUBSEQUENT TO

BIFENTHRIN (CAPTURE 2 EC) RISK CHARACTERIZATION DOCUMENT, 1991

HEALTH ASSESSMENT SECTION
MEDICAL TOXICOLOGY BRANCH
DEPARTMENT OF PESTICIDE REGULATION
CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

March 4, 1997

CONTRIBUTORS AND ACKNOWLEDGMENTS

Principal Author:	Nu-may R. Reed, Ph.D., D.A.B.T. Staff Toxicologist Health Assessment Section Medical Toxicology Branch
Product Data Review:	John Corlett, B.S. Associate Pesticide Review Scientist Product Data Review Section Medical Toxicology Branch
	Thomas B. Moore, Ph.D. Staff Toxicologist Product Data Review Section Medical Toxicology Branch
Dietary Exposure:	Nu-may R. Reed, Ph.D., D.A.B.T. Staff Toxicologist Health Assessment Section Medical Toxicology Branch
Occupational Exposure:	Michael Dong, Ph.D. Exposure Assessment Group Worker Health and Safety Branch
Peer Review:	Keith Pfeifer, Ph.D., D.A.B.T. Senior Toxicologist Medical Toxicology Branch
	Jay P. Schreider, Ph.D. Primary State Toxicologist Medical Toxicology Branch

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RISK ASSESSMENT FOR BIFLEX® TC

I. BACKGROUND

This document contains the risk assessment of Biflex® TC to be used as a subterranean termiticide. Biflex® TC contains 25.1% bifenthrin. The label specifies a maximum Biflex® TC application rate of 0.12% bifenthrin, or, 2 quarts Biflex® TC per 100 gallons finished application emulsion. The maximum volume of application is 1 gallon of emulsion per 10 ft^2, or 4 gallons of emulsion per 10 linear feet per foot of depth. For preconstruction applications, the volume of application is 1.5 gallons of emulsion per 10 ft^2 in horizontal barriers if the fill is washed gravel or other course material, and 2 gallons of emulsion per 10 linear feet in hollow block voids or masonry voids applications.

A risk characterization document (RCD) for bifenthrin, specifically for the Section 3 registration of Capture® 2 EC-Cal for cotton, was completed in 1991 (Reed, 1991). The database on the physical and chemical properties, the environmental fate, and the toxicity profile of bifenthrin were presented in the 1991 RCD. Recently, the registrant requested a reevaluation of the toxicological database with respect to the NOEL determination, although no new data were submitted. The oncogenicity dose-response assessment was also reevaluated based on the re-reading of histopathological slides in 1992. Detailed discussions on these two issues were presented in a recent risk assessment for Talstar® (Reed, 1997). DPR concluded from the reevaluation that, the critical NOEL and oncogenicity dose-response assessment presented in the 1991 RCD remained valid for use in the risk assessment of bifenthrin formulations (i.e., Talstar® and Biflex®).

The use of Biflex® TC as termiticide by itself is not expected to result in dietary exposures. However, the potential for a dietary exposure to bifenthrin exists through the use of Capture® 2 EC-Cal. In addition to its registered use on cotton, Capture® 2 EC-Cal has also been used since 1991 on many food crops in California under Section 18 Emergency Exemption of the Federal Insecticide, Fungicide, and Rodenticide Acts (FIFRA). Therefore, dietary exposures used in the Talstar® T&O risk assessment (Reed, 1997) are also included in the assessment of the total bifenthrin exposures of workers and residents associated with the use of Biflex® TC.

II. HAZARD IDENTIFICATION AND DOSE-RESPONSE ASSESSMENT

The acute toxicity database for Capture® 2 EC formulation was used to support the registration of Biflex® TC since the two formulations are identical. The oral median lethal dose (LD_{50}) for the formulation was 275 mg/kg in rats, the dermal LD_{50} was above 2,000 mg/kg in rabbits, and the inhalation median lethal concentration (LC_{50}) was 1.90 mg/l (4-hr whole body exposures) in rats (Reed, 1991). Based on studies on eye and dermal irritation, Capture® 2 EC was determined to be a category III eye irritant (irritation cleared within 7 days). It is classified in category IV with respect to dermal irritation potential since no dermal irritation was observed after 4 hours of semi-occluded exposures. Capture® 2 EC was determined to be a dermal sensitizer (Dong, 1996), however, a statement on the dermal sensitization potential is not included in the current labels for either Capture® 2 EC-Cal or Biflex® TC.

A detail toxicological profile of bifenthrin was presented in the RCD for Capture® 2 EC-Cal (Reed, 1991). The critical acute NOEL was 1 mg/kg/day based on an oral study in pregnant rats in which tremors were noted at 2 mg/kg/day. The critical endpoint for a long-term exposure was the oncogenicity potential. Based on urinary bladder tumors in mice, the slope of the oncogenicity dose-response relationship was 2.6×10^{-2} $(mg/kg/day)^{-1}$ at the maximum likelihood estimate (MLE) and 4.3×10^{-2} $(mg/kg/day)^{-1}$ at its 95% upper confidence bound (UB). The recent reevaluation resulted in no change in these critical endpoints and dose-response relationships for risk assessment (Reed, 1997).

III. EXPOSURE ASSESSMENT

Dietary exposures from the Section 18 uses are included in the estimates of total acute exposures of workers and residents of treated houses. These crops were not included in the dietary exposure components of the chronic risk assessment. Instead, chronic dietary exposures should be evaluated when these crops are under consideration for Section 3 registrations or when they are reconsidered for Section 18 uses subsequent to the 1996 use permits. Only the dietary exposure from the use of Capture® 2 EC-Cal on cotton was included in the assessment of total lifetime exposures. A detailed dietary exposure assessment was presented in the risk assessment for Talstar® T&O (Reed, 1997). The respective acute dietary exposures for a child and an adult were 3.5 and 2.2 μg/kg/day. The lifetime average dietary exposure was 0.003 μg/kg/day.

The two population groups that could potentially be exposed to bifenthrin from the use of Biflex® TC are: 1) mixer/loaders and applicators and, 2) residents and/or persons who service the house to which Biflex® TC has been applied. A detailed occupational and residential exposure assessment was presented by Dong (1995). Only a brief description of the exposure assessment is presented in this section. The absorbed dose from the occupational/residential exposure was calculated based on the absorption factor of 17.9% for dermal exposures and 50% for inhalation exposures.

The total exposure was the sum of the dietary exposure and the occupational/residential exposures. Because the critical NOEL and the oncogenic potency were determined from oral studies, the absorbed dose from occupational/residential exposure was converted to an oral equivalent exposure based on the oral absorption factor of 28% (Reed, 1991, 1997). A summary of the occupational/residential and total exposures is given in Table 1.

III.A. Occupational Exposures

The exposures for mixer/loaders and applicators were estimated based on dermal and air monitoring studies for both preconstruction applications (11 total sites) and applications to house foundations (17 total houses) at a target application concentration of 0.125% bifenthrin. The studies were conducted in six states (i.e., Delaware, Florida, New Jersey, Pennsylvania, Georgia, Illinois).

III.A.1. Acute Exposure levels

Two exposure estimates of absorbed daily dose (ADD) for each work task were given; the arithmetic mean and the highest value. The dermal and inhalation exposures were estimated based on an 8-hour work day in which a total of 3 pounds of bifenthrin was handled. The default respiratory rate of 0.84 m^3/hr was used in estimating the inhalation exposures.

Table 1. Bifenthrin occupational, residential, and total exposures associated with the use of Biflex® TC[a].

Exposure Groups	Acute Exposure (μg/kg/day)			Lifetime Exposure (μg/kg/day)		
	ADD	Oral equiv.[b]	Total[c]	LADD	Oral equiv.[b]	Total[d]
Mixer/Loader						
Average	1.59	5.68	7.88	0.51	1.82	1.82
High	8.50	30.35	32.55	2.72	9.71	9.72
Applicator						
Average	2.55	9.11	11.31	0.82	2.93	2.93
High	6.97	24.89	27.09	2.23	7.96	7.97
Mixer/Loader/Applicator						
Average	2.07	7.39	9.59	0.66	2.36	2.36
High	7.74	27.64	29.84	2.47	8.82	8.82
Resident - Child						
Average	0.02	0.07	3.57			
High	0.15	0.54	4.04			
Resident - Adult						
Average	0.01	0.04	2.24			
High	0.10	0.36	2.56			
Resident - Service						
Average	0.01	0.04	2.24			
High	0.06	0.21	2.41			

[a]/ Data taken from Dong (1995). ADD: Absorbed Daily Dose for occupational exposures; LADD: Lifetime Absorbed Daily Dose for occupational exposures. These values were estimated based on respective dermal and inhalation absorption factors of 17.9% and 50%.

[b]/ The oral equivalent occupational/residential exposure was the ADD or LADD divided by the oral absorption factor of 28%.

[c]/ The total exposure was the sum of the oral equivalent occupational/residential exposure and the dietary exposure. Dietary exposures were 3.5 μg/kg/day for a residential child and 2.2 μg/kg/day for an adult (Reed, 1997).

[d]/ The total exposure was the sum of the oral equivalent occupational/residential exposure and the dietary exposure. The dietary exposure was 0.003 μg/kg/day (Reed, 1997).

III.A.2. Lifetime exposure levels

The toxicological endpoint for long-term exposures was the oncogenicity potential, the potential to cause tumors and/or cancer. Without data to show otherwise, the current default assumption is that the oncogenic risk is proportional to the daily exposure averaged over a lifetime. Therefore, a lifetime average daily dose (LADD) was estimated. The average and high estimates of LADD were calculated from the average and high ADDs. The exposure frequency was assumed to be 219 days per year and 40 years in a lifetime of 75 years (Dong, 1995).

III.B. Resident Exposures

The exposure of residents living in a house treated with Biflex® TC was expected to be from inhalation of particulates that contain bifenthrin. The exposure was calculated based on indoor air monitoring data collected from 15 homes in four states (i.e., Florida, Georgia, New Jersey, Pennsylvania) (Dong, 1995).

III.B.1. Acute Exposure levels

Three exposure scenarios were assessed:

1) Resident - Child: The inhalation rate of 0.39 m^3/hr for a 6 years old child is the highest among all age groups (Dong, 1995). Therefore, a 6 years old child was used as a model for estimating the high-end of exposure for an individual staying in a treated house for 24 hours.
2) Resident - Service: The exposure of a worker performing services in a treated structure for 8 hours.
3) Resident - Adult: The high-end exposure for a 68.7 kg residential adult was based on a respiratory rate of 0.66 m^3/hr, assuming 16 hours resting time in the living area and 8 hours working time in the treated structure.

III.B.2. Lifetime Exposure levels

A LADD was not calculated for the residential exposure because the exposure was not expected to occur for more than 2 days after each application and that a repeated application for a number of years was unlikely (Dong, 1995).

IV. RISK CHARACTERIZATION

The risk of acute exposures is characterized by the margin of exposure (MOE). MOE is the ratio of the NOEL divided by the exposure. The risk of chronic, long-term exposures was characterized by a quantitative risk estimate. The lifetime oncogenic risk was calculated as the potency value multiplied by the lifetime average daily dose. The MOEs and risk estimates were summarized in Table 2.

Table 2. The characterization of risk associated with the use of Biflex® TC.

Exposure Groups	Acute Risk		Lifetime Oncogenic Risk	
	Exposure (μg/kg/day)	MOE[a]	Exposure (μg/kg/day)	Risk[b]
Mixer/Loader				
Average	7.88	130	1.82	5 to 8 x 10^{-5}
High	32.55	30	9.72	
Applicator				
Average	11.31	90	2.93	8 to 13 x 10^{-5}
High	27.09	40	7.97	
Mixer/Loader/Applicator				
Average	9.59	100	2.36	6 to 10 x 10^{-5}
High	29.84	30	8.82	
Residential - Child				
Average	3.57	280		
High	4.04	250		
Residential - Adult				
Average	2.24	450		
High	2.56	390		
Residential - Service				
Average	2.24	450		
High	2.41	410		

[a]/ The MOE (margin of exposure) was calculated as the ratio of the NOEL (1 mg/kg/day) over the exposure.

[b]/ The lifetime oncogenic risk is calculated as the potency multiplied by the exposure. The given risk levels ranged from the maximum likelihood estimate (MLE) to the 95% upper confidence bound (UB), using the MLE potency of 2.6 x 10^{-2} $(mg/kg/day)^{-1}$ and its UB of 4.3 x 10^{-2} $(mg/kg/day)^{-1}$.

IV.A. Acute Exposures

The MOEs for residential exposures were above 250. The MOEs for mixers/loaders and applicators ranged from 100 to 130 at the average exposures and 30 to 40 at the high end of exposure. For the high end of exposures for workers, dietary exposures contributed less than 9% to the total exposures (Table 1). The MOEs for the high end exposures were below 100, the MOE generally considered as the benchmark for the protection of human health. The MOE of 100 takes into account both the interspecies and the inter-individual variations in sensitivity. In extrapolating data from animals to humans, it is usually assumed that humans could be 10 times more sensitive than laboratory animals. In considering the heterogeneity in human population (e.g., genetic predisposition, age, life style), it is further assumed that the inter-individual differences in sensitivity to a chemical toxicant could be as much as 10-fold.

IV.B. Lifetime Oncogenic Risk

The potential lifetime oncogenic risks of workers were calculated based in the estimated average LADD. A lifetime oncogenic risk was not calculated based on the "high" exposure estimates for mixer/loaders and applicators. This was because they were derived from the high acute exposures (i.e., high ADD values), using the same exposure parameters (i.e., number of days per year and years per lifetime of exposures) as for the average LADD. It is unlikely that the daily "high" exposures would occur repeatedly for a lifetime. The potential lifetime oncogenic risk was 5 to 8 x 10^{-5} for mixers/loaders and 8 to 13 x 10^{-5} for applicators. Dietary exposures contributed less than 2% to the total exposures for all work tasks.

IV.C. Local Dermal Effects

The local dermal effects of bifenthrin cannot be characterized due to the lack of dermal exposure estimates. It should also be noted that a statement of dermal sensitization potential is not included in the current label for Capture® 2EC-Cal or the proposed label of Biflex® TC.

V. RISK APPRAISAL

Uncertainties are introduced into the risk analysis through each component of the risk assessment. When sufficient data were not available, default assumptions were used. The same specific areas of uncertainties regarding the toxicological database presented in the risk assessment of Talstar® T&O (Reed, 1997) are also relevant to the assessment of Biflex® TC. Depending on the toxicological endpoints for risk assessment, using a dermal instead of an oral NOEL could result in 2- to 4-fold higher MOEs. The resulting estimates of MOE could be 60 to 120 for mixer/loaders and 80 to 160 for applicators.

There were also several areas of uncertainties in the exposure assessment. One area of uncertainty was the exposure parameter (e.g., amount of use; hours per day, days per year, years per lifetime). Since the LADD was calculated from the ADD with the presumed frequency of work activities (annual and lifetime), changes in the ADD would proportionally change the LADD and hence, the risk estimates. Detailed discussions on the source of data and the assumptions used in the assessment were presented by Dong (1995).

Bifenthrin also causes local dermal effects of erythema and skin sensitization. However, data on the exposure was insufficient for characterizing the risk of skin effects. This might be an area for

further investigation since the current illness report appeared to indicate that skin effects may be a potential area of concern.

VI. CONCLUSIONS

The MOEs of acute exposures for workers and residents living in the treated houses were calculated based on the oral NOEL of 1.0 mg/kg/day (tremors observed in rats at 2.0 mg/kg/day). Based on the mean estimates of the exposure, the MOEs for mixers/loaders and applicators ranged from 100 to 130. The MOEs based on the high end exposures ranged from 30 to 40. The MOEs for residents were at least 250. A MOE of at least 100 is generally considered protective of human health when the adverse effect is based on animal data.

The potential lifetime oncogenic risk was 5 to 8 x 10-5 for mixers/loaders and 8 to 13 x 10-5 for applicators. The oncogenic risks for residents were not assessed because a repeated application of a number of years was unlikely.

A qualitative presentation of uncertainties in the determination of the critical NOEL was presented. Uncertainties existed when an oral NOEL was used to calculate the MOE for dermal exposures. Adjusting for the route-specific absorption factor and the apparent species sensitivity between test species, the difference between the critical NOEL for oral and dermal routes could be approximately 2- to 4-fold. Therefore, the resulting MOEs could be 2- to 4-fold higher. Uncertainties in the exposure assessment and the oncogenicity data that formed the basis of risk estimates were also presented.

The risk of local dermal effects was not assessed due to insufficient data for assessing the exposures. Capture® 2EC, the same formulation as Biflex® TC, was shown to cause dermal sensitization. However, the current labels for either formulation do not include a statement on the potential for dermal sensitization.

VII. REFERENCES

Dong, M. H. 1995 Human pesticide exposure assessment - Bifenthrin (Biflex™ TC used for subterranean termite control. Worker Health and Safety Branch, Department of Pesticide Regulation, Cal/EPA. HS-1722.

Reed, N. R. 1991 Bifenthrin (Capture 2 EC) Risk characterization document. California Department of food and Agriculture.

Reed, N. R. 1997 Rrisk assessment of Talstar® T&O - Bifenthrin Risk Characterization Document B: Subsequent to bifenthrin (Capture 2 EC) Risk Characterization Document, 1991. Health Assessment Section, Medical Toxicology Branch, Department of Pesticide Regulation, Cal.EPA.