

**ESTIMATION OF DAILY DERMAL EXPOSURE AND ABSORBED DAILY DOSAGE FOR
AGRICULTURAL WORKERS EXPOSED TO BIFENTHRIN IN CALIFORNIA COTTON FIELDS**

**Michael H. Dong, Staff Toxicologist
Tian Thongsinthusak, Staff Toxicologist
John H. Ross, Senior Toxicologist**

HS-1561

February 1, 1990; Revised September 4, 1990; Revised January 31, 1991

**California Department of Food and Agriculture
Division of Pest Management, Environmental
Protection and Worker Safety
Worker Health and Safety Branch
1220 N Street
Sacramento, California 95814**

SUMMARY

Bifenthrin (Talstar[®], Brigade[®], Capture[®]) is an insecticide/miticide which has been synthesized for the control of a wide range of foliar insect pests and mites on ornamentals, fruits, cotton, and other crops. The compound is labelled as a Toxicity Category II, federally restricted use pesticide, and is classified as a Category C oncogen by the U. S. Environmental Protection Agency. A dermal absorption study on the rat demonstrated a 17.9% dermal penetration for bifenthrin. Data on bifenthrin metabolism suggest that fecal excretion is the primary route of elimination of the parent compound (accounting for a major portion) and the metabolites in rats. Surrogate measures of dermal exposure from published exposure studies were used to estimate the expected daily dosages for cotton scouts and for agricultural workers handling bifenthrin for use on cotton. Inhalation exposures from bifenthrin applied to cotton were assumed to be negligible compared to dermal exposures. This report was prepared as Appendix B (i.e., Human Exposure Assessment) to the Department's risk characterization document for bifenthrin applied to cotton. (Bifenthrin is in risk assessment under SB-950 because of its adverse effects observed in animal tests for oncogenicity, maternotoxicity, and acute toxicity.)

APPENDIX B

California Department of Food and Agriculture Worker Health and Safety Branch

Human Exposure Assessment

BIFENTHRIN

February 1, 1990; Revised September 4, 1990; Revised January 31, 1991

PHYSICAL AND CHEMICAL PROPERTIES

Bifenthrin (Talstar[®], Brigade[®], Capture[®], 2-methyl[1,1'-biphenyl]-3-yl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethyl-cyclopropanecarboxylate, CAS No. 82657-04-3, molecular formula C₂₃H₂₂ClF₃O₂, molecular weight 422.88) is an insecticide/miticide which has been synthesized for the control of a wide range of foliar insect pests and mites on ornamentals, fruits, cotton, and other crops. This chemical belongs to the synthetic pyrethroid family and is a non-corrosive substance. It is commercially available as a viscous oil which hardens to a solid, light brown mass. The vapor pressure of bifenthrin is 1.81 x 10⁻⁷ torr at 25°C, with a specific gravity of 1.21 at 25°C and a melting point of 68-70.6°C. Although bifenthrin has very low solubility in water (0.1 µg/L), it is readily soluble in acetone, chloroform, dichloromethane, diethyl ether, and toluene [1].

FORMULATION

All pesticides containing bifenthrin as the active ingredient (a.i.) are manufactured solely by the FMC Corporation. These bifenthrin products are either federally registered or pending federal registration, and are all made available under the trade names Talstar[®], Brigade[®], and Capture[®]. Early on, the technical grade bifenthrin was assigned by FMC the code number FMC 54800. This active ingredient is now available in three different formulations: an EC (emulsifiable concentrate), a WP (wetable powder), and most recently a WSB (water-soluble bag).

Capture-2EC (EPA Reg No. 279-3069) is federally registered for use only on cotton. Talstar-10WP (EPA Reg No. 279-3057) and Talstar-WSB (EPA Reg No. 279-3086, -3087) are federally registered for greenhouse-grown ornamentals. Talstar-2EC (EPA Reg No. 279-3056), which is the exact same formulation as Capture-2EC, is also federally registered for greenhouse uses but has not been marketed. According to FMC, Brigade-10WP and Brigade-WSB have been submitted to the U. S. Environmental Protection Agency (EPA) for registrations on strawberries, walnuts, pears, and pecans. Although the registrations of Brigade products are still pending, federal Experimental Use Permit (EUP) programs for them are currently in place.

No bifenthrin product is yet registered in California. At this time, the only bifenthrin label under review at the California Department of Food and Agriculture (CDFA) is Capture-2EC for cotton. Each gallon of the Capture product contains 2 lbs of the active ingredient. The label for this liquid formulation specifies that a maximum of 0.1 lb a.i. be applied per acre of cotton field, and that no more than 0.5 lb a.i. (or five application each at 0.1 lb a.i.) be applied per acre per season.

EPA STATUS

Insofar as Capture-2EC is concerned, in 1985 the EPA issued a one-year EUP for the use of bifenthrin on cotton. In that same year, the EPA also approved the temporary tolerance of bifenthrin in or on cottonseed at 0.5 ppm (parts per million). The temporary tolerance was issued to permit the marketing of the aforesaid raw agricultural commodity under the terms and conditions that were set forth in the EUP.

In 1988 the EPA then issued a Conditional Registration for use of bifenthrin on cotton with a final expiration date of October 31, 1991, and announced its formal ruling on the aforesaid tolerance [2]. The levels of the tolerance in question remained the same as before but with an expiration date of October 31, 1992. In that issuance the EPA concluded that the proposed use of bifenthrin on cotton would pose extremely small risks to humans, but nonetheless classified it as a Category C (possible human) oncogen. Their classification was based on the observation that there was a statistically highly significant increase in leiomyosarcoma incidence in the male mouse urinary bladder.

USAGE

Capture-2EC has been petitioned for use on cotton in California since 1986 and its registration for such use is still under review. Accordingly, there should be no data available on its usage on cotton in California at the present time. Previously, the registrant also filed for an EUP registration for the use of bifenthrin on other crops (e.g., ornamentals) in California. These other EUP petitions were either withdrawn by the registrant or were denied by the CDFA. As a result, there also should be no data on bifenthrin usage on other crops in California.

LABEL PRECAUTIONS

Capture-2EC is labelled as a Toxicity Category II, federally restricted use pesticide. As noted earlier, the product is also classified by the EPA as a Category C oncogen. The label requires that applicators wear long sleeved shirt and trousers (fabric not specified), and that mixer/loaders wear similar protective clothing plus chemical resistant gloves and goggles (or face shield) and use a *closed* transfer mix/load system. It also warns against workers reentering treated areas unless they wear protective clothing or until the sprays have dried.

The statement of practical treatment advises that no vomiting be induced if the victim accidentally swallows the product. For eye or dermal contact, the label recommends flushing with plenty of water. If poisoning is through inhalation, the victim needs to be immediately removed from the contaminated atmosphere and, if necessary, to be given artificial respiration. In all cases, medical attention should be sought as soon as possible.

WORKER ILLNESSES

For reasons stated in the **USAGE** section, there are no data available on occupational illnesses that have been reported in California as related to bifenthrin exposure. Also, there have been no epidemiological studies reported for bifenthrin.

DERMAL TOXICITY

Two acute dermal toxicity/irritation studies were investigated for bifenthrin in rabbits. In the first study [3], five male and five female young adult New Zealand white rabbits were treated with Capture-2EC

at a dosage level of 2,000 mg/kg. The test material was placed in contact with the intact skin for 24 hrs under an occlusive wrap; the test sites were previously clipped free of hair. Based on the findings of that study, the dermal LD₅₀ of Capture-2EC was determined to be greater than 2,000 mg/kg (Category III toxicity) for both male and female rabbits.

In the second study [4], three male and three female young adult New Zealand white rabbits were each treated topically on two test sites (which were previously clipped free of hair), either abraded or unabraded. A dose of 0.5 ml of Capture-2EC was placed in contact with each test site. Both of the test sites were covered separately with gauze patches and the trunk of the animal was wrapped with an elastic gauze bandage. The test material was in contact with the skin for 4 hrs, after which the animals were unwrapped and the test material removed. Approximately 30 min after the exposure period, the test sites were scored for irritation using the evaluation criteria described by Draize [5]. The test sites were also scored at 24, 48, and 72 hrs. No dermal irritation was found on any test animal after dose application. Capture-2EC was hence considered to be non-irritating to either abraded or intact skin, and was classified as having Category IV toxicity for primary skin irritation.

In addition, a dermal sensitization study [6] was reported in which 10 male Hartley guinea pigs were treated with 0.5 ml of Capture-2EC on their left shoulder (which was previously clipped free of hair). The test material was applied to the test site and left in contact with the skin for approximately 6 hrs, three times a week for a total of 10 treatments. Fourteen days after the 10th treatment, the animals were challenged with the test material at a virgin skin site. Observations for skin reactions were recorded at 24 hrs after each application. Animals which had slight irritation were re-challenged the following day at another virgin site. Dinitrochlorobenzene (DNCB) at 0.15% in ethanol was applied as the positive control to 10 other guinea pigs in a similar manner. Signs of local irritation which were found in the test animals during the induction phase included erythema, desquamation, eschar, exfoliation, and fissuring. At challenge, slight to severe erythema was observed in nine animals treated with the test material, three of which also had necrosis over the test site. DNCB was confirmed as a dermal sensitizer in all of the 10 control animals. Consequently, Capture-2EC was judged to be sensitizing when topically applied to male Hartley guinea pigs.

DERMAL ABSORPTION

A dermal absorption study was submitted to the CDFA in July 1989 in the form of an *unaudited* draft document [7], which was prepared as supplemental information to a previously submitted dermal absorption study [8]. In the earlier study, approximately 50% of the applied dose was found bound to the treated skin at all dose levels ranging from 50-5,000 µg per rat (or per 12.5 cm² skin area); the animals were observed for 24 hrs or less. The registrant then conducted another study with an extended observation period in order to comply with the EPA guidelines [9] regarding the high percent residues that were found *in* the treated skin. This effort led to the submission of the supplemental study, in which the lowest (practical) dose (i.e., 0.05 mg per 12.5 cm²) from the first study was applied to 36 Charles River male CD rats. (An audited final report of this supplemental study has recently been submitted to the CDFA for filing, with results virtually the same as those presented in the draft copy.)

For the most part, the supplemental study was conducted in accord with the EPA study protocol prepared for mammalian dermal absorption [9], although all animals except the 2 controls were dosed at a *single* rate. The single dose used in the supplemental study was still much higher (by approximately 50-fold) than those expected to occur in agricultural workers exposed to bifenthrin in cotton fields.

Sacrifice times in the supplemental study were set at 2, 4, 10 hrs, 1, 7, 14, and 21 days; and a group of 4 rats were used for each of these 7 observation periods. After acclimatization for 8 days, 50 µg of bifenthrin (with radiopurity = 97.0%) in EC blank formulation diluted with distilled water was applied to

12.5 cm² of the animal's shaved back where a dose cell was attached. Treated area was covered with a nonocclusive cover (filter paper) which was affixed to the dose cell with rubber cement. An Elizabethan collar was also placed around each rat's neck in an effort to restrain the animal from licking the test site.

Treated skin was washed at the time of animal sacrifice when the observation period was 10 hrs or less; otherwise, it was washed at 10 hrs after dosing. Excreta, carcass, and the skin in the dosed area were radioassayed for absorbed ¹⁴C. The skin wash and protective coverings were radioassayed for the nonabsorbed radiolabel.

The overall material balance in the supplemental study was greater than 86% (of the total dose administered) for the animals sacrificed at 4 hrs or earlier. However, for the animals observed for 10 hrs or longer, the recovery of ¹⁴C from all sources was unacceptably low, ranging from only 55-68%. In light of this low recovery of radioactivity, the Worker Health and Safety Branch (WH&S) made a recommendation that a more acceptable study be conducted which should be similar in design to the one submitted here but with higher dose recovery [10]. That recommendation resulted in the submission of yet another study on dermal absorption of bifenthrin in the rat, which was judged by WH&S to be acceptable [11]. The dermal absorption for bifenthrin calculated from this third study was found to be approximately 17.9% of the total dose applied. As shown later, this dermal absorption rate was used in the worker exposure assessment.

ANIMAL METABOLISM

A series of nine metabolism studies were provided for review. In all of these studies, the biologic fate of bifenthrin was investigated in rats only. The Medical Toxicology Branch has given an extensive review of these studies and has found them all *individually* unacceptable [12]. That Branch has nonetheless concluded that *as a group*, these studies provide sufficient information to fulfill the metabolism data requirements.

In the first study [13] submitted, the distribution of radioactivity in eight nulliparous female Sprague-Dawley rats was investigated by the whole-body autoradiography technique. The rats were each given a single oral dose of ¹⁴C-bifenthrin (with radiopurity = 99.0%) at a dose level of 0.5 mg/kg. Absorption of radioactivity from the upper gastrointestinal tract (GI) was found to be relatively slow throughout the first 2 hrs after dosing, but was maximized within 6 hrs. At 6 hrs after dosing, radioactivity was found present in the GI, liver, and the urinary systems, which were the main organs of excretion and biotransformation. Other tissues or organs where radioactivity was found included blood, muscle, bone marrow, fat, and brown fat. Excretion of radioactivity was found to be relatively rapid after absorption; much of the radioactivity (amount not specified) was reported to have been eliminated by 24 hrs after dosing. On the other hand, relatively high levels (amount also not specified) of radioactivity were found to have persisted in fat deposits, areas of brown fat, and the intestinal tract, even at 192 hrs (i.e., 8 days) after dosing.

The second study [14] was conducted to determine the material balance of a single oral dose of alcohol(phenyl)-¹⁴C-bifenthrin (with radiopurity > 98.0%) in Sprague-Dawley rats at 5 mg/kg. Radiocarbon in excretion was monitored for 7 days. Rats were sacrificed at the end of the monitoring period, and tissues from three male and three female rats were radioassayed for total ¹⁴C. Fecal excretion was found to be the primary route for the elimination of bifenthrin and of its metabolites in rats (76-79% of the total dose applied), whereas urinary excretion accounted for only 6-7% during the first 48 hrs after dosing. A total of 91-92% of the administered dose was recovered in excreta after 7 days. Unchanged bifenthrin constituted a significant portion of the feces residue (75-88% of recovered ¹⁴C). Radiocarbon residues in most tissues were found to be low (< 0.1 ppm ¹⁴C-bifenthrin equivalents) except for liver, skin, lungs, and fat, with the last tissue having the highest residue of 0.8-1.0 ppm.

In the third study [15] of this metabolism series, 10 adult female Sprague-Dawley rats were each given a single oral dose of the aforesaid alcohol labelled compound. The rats were dosed with either 4 mg/kg (n = 5) or 35 mg/kg (n = 5). Ten adult male rats were also treated similarly but with the acid(cyclopropyl)-¹⁴C label (with radiopurity > 97.0%). In addition, five male and five female rats were each dosed orally for 14 days with 4 mg/kg of nonlabelled bifenthrin and on the 15th day, with 4 mg/kg of the radiolabel. On the 7th day after dosing with the radiolabel, the animals were sacrificed and their tissues were radioassayed for residual radioactivity. All rats were found to excrete the majority of the administered radioactivity via feces. For the 4 mg/kg single oral dose, female rats excreted 19.7% of dosed radioactivity in their urine and 72.9% in their feces, whereas male rats excreted 13.4% dosed radioactivity in their urine and 82.8% in their feces. For the 35 mg/kg single oral dose, female rats excreted 21.8% of dosed radioactivity in their urine and 70.9% in their feces, whereas male rats excreted 21.6% of dosed radioactivity in their urine and 68.9% in their feces. For the multiple dose (i.e., with nonlabel preceding radiolabel), female rats excreted 25.0% of dosed radioactivity in their urine and 65.8% in their feces, whereas male rats excreted 18.4% of dosed radioactivity in their urine and 73.2% in their feces. In general, residual ¹⁴C in tissues was found higher than twice the background. The highest level of radioactivity found in the tissues, as expressed in ppm, was in the adipose, which was 100 times the blood concentration; the highest value of radioactivity found in whole blood was 0.23 ppm.

The fourth study [16] was an extension of the third study. In this extended study an effort was made to identify the products in the excreta collected from animals tested in the third study. Representative samples of fecal and urinary excreta were analyzed by TLC, HPLC, GC/MS, NMR, and liquid scintillation counting. Results of this metabolite analysis study showed that fecal metabolites were mainly derived from mono- and di-hydroxylated intact parent chemical. These metabolites included the 3'-OH-hydroxymethyl-bifenthrin, 4'-OH-hydroxymethyl-bifenthrin, 4'-OH-bifenthrin, hydroxymethyl-bifenthrin, 3'-monomethyl-catechol-bifenthrin, and 4'-monomethyl-catechol-bifenthrin, along with hydrolytic/oxidative products of bifenthrin; these hydrolytic-related products included biphenyl alcohol, biphenyl acid, TFP acid, and biphenyl aldehyde. Some of these metabolites were also found in the rat urine.

The fifth study [17] of the series was in effect a continuation of the third study. The objective of this fifth study was to determine the *kinetics* of bifenthrin in the blood of rats. In this study female rats were not used, however; and 50 male rats were each dosed with the alcohol radiolabel, at either 4 mg/kg (n = 25) or 35 mg/kg (n = 25). Five rats per dose group were then serially sacrificed (through heart puncture) at 4 different time intervals ranging from 2 to 24 hrs after dosing. In addition, five rats per dose group were isolated for the continuous monitoring of ¹⁴C in the blood. Blood samples from the isolated rats were taken from the tip of the tail of each animal. The blood was then transferred into combustion cones and processed for combustion. The isolated animals were not sacrificed until the completion of the blood kinetic studies. The alcohol ¹⁴C-labelled compound was found slowly absorbed, with radioactivity in the blood peaking (0.66 µg/ml and 3.29 µg/ml) after 4 and 6 hrs, respectively, for the 4 mg/kg and 35 mg/kg single oral doses. After 10 hrs from dosing, the radioactivity in blood declined to less than 50% of the concentration at peak in both doses. At the end of the study, the plasma samples were collected for metabolite analyses which all took place in the sixth study [18] of this metabolism series.

The sixth study was thus an extension of the fifth study and was the second of the three metabolite analysis studies included for review. In this sixth study, plasma samples were deproteinized and extracted with acetone. Representative samples of whole plasma were then analyzed by HPLC and liquid scintillation counting. The major products found were the parent chemical, the hydrolysis product BP alcohol, the oxidized hydrolysis product, and BP acid, with *each* present as roughly 20-30% of total radioactive residue at peak plasma intervals from both high and low doses. The percentage of extractable material was found to decline with time; this was believed to be due primarily to plasma protein binding.

The seventh study [19] was conducted as a supplement to the third as well as the fifth study. In this study an effort was made to investigate the *bioaccumulation* of ¹⁴C-bifenthrin (with radiopurity = 99.0%) in the rat tissues and organs. The radiolabelled compound was administered orally to 60 female Sprague-Dawley rats once daily for 70 days at a dose level of 0.5 mg/kg/day. Animals were sacrificed in groups of 4 (3 test and 1 control) on 20 different days ranging from days 1 to 155. On these sacrifice days radioactivity concentrations were measured in several tissues and organs including blood. Levels of radioactivity for the various organs studied were all found to have peaked on day 70, the last dosing day; the levels measured on this final dosing day were 9.62, 1.74, 0.40, 0.32, 1.69, 3.25, 0.06, and 0.06 ppm for fat, skin, liver, kidney, ovaries, sciatic nerve, whole blood, and plasma, respectively. Half-lives for elimination of the radiolabelled compound were 51, 50, 19, 28, 40, and 40 days, respectively, for fat, skin, liver, kidney, ovaries, and sciatic nerve. Accumulation was reported to have occurred over the dosing period in the fat, skin, ovaries, and sciatic nerve. Levels of radioactivity in the plasma were found similar from days 21 to 70 (0.04 - 0.06 ppm) and decreased to < 0.01 ppm after day 78. Whole blood levels were found similar to plasma, thus indicating some uptake of radioactivity into blood cells but no specific accumulation. The highest concentrations of radioactivity were found in the fat of rats at all sacrifice times. Analysis of fat by TLC indicated that the parent chemical accounted for a majority (65-85%) of the (acetonitrile-soluble) ¹⁴C residues in fat (with three major metabolites quantified but not identified).

The final two studies [20,21] of the series were submitted in response to the CDFA's concern that male and female rats were not dosed with the same labelled test material. These eighth and ninth studies were similar to the third and fourth studies in design, respectively, except that the sex dosing regimen was *reversed*. A comparison of the results of these studies revealed that the excretion and metabolic fate of bifenthrin were essentially the same regardless of sex or type of radiolabel.

WORKER EXPOSURE

Several groups of agricultural workers are of principal concern in the assessment of worker exposure to bifenthrin applied to cotton. Workers may be exposed to bifenthrin when they mix/load the pesticide or apply it to cotton. These include mixer/loaders, ground boom applicators, aerial applicators (i.e., pilots), and flaggers. In addition, cotton scouts and irrigators are subject to occupational exposure from contact with dislodgeable bifenthrin residues that have been accumulated on treated cotton foliage.

Measurements of bifenthrin exposure for these workers had not been made available to the WH&S. Accordingly, the WH&S reviewers used surrogate data for their worker exposure assessment for bifenthrin. The surrogate data submitted by the registrant were used by the WH&S reviewers in the exposure assessment for mixer/loaders and applicators. These surrogate data were made available from two recent EPA documents [22,23], the latter of which was prepared especially for bifenthrin applied to cotton. For cotton scouts, the surrogate exposures were based on a set of transfer factors derived from a series of field studies by Ware *et al.* [24-26]. In the Ware *et al.* series, cotton scouts were monitored for dermal exposure to monocrotophos, ethyl parathion, and methyl parathion.

The expected daily exposures and absorbed daily dosages for mixer-loaders and applicators using label required protective clothing/equipment are presented in Table 1; and those for cotton scouts, in Tables 2 and 3. For comparison purposes, also included in Table 1 are the expected daily exposure and absorbed daily dosage for cotton scouts under the extreme-case scenario. The 17.9% dermal absorption was assumed in all calculations of absorbed dosages, as mentioned earlier. The assumption that inhalation exposures from bifenthrin applied to cotton were negligible (compared to dermal exposures) [23] was followed. Some of the assumptions used in the calculations were consistent with common practice and hence are mentioned as table footnotes only. Others that require clarification or appear to be unique to cotton-based bifenthrin exposure are discussed below, along with a brief description of the calculations involved.

Table 1. Expected Daily Dermal Exposure and Expected Absorbed Daily Dosage for Cotton Scouts and for Workers Handling Bifenthrin in California Cotton Fields^a

Job Class	No. of Days Exposed per Year ^b	Dermal Exposure (mg/day) ^{c,d}	Absorbed Daily Dosage (µg/kg BW/day) ^e	Annual Average Daily Dosage (µg/kg BW/day)
Aerial Application				
Mixer/Loaders				
Open Pour Loading	40	11.61	29.68	3.255
Closed System Loading	40	0.232	0.592	0.065
Pilots	40	0.058	0.149	0.016
Flaggers	40	0.32	0.818	0.090
Ground Boom Application				
Mixer/Loaders				
Open Pour Loading	20	1.79	4.58	0.252
Closed System Loading	20	0.036	0.092	0.006
Applicators	20	0.46	1.176	0.065
Cotton Scouts (no gloves)	40	2.29	5.86	0.642

Dong, WH&S, 1990

^a for workers wearing long-sleeved shirt and long pants and, where applicable, chemical resistant gloves (as specified on the label).

^b as estimated by Meinders and Krieger [27] in their study in which monocrotophos applied to cotton was assumed to be by *commercial* applicators, *commercial* mixer/loaders, and *commercial* flaggers; also assumed in their study were *commercial* cotton scouts.

^c based on the following application/usage rates as provided by the registrant [28]: 0.1 lb a.i. per acre; 96.4 acres per day for ground application; 625 acres per day for aerial application; and 5 hrs per day.

^d based on the following mean surrogate exposures (*per 0.1 lb a.i. handled/acre adjusted for 90% clothing protection*) provided by the EPA [22,23]: 0.019 mg for mixer/loaders under *open pour* loading (ground or aerial application), 0.012 mg/hr for pilots, 0.064 mg/hr for flaggers, and 0.092 mg/hr for ground applicators; for mixer/loaders under *closed* system loading, the exposure estimate was taken from a 98% reduction of the mean surrogate exposure assumed for those under *open pour* loading (as common practice); and for cotton scouts, see Table 3 under the *extreme-case* scenario (with daily exposure estimated for *day 1* after the *fifth* application).

^e based on a male body weight (BW) of 70 kg and on a dermal absorption rate of 17.9% (see discussion in text and [11]).

The surrogate estimates of dermal exposure for applicators and mixer-loaders wearing work clothing are footnoted in Table 1. These estimates were based on a weighted average or geometric mean taken over the exposure estimates computed from several field studies on various pesticides. Because the inclusion of pesticides as bifenthrin surrogates was not without deliberation, a controversy over the applicability of these surrogate data appeared inevitable. For workers with aerial application, the registrant had suggested that the *lower*, cypermethrin exposures from the study by Chester *et al.* [29] be used. They argued [28] that because cypermethrin was also a synthetic pyrethroid, it would be more similar to bifenthrin than the surrogate pesticides included in the EPA evaluation. The WH&S reviewers contended, however, that cypermethrin as used in the study was not a proper surrogate for bifenthrin, since it was applied as an ultra low volume (ULV) formulation utilizing special equipment different from bifenthrin. (Note that although both the chemigation and ULV applications are on the federally approved label for Capture-2EC, neither process is typically employed by California cotton growers. These types of application are mainly practiced by cotton growers in other parts of the country.)

The application and usage rates for bifenthrin on cotton were the maximum label rates [28,30], which are footnoted in Table 1. As shown in Table 1, the mixer/loaders under *open pour* loading appeared to have attained the highest daily dermal exposure (i.e., 11.61 mg/day for aerial application). Exposure for mixing/loading/applying by ground boom equipment was assumed to be approximately the *sum* of the individual task exposures, since the applicators were expected to work only up to 5 hrs per day (because of the maximum daily acreage assumed). Mixing/loading, flying, and flagging were on the other hand assumed to be done by different workers.

As noted earlier, the surrogate exposures for cotton scouts were based on a series of transfer factors derived from the Ware *et al.* studies [24-26]. The procedure used for the computation of these surrogate exposures may be described briefly as follows. The term dislodgeable foliar residues (DFR) is defined as the amount of pesticide residues that can be removed from *both* sides of treated leaf surfaces using aqueous surfactant. When coupled (multiplied) with a proper predetermined dermal transfer factor, the DFR under study may be readily converted to hourly dermal exposure of a worker reentering a treated area. Dermal transfer factor is defined here simply as the ratio (or sometimes some other relation) of hourly dermal exposure ($\mu\text{g/hr}$) to DFR ($\mu\text{g/cm}^2$) estimated at a given time. The calculations of the transfer factors used in this exposure conversion were described in detail in a Branch memorandum [31].

The expected *potential* daily exposures for cotton scouts, as shown in Table 2, were estimated from the *geometric mean* transfer factors computed for *bare* hands ($950 \text{ cm}^2/\text{hr}$), the *clothed* upper body ($1,020 \text{ cm}^2/\text{hr}$), and the *clothed* lower body ($9,640 \text{ cm}^2/\text{hr}$). The *potential* dermal transfer factor for *the whole body* of cotton scouts is simply the sum of these individual geometric mean transfer factors. The *potential* daily dermal exposures by body part, as provided in Table 2, were prepared for risk mitigation purposes.

The expected daily dermal exposures for cotton scouts wearing work clothing, with or without gloves, are presented in Table 3. As in the case of mixer-loaders and applicators, it was assumed that the cotton scouts would wear a long-sleeved shirt and a pair of long pants. The *percentage* of clothing permeation for the three body parts was assumed to be 10, which has been the default value adopted by the WH&S (unless there is evidence to the contrary).

The *predicted* (cotton-based) bifenthrin DFR, from which their corresponding hourly dermal exposures were estimated, were provided by the registrant through log-linear regression analyses based on actual field data [30]. In their regression analyses, they accounted for the build-up of residues after five sequential applications to the crop while assuming no growth dilution of residues (for the first four applications from day 8 and thereafter) or loss of treated foliage from earlier applications. Dislodgeable bifenthrin residues were predicted *separately* for each of the five applications given at 7 day intervals, which were the maximum number of applications (per season) specified by the label. The time that a cotton scout is expected to be in *actual* contact with treated cotton foliage was assumed to be 6 hrs per

Table 2. Expected Potential Daily Dermal Exposure (mg) by Body Part for California Workers Scouting Maturing Cotton Treated with Bifenthrin^a

Days After Each Spray	Predicted DFR ($\mu\text{g}/\text{cm}^2$) After Application No. ^b			Bare Hands Dermal Exposure After Application No. ^c			Potential Upper Body Dermal Exposure After Application No. ^d			Potential Lower Body Dermal Exposure After Application No. ^e		
	1	3	5	1	3	5	1	3	5	1	3	5
0 ^f	0.1471	0.1696	0.2148	*	*	*	*	*	*	*	*	*
1	0.1244	0.1339	0.1897	0.71	0.76	1.08	0.76	0.82	1.16	7.20	7.74	10.97
2	0.1050	0.1056	0.1695	0.60	0.60	0.97	0.64	0.65	1.04	6.07	6.11	9.80
3	0.0887	0.0833	0.1515	0.51	0.47	0.86	0.54	0.51	0.93	5.13	4.82	8.76
4	0.0749	0.0657	0.1354	0.43	0.37	0.77	0.46	0.40	0.83	4.33	3.80	7.83
5	0.0632	0.0518	0.1210	0.36	0.30	0.69	0.39	0.32	0.74	3.66	3.00	7.00
6	0.0534	0.0409	0.1082	0.30	0.23	0.62	0.33	0.25	0.66	3.09	2.37	6.26
7	0.0451	0.0322	0.0967	0.26	0.18	0.55	0.28	0.20	0.59	2.61	1.86	5.59
14	0.0138	0.0061	0.0440	0.08	0.03	0.25	0.08	0.04	0.27	0.80	0.35	2.54
21	0.0042	0.0011	0.0206	0.02	0.01	0.12	0.03	0.01	0.13	0.24	0.06	1.19
28	0.0013	0.0002	0.0094	0.01	0.00	0.05	0.01	0.00	0.06	0.08	0.01	0.54
35	0.0004	0.0000	0.0043	0.00	0.00	0.02	0.00	0.00	0.03	0.02	0.00	0.25

Dong, WH&S, 1990

^a daily dermal exposure for the unprotected whole body is simply the sum of the individual dermal exposures calculated for the above three body parts.

^b based on log-linear regression analyses performed by the registrant [30].

^c based on 6 hrs per day [see discussion in text] and on a dermal transfer factor of 950 cm^2/hr [31].

^d based on 6 hrs per day [see discussion in text] and on a dermal transfer factor of 1,020 cm^2/hr [31].

^e based on 6 hrs per day [see discussion in text] and on a dermal transfer factor of 9,640 cm^2/hr [31].

^f assuming a reentry interval of at least 24 hrs (as common practice for cotton scouts).

Table 3. Expected Daily Dermal Exposure and Expected Absorbed Daily Dosage for California Workers Scouting Maturing Cotton Treated with Bifenthrin^a

Days After Each Spray	<i>With Gloves</i>						<i>Without Gloves</i>					
	Dermal Exposure (mg/day)			Absorbed Daily Dosage (µg/kg BW/day)			Dermal Exposure (mg/day)			Absorbed Daily Dosage (µg/kg BW/day)		
	After Application No. ^b			After Application No. ^c			After Application No. ^b			After Application No. ^c		
	1	3	5	1	3	5	1	3	5	1	3	5
0 ^d	*	*	*	*	*	*	*	*	*	*	*	*
1	0.87	0.93	1.32	2.225	2.378	3.375	1.51	1.62	2.29	3.861	4.143	5.856
2	0.73	0.74	1.18	1.867	1.892	3.017	1.27	1.28	2.05	3.248	3.273	5.242
3	0.62	0.58	1.05	1.585	1.483	2.685	1.08	1.00	1.83	2.762	2.557	4.680
4	0.52	0.46	0.94	1.330	1.176	2.404	0.91	0.79	1.64	2.327	2.020	4.194
5	0.44	0.36	0.84	1.125	0.921	2.148	0.77	0.63	1.46	1.969	1.611	3.733
6	0.37	0.29	0.75	0.946	0.742	1.918	0.64	0.49	1.31	1.637	1.253	3.350
7	0.32	0.22	0.67	0.818	0.563	1.739	0.55	0.39	1.17	1.406	0.997	2.992
14	0.10	0.04	0.31	0.256	0.102	0.793	0.17	0.07	0.53	0.435	0.179	1.355
21	0.03	0.01	0.14	0.077	0.026	0.358	0.05	0.02	0.25	0.128	0.051	0.639
28	0.01	0.00	0.07	0.026	0.000	0.179	0.02	0.00	0.11	0.051	0.000	0.281
35	0.00	0.00	0.03	0.000	0.000	0.077	0.00	0.00	0.05	0.000	0.000	0.128

Dong, WH&S, 1990

^afor workers wearing long-sleeved shirt, long pants, and gloves (where applicable).

^bbased on 6 hrs per day [see discussion in text]; on a 10% clothing permeation (as common practice); and on the transfer factors of 950, 1,020, and 9,640 cm²/hr, respectively, for bare hands, the clothed upper body, and the clothed lower body [31].

^cbased on a male body weight (BW) of 70 kg and on a dermal absorption rate of 17.9% (see discussion in text and [11]).

^dassuming a reentry interval of at least 24 hrs (as common practice for cotton scouts).

day. This scout exposure time appears to be reasonable, given that cotton scouts are almost always required to travel *daily* between fields which may be miles apart. Table 3 suggests that the dermal exposure for a cotton scout could be as high as 2.29 mg per day, if he were to be exposed on *day 1* after the *fifth* application to cotton (in the same field and not wearing gloves). On the other hand, the daily dermal exposure for the same individual could be as low as 0.05 mg, if he were to be exposed on *day 21* after the *first* application to cotton. As shown in Table 1, for a cotton scout with work clothing but not wearing gloves the annual average daily dosage could be as high as 0.642 µg per kg of body weight.

REFERENCES

1. FMC Corporation. Product Chemistry (Technical Chemical). California Department of Food and Agriculture Registration Document No. 50429-007, 1984.
2. U. S. Environmental Protection Agency. Pesticide Tolerances for Bifenthrin. 40 *CFR* 180:30676-30678, 1988.
3. FMC Corporation. Acute Dermal Toxicity of FMC 54800-2EC (Capture[®]-2EC) in Rabbits. California Department of Food and Agriculture Registration Document No. 50429-022, 1985.
4. FMC Corporation. Primary Skin Irritation of FMC 54800-2EC (Capture[®]-2EC) in Rabbits. California Department of Food and Agriculture Registration Document No. 50429-022, 1985.
5. Draize JH. Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics. *Assn Food & Drug Officials of the U.S.*, 1959.
6. FMC Corporation. Skin Sensitization of FMC 54800-2EC (Capture[®]-2EC) in Guinea Pigs. California Department of Food and Agriculture Registration Document No. 50429-022, 1985.
7. Hazleton Laboratories America Inc.. Dermal Penetration and Distribution of ¹⁴C Capture[®]-2EC (FMC 54800) in Skin of Male Rats [an unaudited report]. California Department of Food and Agriculture Registration Document No. 50429-109, 1989.
8. FMC Corporation. Dermal Absorption Study in Rats with ¹⁴C FMC 54800 (Capture[®]-2EC). California Department of Food and Agriculture Registration Document No. 50429-080, 1986.
9. Zendzian RP. Procedure for Studying Dermal Absorption. U. S. Environmental Protection Agency Office of Pesticide Programs (Washington, D.C.), 1987.
10. Thongsinthusak T. Dermal Absorption Review for Bifenthrin. Memorandum from the Worker Health and Safety Branch to the Pesticide Registration Branch (within the California Department of Food and Agriculture), dated July 31, 1989.
11. Thongsinthusak T. Dermal Absorption Review for Bifenthrin. Memoranda from the Worker Health and Safety Branch to the Pesticide Registration Branch (within the California Department of Food and Agriculture), dated July 27, 1990 and December 20, 1990.
12. Morgan RL. Data Package Summary and Recommendation Sheet - New Active Ingredient. Memorandum from the Medical Toxicology Branch to the Pesticide Registration Branch (within the California Department of Food and Agriculture), dated September 13, 1989.
13. FMC Corporation. The Determination of Whole Body Autoradiography of the Distribution of the Insecticide/Miticide ¹⁴C-FMC 54800 in Rats. California Department of Food and Agriculture Registration Document No. 50429-071, 1986.

14. FMC Corporation. Excretion/Tissue Distribution of Alcohol-¹⁴C FMC 54800 in the Rat. California Department of Food and Agriculture Registration Document No. 50429-079, 1986.
15. FMC Corporation. Absorption, Distribution and Excretion Studies of FMC 54800 in the Rat. California Department of Food and Agriculture Registration Document No. 50429-079, 1986.
16. FMC Corporation. Metabolism of FMC 54800 in Rats - Identification of Products in Excreta. California Department of Food and Agriculture Registration Document No. 50429-079, 1986.
17. FMC Corporation. The Kinetics of FMC 54800 in the Blood of Rats Following a Single Oral Dose. California Department of Food and Agriculture Registration Document No. 50429-080, 1986.
18. FMC Corporation. Analysis of FMC 54800 Residues in Plasma from Rats Dosed Orally with ¹⁴C FMC 54800. California Department of Food and Agriculture Registration Document No. 50429-080, 1986.
19. FMC Corporation. Bioaccumulation Study of ¹⁴C FMC 54800 in the Rat. California Department of Food and Agriculture Registration Document No. 50429-080, 1986.
20. Hazleton Laboratories America Inc. Metabolism of ¹⁴C-Bifenthrin (FMC 54800) in Rats. California Department of Food and Agriculture Registration Document No. 50429-112, 1989.
21. Xenobiotic Laboratories Inc.. Metabolism of ¹⁴C-Bifenthrin (FMC 54800) in Rats - Analysis and Quantitation of Metabolites in Excreta. California Department of Food and Agriculture Registration Document No. 50429-112, 1989.
22. Lunchick C. A Summary of Surrogate Worker Exposure Data Prepared in Anticipation of Dinoseb Cancellation Hearings, U. S. Environmental Protection Agency Office of Pesticide Programs (Washington, D.C.), 1988.
23. Kutney LL. Handler Exposure Assessment for Bifenthrin Use on Cotton. Memorandum from the Health Effects Division to the Registration Division (within the U. S. Environmental Protection Agency), dated March 14, 1989.
24. Ware GW, Morgan DP, Estes BJ, *et al.* Establishment of Reentry Intervals for Organophosphate-Treated Cotton Fields Based on Human Data: I. Ethyl- and Methyl Parathion. *Arch Environ Contam & Tox* 1:48-59, 1973.
25. Ware GW, Morgan DP, Estes BJ, *et al.* Establishment of Reentry Intervals for Organophosphate-Treated Cotton Fields Based on Human Data: II. Azodrin, Ethyl and Methyl Parathion. *Arch Environ Contam & Tox* 2:117-129, 1974.
26. Ware GW, Morgan DP, Estes BJ, *et al.* Establishment of Reentry Intervals for Organophosphate-Treated Cotton Fields Based on Human Data: III. 12 to 72 Hours Post-Treatment Exposure to Monocrotophos, Ethyl- and Methyl Parathion. *Arch Environ Contam & Tox* 3:289-306, 1975.
27. Meinders D and Krieger RI. Estimation of Exposure of Persons in California to Pesticide Products that Contain Monocrotophos and Estimation of Effectiveness of Exposure Reduction Measures. HS-1472. The Worker Health and Safety Branch, California Department of Food and Agriculture, 1988.
28. Orius Associates Inc. Acute and Chronic Margin of Safety Assessments Based on Surrogate Exposure Models for Workers Treating Cotton with Bifenthrin Insecticide/Miticide by Ground Boom

and Aerial Equipment. California Department of Food and Agriculture Registration Document No. 50429-117, 1990.

29. Chester G, Hatfield LD, Hart TB, *et al.* Worker Exposure to, and Absorption of, Cypermethrin During Aerial Application of an "Ultra Low Volume" Formulation to Cotton. *Arch Environ Contam & Tox* 16:69-78, 1987.
30. Orius Associates Inc. Acute and Chronic Margins of Safety Risk Assessment Based on Surrogate Exposure Models for Workers Reentering Cotton Treated with Bifenthrin Insecticide/Miticide. California Department of Food and Agriculture Registration Document No. 50429-117, 1990.
31. Dong MH. Dermal Transfer Factor for Cotton Scouts. Memorandum to Dr. John H. Ross within the Worker Health and Safety Branch, California Department of Food and Agriculture, dated June 8, 1990.