UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR - 1 1993

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: 041701. Fonofos. Comments on the Hazard Associated With Exposure to Fonofos or Its Degradates in Groundwater

Tox. Chem. No. 454B
Project No. D185321

TO: Judith Loranger, PM Team # 73
Special Review and
Reregistration Division (H7508W)

FROM: Pamela M. Hurley, Toxicologist Pamela M. Hurley 2/24/93
Section I, Toxicology Branch I
Health Effects Division (H7509C)

THRU: Roger L. Gardner, Section Head Roger Gardner 3-23-93 KB 3/25/93
Section I, Toxicology Branch I
Health Effects Division (H7509C)

Submission No(s). S430472

Background and Request: The Environmental Fate and Ground Water Branch (EFGWB) is considering requesting a small-scale ground-water study for fonofos. The Toxicology Branch has been asked to comment on the "hazard associated with exposure to fonofos or its degradates in groundwater".

Toxicology Branch Response:

Hazard From Parent Compound: The toxicology data base on fonofos is nearly complete. This is summarized in the Toxicology Profile attached to this memorandum. The data gaps consist of a dermal sensitization study, a series of neurotoxicity studies and a chronic feeding study in the dog.

Fonofos is highly acutely toxic, with a toxicity category rating of I for the acute oral, dermal and inhalation studies. The primary dermal and eye irritation studies had to be tested at concentrations ten times lower than those specified in the guidelines because all of the animals died at the specified concentrations.

Fonofos is a cholinesterase inhibitor. Although some delayed neurotoxicity studies have been conducted, the Toxicology

Branch (TB-I) has not received enough data to provide a complete assessment of delayed neurotoxicity.

The present RfD is based on a two-year feeding study in the dog, which has recently been downgraded to Core Supplementary, partly due to the unusual feeding pattern, the lack of consistency in design and conduct of the study for replacement dogs, incomplete clinical chemistry studies and incomplete microscopic examinations. The NOEL is 0.2 mg/kg/day and the LEL is 0.4 mg/kg/day based on red blood cell cholinesterase inhibition, cholinergic symptoms, increased liver weights and microscopic changes in the liver and small intestine. At higher dose levels, deaths, decrease in body weight, increase in serum alkaline phosphatase, acute tissue congestion and liver pathology were observed.

The dog is the most sensitive species. The NOEL's for mice and rats, also based on cholinesterase inhibition in long-term feeding studies were both 0.75 mg/kg/day. Fonofos was not oncogenic in either the rat or mouse oncogenicity studies. It did not induce reproductive effects at dose levels up the 1.58 mg/kg/day (the highest dose tested (HDT)). In a rabbit developmental toxicity study, the NOEL for both maternal and developmental toxicity is 1.5 mg/kg/day (HDT). In mice, the NOEL for maternal toxicity is 6 mg/kg/day and the LEL is 8 mg/kg/day, based on symptoms of neurotoxicity, including tremors and chromodacryorrhea. The NOEL for developmental toxicity in mice is 4 mg/kg/day and the LEL is 6 mg/kg/day, based on sternebral malalignment and slight dilation of the 4th cerebral ventricles.

Fonofos is not mutagenic in a gene mutation test in Salmonella and it tested negatively in both an in vivo structural chromosomal aberration assay and in a mouse micronucleus assay.

Single oral doses of dyfonate to rats produced the following metabolites in the urine and feces: o-ethylethanephosphonothioic acid (ETP), o-ethylethanephosphonic acid (EOP), methylphenylsulfone and its phenyl hydroxylates. Single i.p. doses produced $MPSO_2$ and its hydroxylates.

In an in vitro metabolism study with induced male rat liver homogenates in the presence of $NADPH_2$, the oxon analogue, ETP, EOP and thiophenol were obtained. It appears that chemical oxidation with m-chloroperbenzoic acid yields the same results with the addition of sulfur. The other available metabolism studies did not identify specific metabolites.

Hazard From Degradates: The following products from fonofos were listed in the EFED one line summary tables:

Hydrolysis (Study # 161-1): DPDS*, OXON*, OEPTA* and OEPA*.

Photolysis (Study #'s 161-2,-3,-4): Water - OXON, OEPA and OEPTA; Soil - PEPA*, OXON and diphenyl disulfide; Air - no data.

Anaerobic Soil Metabolism (Study # 162-2): OXON, 2-,3-, and 4-hydroxyphenyl methyl sulfone.

Other degradation products include thiophenol, methylphenyl sulfoxide, o-ethyl s-phenyl ethylphosphothioate and methylphenyl sulfone.

* OXON = o-ethyl-S-phenyl ethylphosphonothioate
OEPA = ethylethoxy phosphonic acid
DPDS = diphenyl disulfide
OEPTA = o-ethylethylphosphonothioic acid
PEPA = s-phenyl phosphonodithioic acid

When the above list is compared with the metabolites listed in the available metabolism studies conducted with fonofos, at least part of the list matches with mammalian metabolites. TB-I cannot specify their potential hazard other than the fact that the ones that match have been tested in the chronic studies along with the parent compound because the parent compound was presumably metabolized to these compounds during the exposure period.

TB-I has checked the available exposure data that are available. Although the attached memoranda are not necessarily related to this particular request, they are included for information purposes only.

The following toxicology profile for fonofos lists the studies that are required and those that have been satisfied with accompanying comments. In addition, one-line summaries of each study are provided.

	Required	Satisfied
Technical Product		
Acute oral LD_{50}	Yes	Yes
Acute dermal LD_{50}	Yes	Yes
Acute inhalation LC_{50}	Yes	Yes
Primary eye irritation	Yes	Yes
Primary dermal irritation	Yes	Yes
Dermal sensitization	Yes	No
Acute delayed neurotoxicity (hen)	Yes	No (comment 1)
Acute neurotoxicity screening (mammalian)	Yes	No (comment 2)
90-day subchronic oral		
rodent	Yes	Yes (comment 3)
nonrodent	Yes	No (comment 4)
28-day delayed neurotoxicity (hen)	Yes	Reserved (comment 5)
Subchronic neurotoxicity screening (mammalian)	Yes	No (comment 2)
6-month dog (ocular effects)	Yes	No (comment 6)
Chronic feeding		
rodent	Yes	Yes
nonrodent	Yes	No (comment 4)
Oncogenicity		
rat	Yes	Yes
mouse	Yes	Yes
Teratology		
rabbit	Yes	Yes
mouse	Yes	Yes
2-Generation reproduction	Yes	Yes
Gene mutation	Yes	Yes
Chromosome aberration	Yes	Yes
Other genotoxic effects	Yes	Yes
Metabolism	Yes	Yes

Comments

1. This study has been requested in the FIFRA '88 requirements.

2. This study has been requested in the FIFRA '88 requirements. The Agency has previously reviewed the submitted protocol for this study.

3. An acceptable chronic/oncogenicity feeding study in the rat is available. Therefore, the requirement for a 90-day oral study in the rat has been satisfied.

4. Although a 2-year chronic feeding study in dogs is available, it is not acceptable for regulatory purposes. Therefore, the requirement for a subchronic feeding study in dogs has not been satisfied.

5. A 90-day delayed neurotoxicity study is available in the hen. This study has been classified as Supplementary until data from an acute delayed neurotoxicity study has been received and reviewed. The 90-neurotoxicity study was based on the old neurotoxicity testing guidelines. The Office of Pesticide Programs (OPP) is in the process of finalizing new guidelines for neurotoxicity testing. The 90-day hen study published in OPP's previous guidelines is missing the assays for acetylcholinesterase (AchE) and neuropathy target esterase (NTE). This assay is included in the new guidelines for hen studies. Therefore, the 90-day hen study will apply to the previously published OPP neurotoxicity testing guidelines. TB-I notes that the Registrant has added the AchE and NTE assays in their protocols for the rat neurotoxicity screening battery for Fonofos. Therefore, the requirement for a 28-day delayed neurotoxicity study in hens will be reserved until review and evaluation of the other neurotoxicity data requirements have been received and reviewed.

6. This study has been requested in the FIFRA '88 requirements. The Agency has approved a deferral for ocular effects testing until further guidance can be provided.

Last Updated:

Technical grade

Guide-line #	Study Identification and Classification	Results
81-1	Acute Oral Toxicity in Rats Lab: Stauffer Chemical MRID 00078777 Report # T-6461 Date: 2/12/79 Acceptable	LD_{50}: 24.5 (21.4-28.0) mg/kg (males) LD_{50}: 10.8 mg/kg (9.6-12.2) (females) TOXICITY CATEGORY: I Tremors, salivation, diarrhea, lacrimation & labored breathing.
81-2	Acute Dermal Toxicity in Rabbits Lab: Stauffer Chemical MRID 00078777 Report # T-6461 Date: 2/12/79 Acceptable	LD_{50}: 159 (40-615) mg/kg TOXICITY CATEGORY: I Tremors, salivation, diarrhea, rapid breathing and miosis.
81-3	Acute Inhalation Toxicity in Rats MRID 419359-01 Lab: ICI Central Tox. Lab Report # HR2047 Date: 04/11/91 Acceptable	LC_{50}: 51.0 (33.5-77.7) µg/l (males) LC_{50}: 17.9 (8.6-37.0) µg/l (females) (Four hour exposure) TOXICITY CATEGORY: I Median lethal concentration was based on atmospheric concentrations. Clinical signs of toxicity and cholinesterase inhibition were evident and were consistent with the combination of neurological and irritancy effects which are typical of those seen following exposure to organophosphorus compounds.

Last Updated:

Technical grade

Guide-line #	Study Identification and Classification	Results
81-4	Primary Eye Irritation in Rabbits Lab: Stauffer Chemical MRID: 00078777 Report # T-6461 Date: 2/12/79 Acceptable	Primary Irritation Score: Not given in DER. TOXICITY CATEGORY: IV Moderate irritation for 1/6 animals. 0.01 ml tested because in other studies with technical dyfonate, all animals died with a dose of 0.1 ml with no irritation. 0/6 died in this study.
81-5	Primary Dermal Irritation in Rabbits Lab: Stauffer Chemical MRID: 00078777 Report # T-6461 Date: 2/12/79 Acceptable	Primary Irritation Score: Not given. TOXICITY CATEGORY: IV 2/6 animals died. No irritation. 0.05 ml given as a dose. The required dose is 0.5 ml. However, all animals had died with a previous dose of 0.5 ml of the 93% Technical with Aliquot 335. The Tox. Category was I in the previous study.
81-7	Acute delayed neurotoxicity - chickens Lab: Woodward Research MRID: Not available Report # Not available Date: 1/10/69 Core Grade: Minimum (original assessment).	NOEL: 6.32 mg/kg LOEL: 20 mg/kg Effects: Dose levels tested: 2, 6.32, 20 mg/kg. Slow locomotion, curling under of toes, head lowering, squatting, loss of equilibrium, possible demyelination of peripheral nerve for 1 chicken. Study not currently acceptable for regulatory purposes.

Last Updated:

Technical grade

Guideline #	Study Identification and Classification	Results
82-5	90-day delayed neurotoxicity study in hens Lab: Stauffer Chemical Company MRID: 401501-20 Report # T-6237 Date: 11/8/78; reformatted and reissued: 3/24/87 Core Grade: Supplementary	NOEL for inhibition of plasma cholinesterase: < 2.0 mg/kg/day (LDT). NOEL for other acute neurotoxic effects: < 2.0 mg/kg/day. Effects: Dose levels tested: Administered orally to adult hens for 90 days at 2, 4 and 8 mg/kg/day. Positive control group administered tri-o-cresyl phosphate (TOCP). No evidence of delayed neurotoxicity observed in any of the treated hens. Treated animals exhibited significant weight loss in high dose group, clinical signs of toxicity in mid- and high dose groups (possibly the low dose group), inhibition of plasma cholinesterase in all dose groups and impaired egg production in all dose groups. Since results from microscopic examination slightly unclear, it would be helpful for an overall assessment of delayed neurotoxicity to have data from an acute delayed-neurotoxicity study in the hen. 90-day neurotoxicity study classified as Core Supplementary, upgradable when data on the acute delayed neurotoxicity study are submitted.

Last Updated:

Technical grade

Guideline #	Study Identification and Classification	Results
83-1	Chronic feeding study in dogs Lab: Woodward Research MRID: 00082233 Report # T-2153? Date: 1/10/69 Core Grade: Supplementary	NOEL: Cholinesterase NOEL: 8.0 ppm LOEL: 16.0 ppm. Systemic NOEL: 16.0(8.0) ppm. LOEL: 60 ppm Effects: Dose levels tested: 0, 16(8.0), 60 and 240 ppm for 2 years. 240 ppm: deaths, clinical signs, decrease in body weight, increase in serum alkaline phosphatase, possible liver effects (organ weights and histopathology) and acute tissue congestion; at 60 ppm: a few clinical signs, liver weight increases and some possible body weight decreases, however, there were no major systemic effects. Quality of study not sufficient for regulatory purposes.
83-2 (a)	Oncogenicity study in mice Lab: Stauffer Chemical MRID: 401501-21 Report # T-11995 Date: 3/12/87 Core Grade: Guideline	NOEL: 5 ppm LOEL: 25 ppm Effects: Dose levels tested: 0, 5, 25, 100 ppm for 18 months. Cholinesterase inhibition (brain, erythrocyte and serum). Hyperplasia and hypertrophy of duodenum, reductions in body wt. gain & food consumption in high dose males.

Last Updated:

Technical grade

Guide-line #	Study Identification and Classification	Results
83-3	Teratology Study in Rabbits MRID 401501-22 Lab: Wil Research Labs Report # WIL-27027 Date: 2/23/87 Core Grade Minimum	Maternal NOEL: 1.5 mg/kg/day (HDT) Effects: Dose levels tested: 0, 0.2, 0.5, 1.5 mg/kg/day. Tested at sufficiently high dose level because in range-finding study at: 0 - 10.0 mg/kg/day, maternal toxicity observed at 2.0 mg/kg/day and above (death). Developmental NOEL: 1.5 mg/kg/day (HDT). NOEL borderline because there was a non-statistically significant increase in number of resorptions/doe in high dose group. Increase within historical control range & standard deviation for measurement was large.
83-3	Teratology Study in Mice Lab: Stauffer Chemical MRID: 420576-01 Report # T-10192 Date: 4/2/92 Core Grade Minimum	Maternal NOEL: 6 mg/kg/day Maternal LOEL: 8 mg/kg/day Effects: Dose levels tested: 0, 2, 4, 6, 8 mg/kg/day. Some symptoms of neurotoxicity, including tremors, chromodacryorrhea. Developmental NOEL: 4 mg/kg/day Developmental LEL: 6 mg/kg/day Effects: Sternebral malalignment & slight dilation of 4th cerebral ventricles.

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Technical grade

Guide-line #	Study Identification and Classification	Results
83-4	Multigeneration Reproduction Toxicity in Rats MRID 00082234 Lab: Woodward Research Report # Not given Date: 1/10/69 Core Grade Not given	NOEL: > 31.6 ppm (HDT) Effects: Dose levels tested: 0, 10 or 31.6 ppm. No effects. Reproductive NOEL: > 31.6 ppm (HDT). DER not sufficient. Study checked against acceptance criteria. New DER needs to be written.
83-5	Chronic/oncogenicity feeding study in rats Lab: ICI Americas, Inc. MRID: 406179-01 Report # T:11997 Date: 05/02/88 Core Grade: Minimum	NOEL: 15 ppm LOEL: 60 ppm Effects: Dose levels tested: 0, 4, 15, 60 ppm for 2 years and 120 ppm for 12 months. Not oncogenic. Cholinesterase inhibition (brain, serum and erythrocyte). Decreases in body weight gain in females at 120 ppm.
84-2 (a)	Gene Mutation Assay (Ames Test) Lab: ICI Central Toxicology Lab MRID: 417692-01 Report # CTL/P/3153 Date: 12/21/90 Acceptable	Dose levels tested: Tested with and without activation at 0.32, 1.6, 8.0, 40, 200, 1000, 5000 µg/plate. Tested up to levels of cytotoxicity. Results negative when compared to vehicle (DMSO) and absolute controls.

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Technical grade

Guide-line #	Study Identification and Classification	Results
84-2 (b)	Structural Chromosomal Aberration Assay: In vitro cytogenetics in human lymphocytes Lab: ICI Central Tox. Laboratory MRID: 418371-01 Report # SV0481 Date: 3/13/91 Acceptable	Dose levels tested: 10, 50, 100 µg/ml both with and without metabolic activation. Tested up to levels of cytotoxicity. Results negative. Positive controls verified sensitivity.
84-2 (c)	Other Genotoxicity Assays: Mouse micronucleus assay Lab: ICI Central Tox. Laboratory MRID: 418133-01 Report # CTL/P/3153 Date: 01/17/90 Acceptable	Dose levels tested: 6 and 9.5 mg/kg. No increases in micronucleated PCE's. Indications that it was tested up to level of cytotoxicity.
85-1	Metabolism Lab: Stauffer Chemical MRID: 00090876 Report # Pest Bio Path1:256 Date: 1971 Acceptable	Dose levels tested: Single oral dose of 2.0, 4.0, 8.0 mg/kg to male rats were eliminated greater than 94% in urine and feces at 48 hrs. (C^{14} in the ethyl moiety).
85-1	Metabolism Lab: Stauffer Chemical MRID: 00043508, 00090824 Report # ARC-B-14 Date: 1/12/67 Supplementary	Results: One minor water soluble metabolite (not identified) in corn was not observed in rat urine.

Last Updated:

Technical grade

Guide-line #	Study Identification and Classification	Results
85-1	Metabolism Lab: Stauffer Chemical MRID: 00090875 Report # Not given Date: 12/13/77 Supplementary	Results: No significant influence on excretion of dyfonate (2.0 mg/kg, oral, periodically over 16 days) due to 3-day hepatic enzymes at 0.5 mg/kg/day. Biliary excretion shows 15% enterohepatic recirculation in noninduced rats.
85-1	Metabolism Lab: Stauffer Chemical MRID: 00090877 Report # Life Sci. 10:1311 Date: 1971 Supplementary	Results: Chemical oxidation with m-chloroperbenzoic acid yields o-ethyl-ethanephosphonothioc acid (ETP), o-ethylethanephosphonic acid (EOP), thiophenol and sulfur.
85-1	Metabolism Lab: Stauffer Chemical MRID: 00090879 Report # J.J. Mimm ARC-B-17 Date: 1967 Supplementary	Results: 60 hrs. after single oral doses of either 0.5 or 6 mg/kg to rats (male and female), radiolabel was excreted at 94.4% and 75.8% for the low and high dose respectively, mostly hair and hide.
85-1	Metabolism Lab: Stauffer Chemical MRID: 00090800 Report # Not given Date: 12/12/66 Supplementary	Results: Both C^{14} and S^{35} labels were 90-97% recovered at 96 hours from either oral or i.p. administration in either sex. Tissue retention was 2.3% mostly in blood, liver, kidney, and intestines.

Last Updated:

Technical grade

Guide-line #	Study Identification and Classification	Results
85-1	Metabolism Lab: Stauffer Chemical MRID: 00092025 Report # Life Sci. 10:947 Date: 1971 Supplementary	Results: In vitro microsomal metabolism yields oxon analogue, ETP, EOP & thiophenol.

Data Gaps: Dermal sensitization study, acute and subchronic delayed neurotoxicity studies in hens, mammalian neurotoxicity screening battery, subchronic and chronic dog feeding studies and the 6-month dog ocular study.

Actions Being Taken to Obtain Additional Information or Clarification: These studies have been requested through the FIFRA '88 process.

Reference Dose (RfD):

The recommended provisional RfD (to the RfD Workgroup) is 0.002 mg/kg/day. This value was calculated by using the 2-year dog feeding study NOEL of 0.2 mg/kg/day and a safety factor of 100. This RfD has been verified or approved by a Health Effects Division or Agency RfD Committee. The NOEL and LOEL are based on RBC cholinesterase inhibition, cholinergic symptoms, increased liver weights and microscopic changes in the liver and small intestine.

Pending Regulatory Actions: None

Toxicologic Issues Pertinent to This Request: Toxicologic issues pertain to either missing or inadequate studies. These are explained further in the profile summary.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OCT 29 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Decisions on the Ecological, Fate, and Effects Task Force

FROM: Linda J. Fisher
Assistant Administrator

TO: Douglas Campt, Director
Office of Pesticide Programs

In May 1992, I initiated the Ecological, Fate and Effects Task Force to evaluate the testing requirements for ecological and environmental fate with respect to their impact upon OPP's regulatory programs. For the past several months, numerous OPP managers and analysts, as well as participants from OPPE, OPPT, OGC, and ORD have put an extraordinary amount of time and effort into this workgroup. These decisions, once implemented, will result in protective and timely decisions in the area of ecological risk management. The attached document outlines the specific decisions on the very important issues of ecological risk management raised by the Task Force. There are still many details to resolve as this new paradigm is implemented. I have asked Deputy Assistant Administrator Vic Kimm to chair an implementation committee.

The effort put into the Task Force deliberations was clearly monumental. The Program showed a remarkable commitment to analyzing and addressing these issues. In addition, the support provided by OPPT, OPPE, ORD, and OGC was outstanding, as were their contributions to our policy discussions.

The principle issue addressed by the Task Force is the effect of the data generated from OPP's ecological and environmental fate data requirements on the Reregistration program. As a regulatory agency, we must have a clear sense of how to use the data which we require. The value added by these data on regulatory decisions (registration and reregistration) was carefully reviewed. Secondly, the Task Force evaluated the effect of collecting and reviewing ecological and environmental fate data on the legislative deadlines established for reregistration. Although the Task Force focused much of its attention on reregistration, many of its findings apply to the registration program.

OPP will begin to develop a strategy for making regulatory decisions on the long-term ecological effects of pesticide use. In this effort, OPP should consider a longer time frame for field studies as well as the possibility of testing a single representative of a class of pesticides. The current field studies have a duration of about two years and are performed on a chemical by chemical basis. These studies do not provide risk managers with information which greatly enhances the risk management decision-making process.

For future reregistration and registration purposes, OPP should use risk mitigation to the extent feasible to achieve acceptable risk. Risk mitigation includes all practices which reduce hazard or exposure. Mitigation can be in the form of reduced application rates, mandatory tillage practices or a change in the pesticide's formulation, to name a few. With respect to the current aquatic triggers or "levels of concern", the AA supports the workgroup's recommendation to continue using the existing triggers. However, risk assessments should include a small stream as the receiving body of water. Risk management decisions should be based on the effects to flowing bodies of water unless a risk case, on a use specific basis, can be made as to the relevance of protecting small, closed water systems (such as a pond, wetland, or a small lake).

issues which will need to be addressed, beyond those identified here, in the implementation plan. It is my goal to have a final implementation plan by January 5, 1993.

Again, I wish to thank you and your staff for the commitment you have brought to this very important effort.

3. Effect on Reregistration

How will this policy change affect decision-making in the reregistration program? OPP will make regulatory decisions for aquatic risk following the guidelines established in the Levels of Concern (LOC) project. If a risk exceeds the LOC, the risk assessment should be refined using standard approaches such as application of more sophisticated models to estimate exposure and the EEC. If the LOC exceedance is supported, risk managers should require or negotiate risk reduction measures. It may be necessary to calculate the cost of mitigation in a very crude form prior to negotiating risk mitigation. This will help the Agency decision makers to make better informed decisions regarding mitigation measures to pursue in discussions with registrants. If the LOC is still exceeded after risk reduction measures are evaluated, a risk/benefit based decision, leading to specific regulatory determination, is necessary. A risk/benefit determination is necessary at this point because the concept of "acceptable risk" takes into consideration benefits. Thus acceptable risk may exceed the level of concern, and cannot be defined with a simple numerical standard. To define acceptable risk, a preliminary benefits assessment must be conducted. If it becomes clear that an in depth review of the risks and benefits is necessary to make a determination, then the chemical will be declared ineligible for reregistration, pending a Special Review or other regulatory action.

4. Status of Mesocosm DCIs (Data Call-Ins)

At this point, complete, acceptable mesocosms will not normally be required for purposes of regulatory decision making (reregistration or registration), as these studies do not generally provide regulatory managers with information to make better regulatory decisions. RED decisions can and should be made in the absence of mesocosm studies. If SRRD or RD (Registration Division) feel that a regulatory decision cannot be made in the absence of an aquatic field study, the mesocosm can be required. OPP will continue to accept mesocosm studies which registrants submit to the Agency. These studies will be evaluated and used as confirmatory information in the aquatic risk assessment to the extent that the mesocosm provides relevant information with respect to the aquatic levels of concern. If the registrant believes that a mesocosm will refute a presumption of risk, they can pursue such a study. However, the Agency does not need to wait for such a study before making regulatory decisions.

5. Future Directions in Aquatic Risk Assessment/ Risk Management

Over the next five to ten years (period of FIFRA 88 reregistration) OPP should aim to greatly reduce the direct acute and chronic risks to aquatic environments. During that timeframe, OPP should develop a regulatory scheme for protecting aquatic ecosystems from the long-term effects of pesticide use based upon

If 1/5LC50 <= EEC <= 1/2LC50, then the pesticide is considered for classification as a restricted use pesticide.

If EEC < 1/5LC50, then the pesticide has low avian risk and no additional regulatory action will be pursued.

CHRONIC:

For chronic avian tests, the level of concern is reached if the EEC >= LEL.

Qualitative Factors: Incident reports play a critical role in the avian risk management process. Also important are extent of use, proximity to high value habitat, the fate of the chemical, the species exposed, and the availability of safer substitutes.

3. Effect on Reregistration

RED decisions will be made in the absence of avian field studies. If the chemical exceeds a level of concern for an avian endpoint, OPP will follow the same basic framework as for aquatic risk management. First, OPP will refine its hazard and exposure calculations. Secondly, OPP will evaluate risk reduction techniques (including the costs of mitigation). If mitigation is

qualitative or quantitative information to the risk manager.

4. Status of Avian Field Studies DCIs

Avian field studies will not be required for a substantially complete data base except in highly unusual circumstances (the regulatory management divisions are unable to make a regulatory decision in the absence of such a study). Thus registrants will not be required to complete such studies.

5. Future Directions in Avian Risk Assessment/ Risk Management

OPP needs to develop a long-term strategy for improving the scientific risk assessment methodologies, building on findings of the most recent avian risk dialogue group. In addition, OPP should begin to evaluate the viability and usefulness of longer term avian monitoring in high use areas as well as a research plan for better understanding the impacts of pesticide use on birds.

Avian and aquatic levels of concern (acute and chronic) have been established in regulation and guidance over the last 10 to 15 years. As far as the Agency knows, these levels are appropriate, and OPP should continue to use these "triggers" for regulatory purposes. As a normal part of the scientific and regulatory process, these numbers will be subject to periodic review.

A risk based (human health or ecological) trigger is exceeded, or has a high potential to be exceeded, ((OPP is currently working to define this trigger based on some fraction of a Maximum Contaminant Level (MCL) or Health Advisory (HA), and as appropriate, frequency of detections in high use areas).

3. Effect on Reregistration

The new process will involve a risk management decision before requiring the monitoring study. The following steps will be followed in the risk management process:

1) Determine if there is a known human health or environmental concern with the compound. If not, do not require the monitoring study, if so, go to 2);
2) evaluate the likelihood of the compound reaching a level of concern in a vulnerable area, given the entire data base of the compound (lab data, other monitoring, modelling, etc...); if it appears unlikely that the compound will reach ground water at a level of concern, do not require the monitoring study, if it appears feasible or likely, go to 3);
3) if the existing evidence indicates that a pesticide exceeds the Agency's threshold (level of concern), then regulate without the monitoring study; if the evidence is equivocal, then go to 4);

4. Status of Existing Monitoring DCIs

OPP should perform a cursory review of the 45 chemicals which already have ground water monitoring DCIs to determine if a regulatory decision could be made in the absence of such studies. In particular, if the existing data base on a chemical indicates that regulatory action is warranted, we should pursue such action, and classify the monitoring study as optional. Where such studies are submitted to OPP, they should be evaluated and considered confirmatory. For chemicals which do not have a ground water DCI, we should go through the five step process outlined above.

IV. RISK MITIGATION

1. AA Decision

The Assistant Administrator fully supports the concept of using risk mitigation for pesticides which pose risks of concern. Over the next few weeks, OPP should develop a process which details how and when mitigation will be used. Of greatest importance should be how the program will evaluate risk reduction measures. This plan should also identify where in the risk management process mitigation will be imposed as well as who should be responsible for identifying appropriate measures. For both avian and aquatic risk mitigation, OPP should consider post-mitigation monitoring to evaluate the effectiveness of the mitigation measures.

policies to guide risk assessment and risk management in the ecological area. This document should serve as a first step in providing such guidance. In addition, the Assistant Administrator finds that the roles of the risk assessors and risk managers in the area of ecological effects are not as clearly defined or well understood as they should be. OPP should begin to work through the recommended options with respect to risk assessment/ risk management interaction which are identified in the risk assessment/ risk management chapter.

VII. IMPLEMENTATION

OPP should develop a workplan which describes the process by which these decisions will be implemented. An implementation plan should be in final form by January 5, 1993. An implementation committee should operate under the direction of the Deputy Assistant Administrator of OPPTS. A preliminary plan and schedule should be presented to the AA by December, 1992. In the interim, program managers should strongly consider the direction of this guidance when making regulatory decisions in the areas of ecological risk management and assessment.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 28 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

SUBJECT: EVALUATE REQUEST TO REMOVE THE 24-HOUR RESTRICTED REENTRY INTERVAL STATEMENT FROM THE LABEL OF DYFONATE-TILLAM 1-4E FOR THE ACTIVE INGREDIENT FONOFOS

FROM: Bruce F. Kitchens, Chemist Bruce Kitchens

TO: Rob Forrest, PM 14
Insecticide-Rodenticide Branch
Registration Division (H7505C)

THRU: Mark I. Dow, Ph.D., Section Head
Special Review and Registration Section II

Larry C. Dorsey, Acting Chief
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Please find below, the OREB review of:

DP Barcode: D169278

Pesticide Chemical Code: 41701

EPA Reg. No.: 010182-00195

EPA MRID No.: N/A

Review Time: 3.5 DAYS

PHED: NO

I. INTRODUCTION:

ICI Americas Incorporated submits a request for a label amendment on its product Dyfonate®-Tillam® 1-4E. The label amendment specifically requests removal of the 24-hour restricted reentry interval from the Dyfonate-Tillam 1-4E label for the active ingredient in Dyfonate, fonofos. The registrant intends to replace the 24-hour restricted reentry statement with:

> **Do not enter treated areas without protective clothing until treatments have been completed.**

Dyfonate-Tillam 1-4E is an emulsifiable liquid which contains 1 lb/gal fonofos and 4 lbs/gal pebulate as the active ingredients. Dyfonate-Tillam 1-4E is applied at an application rate of 1.0 gal/acre and is used as an insecticide/herbicide in tobacco. Dyfonate-Tillam 1-4E is incorporated into the soil immediately after application to prevent loss by evaporation of the herbicide (Tillam).

A. Background:

The registrant bases their request on an OREB review of fonofos Postapplication/Reentry and Applicator Exposure Monitoring Data dated March 27, 1991 (P. Perreault). The registrant submitted foliar dissipation studies on corn, sorghum, turfgrass. A soil dissipation study and an applicator exposure monitoring study was also submitted in this package. The soil dissipation study relates to this label amendment since Dyfonate-Tillam 1-4E is soil incorporated. Therefore, only the soil dissipation study will be considered in the evaluation of this label amendment.

B. Purpose:

The purpose of this registration action is to evaluate the registrant's request to remove the 24-hour restricted reentry interval for the active ingredient fonofos from the label of Dyfonate-Tillam 1-4 E.

II. DETAILED CONSIDERATIONS:

In the previously mentioned memo, OREB evaluated the foliar and soil dissipation studies. The soil dissipation study was acceptable. A reentry interval of zero days was established for preemergent soil incorporated applications. This reentry interval applied to the 20G and 4G formulations of Dyfonate when applied to crops via soil incorporation. The corresponding post-application dermal exposure estimate for soil, while not based on an actual field worker exposure monitoring study, was calculated from measured dislodgeable soil residues of fonofos and fonofos oxon

using acceptable transfer factors. Post-application inhalation exposure to soil residues was not determined. Dyfonate is applied preemergent and is incorporated into the soil, consequently, post-application inhalation exposure to soil residues is expected to be negligible. Fonofos has a vapor pressure of 2.10×10^{-4} Torr. Table 1 summarizes average soil residues and post-application dermal exposure to fonofos and fonofos oxon following one preemergent soil incorporated application of Dyfonate 20G and Dyfonate 4EC at 1.0 and 4.0 lb ai/A, respectively.

TABLE 1
Average Estimated Soil Residues and Dermal Exposures to Dyfonate 20G and 4EC at 1lb ai/acre and 4lb ai/acre, respectively

Day	Dyfonate 20G Soil Residues ($\mu g/ft^2$)	Estimated dermal exposure[a] (mg/kg/day)	Dyfonate 4EC Soil Residues ($\mu g/ft^2$)	Estimated dermal exposure[a] (mg/kg/day
0	199.8	0.00023	271.6	0.00032
1	160.2	0.00019	315.0	0.00037
3-28	209.2 - 6.3	0.00024 - 0.000007	236.6 - 9.6	0.00028 - 0.00001

[a] Calculated based on a body weight of 60 kg as follows: soil residues ($\mu g/ft^2$) x 0.07 $\mu g/day/\mu g/ft^2$ (Spear, 1977 correlation developed for estimating full day exposure to parathion and paraoxon residues in soil).

Sample Calculation Day Zero Dyfonate 20G

$$199 \frac{\mu g}{ft^2} \times 0.07 \frac{\mu g/day}{\mu g/ft^2} / 60 \text{ kg} \times \frac{1 \text{ mg}}{1000 \ \mu g} = 0.00023 \text{ mg/kg/day}$$

III. CONCLUSIONS:

OREB concludes that the request to remove the 24 hour reentry interval for the active ingredient fonofos from the label of Dyfonate-Tillam 1-4E is acceptable. Day zero estimated dermal exposures of 0.00023 mg/kg/day and 0.00032 mg/kg/day were obtained for Dyfonate 20G and Dyfonate 4EC, respectively. This amendment is acceptable because the registrant has demonstrated through the submission of acceptable data that dermal exposure resulting from soil residues to reentry workers is minimal. Inhalation exposure is expected to be minimal compared to dermal exposure. This label amendment is applicable only to the soil incorporation of Dyfonate-Tillam 1-4E. The 24 hour reentry restriction will be replaced by the following statement:

Do not enter treated areas without protective clothing as specified by the provisions of the Worker Protection Standards until treatments have been completed.

A zero time reentry interval has been established for preemergent soil incorporated Dyfonate 20G and 4EC in the previous OREB review entitled Postapplication/Reentry and Applicator Exposure Monitoring Data Submitted to Support the Reregistration of Fonofos dated March 27, 1991 (P. Perreault). Dyfonate-Tillam 1-4E's application method of soil incorporation is similar to the preemergent soil incorporation of Dyfonate 20G and Dyfonate 4EC. Therefore, reentry exposure to Dyfonate-Tillam 1-4E is expected to be similar to the reentry exposure to Dyfonate 20G and Dyfonate 4EC. Tobacco seedlings are transplanted mechanically; consequently dermal exposure is expected to be minimal.

IV. REFERENCES:

1. Perreault, P. Postapplication/Reentry and Applicator Exposure Monitoring Data Submitted to Support the Reregistration of Fonofos. Occupational and Residential Exposure Branch/HED. March 1991.

cc: B. Kitchens
Chemical File: FONOFOS
Circulation
Correspondence

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 13 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: CHECK REQUESTED LABEL REVISION FOR DYFONATE GRANULAR TURF INSECTICIDE (HED PROJECT # 1-1428)

TO: Barbara Madden PM 14
Insecticide/Rodenticide Branch
Registration Division (H7505C)

FROM: Bruce F. Kitchens, Chemist
Special Review and Registration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

THRU: Curt Lunchick, Section Head
Special Review and Registration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Charles L. Trichilo, Ph.D., Chief
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Please find below the OREB review of.....

HED Project #: 1-1428

Reg File/Rec #: 165015

Caswell #: 454B

Company Name: ICI AMERICAS INC.

Date Received: 6/12/91 Reviewing Time: 3 days

1.0 INTRODUCTION

ICI Americas Incorporated submitted an application for a label amendment for Dyfonate/Crusade 5-G. The registrant requested a change in the reentry statement **from:** Do not allow people or pets on treated area for 24-hours and unless grass is dry **to:** Do not allow people or pets on treated area unless grass is dry. The registrant states that the 24-hour reentry interval established by the registration standard is not necessary since a recent 21 day dermal study submitted demonstrated that repeated exposure did not result in dermal irritation and that a wide safety margin exists for use of Dyfonate/Crusade 5-G on turfgrass.

The 21-day dermal exposure on rats had a NOEL of 100 mg/kg/day and a LOEL of 1000 mg/kg/day. These values were established by Tox Branch I in a review of a recently submitted 21-day subchronic dermal exposure study dated 2/5/91.

2.0 CONCLUSIONS

OREB concluded that to remove the Dyfonate/Crusade 5-G 24 hour reentry statement a new reentry interval needed to be calculated based on a 21-day dermal exposure. Any recalculated reentry level less than 24 hours can be revised on the label.

A previously submitted dislodgeable foliar residue study (MRID # 40150124) showed that 0.99 ug/cm^2 was the highest dislodgeable foliar residue level found when dosed at the maximum label rate of 4 lbs. a.i./acre. The registrant then converted the DFR into total exposure by multiplying by the total surface area exposed and dividing by the average weight of a fieldworker resulting in a total exposure of 0.02 mg/kg. OREB could not accept the assumption that the feet (1200 cm^2) would constitute the total exposure area. Consequently, a transfer coefficient which accounts for whole body exposure will be used to calculate the reentry interval.

3.0 RECOMMENDATIONS

OREB finds the proposed reentry statement," Do not allow people or pets on treated areas until grass is dry" to be acceptable for uses of Crusade 5G on golf courses and sod farm turf.

4.0 CALCULATIONS

Registrant's

1) Total Dislodgeable Foliar Residues (DFR)

Fonofos Equivalent Oxon Residue ug/cm^2 + Mean Fonofos Residue ug/cm^2 =

Total Fonofos Residue ug/cm^2

2) Total Fonofos Residue x Exposed Surface Area / Weight of Average Fieldworker =

Total Exposure mg/kg

Zero Day (Values from Table 8 in the study MRID # 40150124)

1) 0.034 ug/cm^2 + 0.96 ug/cm^2 = 0.99 ug/cm^2

2) 0.99 ug/cm^2 x 1200 cm^2 / 60 kg = 0.020 mg/kg

OREB's Reentry Calculation (based on two-sided calculation)

1) Allowable Exposure Level (mg/hr) =

$$\frac{\text{subchronic dermal NOEL (mg/kg/day) x 70 kg}}{\text{8 hours}}$$

assumptions: avg. fieldworker wights 70 kg
avg work day is 8 hours
100% dermal absorption

2) Reentry Level

AEL (mg/hr) x 1,000 = AEL (ug/hr)

$$\text{Reentry Level (ug/cm}^2\text{)} = \frac{\text{AEL (ug/hr)}}{\text{10,000 cm}^2\text{/hr (Zweig, et. al 1984)}}$$

3) Using a safety factor of 10 for cholinesterase inhibition, the Reentry Level becomes:

Reentry Level ug/cm^2 x 0.1

4) Compare this Reentry Level with the foliar dislodgeable residue (FDR) data which is also in ug/cm^2 to determine the Reentry Interval (days posttreatment).

1) $\frac{100 \text{ mg/kg/day} \times 70 \text{ kg}}{8 \text{ hours}}$ = 875 mg/hr

2) 875 mg/hr x 1,000 ug/mg = 875000 ug/hr

$\frac{875000 \text{ ug/hr}}{10{,}000 \text{ cm}^2/\text{hr}}$ = 87.5 ug/cm^2

3) ug/cm^2 x 0.1 = 8.75 ug/cm^2

4) Compare to highest residue level reported (0.99 ug/cm^2) and assuming fonofos oxon residues x 5.93 = fonofos equivalent oxon residues

5) Reentry Interval = After grass dries

cc: Bruce Kitchens
Pamela Hurley (H7509C)
Chemical File: FONOFOS
Correspondence
Circulation

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 27 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: IN-DEPTH REVIEW OF POSTAPPLICATION/REENTRY AND APPLICATOR EXPOSURE MONITORING DATA SUBMITTED TO SUPPORT THE REREGISTRATION OF FONOFOS (HED PROJECT # 0-0978)

TO: Lois Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division (H7508C)

FROM: Peg Perreault
Reregistration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

THRU: Alan P. Nielsen, Chief
Reregistration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Charles L. Trichilo, Ph.D., Chief
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Please find below the OREB review of ....

RD Record #: 261742

Caswell #: 454B

Date Received: 3/27/90 Review Time: 15 days

Deferral to: _____ Biological Analysis Branch/BEAD

_____ Science Analysis and Coordination Branch

_____ TB - Insecticide/Rodenticide Support Section

_____ TB - Herbicide/Fungicide/Antimicrobial Support Section

1.0 INTRODUCTION

Postapplication/reentry data are required under 40 CFR 158.390 when both toxicity and exposure criteria are met. In addition, mixer/loader/applicator exposure monitoring data are required when toxicity criteria are met. Fonofos meets the criteria for requirement of both postapplication/reentry and mixer/loader/applicator exposure monitoring data; it is an insecticide registered for use on terrestrial food and nonfood and domestic outdoor sites where occupational and/or residential postapplication exposure can be expected, and technical fonofos is in TOX Category I for acute dermal toxicity and TOX Category II for acute inhalation toxicity. The March 1984 Guidance Document required the following reentry data to support the reregistration of fonofos: foliar dissipation (Guideline requirement 132-1a), soil dissipation (Guideline requirement 132-1b), dermal exposure (Guideline requirement 133-3), and inhalation exposure (Guideline requirement 133-4). In addition, an interim reentry interval of 24 hours was established for all uses of fonofos. In response to the Guidance Document, the registrant submitted foliar dissipation studies on corn, sorghum, and turfgrass, each containing postapplication exposure estimates (MRID #s 401501-23, 402087-07, and 401501-24, respectively), a soil dissipation study, also containing postapplication exposure estimates (MRID #402087-08), and an applicator exposure monitoring study (MRID #402087-03).

2.0 CONCLUSIONS/RECOMMENDATIONS

OREB has evaluated the foliar and soil dissipation studies, the estimated postapplication exposure data, and the applicator exposure monitoring study submitted by Stauffer Chemical Company to support the reregistration of fonofos. The foliar dissipation studies on corn and sorghum and the soil dissipation study are acceptable. The corresponding postapplication dermal exposure estimates for corn, sorghum, and soil, while not based on actual fieldworker exposure monitoring studies, were calculated from measured foliar dislodgeable or soil residues of fonofos and fonofos oxon using acceptable transfer factors. Postapplication inhalation exposure estimates for corn and sorghum were calculated directly from measured air concentrations of fonofos and fonofos oxon assuming inhalation of 10 m^3 of air during an 8 hour work day. Postapplication inhalation exposure to soil residues was not determined; however, for soil application, fonofos is applied preemergence and is incorporated into the soil, thus, postapplication inhalation exposure to soil residues is expected to be negligible. Postapplication exposure to fonofos on corn, sorghum, and soil and reentry intervals derived from these data are summarized below in Section 4.0.

The foliar dissipation study on turfgrass is acceptable; however, the corresponding postapplication exposure estimates for turf grass are unacceptable because several of the assumptions on which the exposure estimates are based are invalid. Estimates of exposure were based on the following assumptions: 1) the only exposed body part would be the feet, as a result of walking on the lawn; and 2) the maximum exposure to fonofos (mg/kg/day) would be the measured level of dislodgeable residues on turfgrass ($\mu g/cm^2$) multiplied by the surface area of the feet (1200 cm^2). Since fonofos is registered for residential use on home lawns where children play, the assumption that exposure will be solely through the feet is not acceptable. In the case of exposure to children, there will also be a large increase in the ratio of exposed skin surface to body weight compared to the ratio of the surface area of the feet to adult body weight (the ratio on which the exposure estimates were based). In addition, the assumption that the maximum daily exposure to the feet will be equal to the level of dislodgeable residues of fonofos on turfgrass is not acceptable; as a person walks across an area of treated turfgrass with bare feet, the skin surface will fractionally accumulate the residues and the level of exposure will eventually be greater than the level of residues on the grass. Two additional studies, one measuring dislodgeable residues on turfgrass (Guideline No. 132-1), and the second measuring actual postapplication dermal exposure to residues on turfgrass (Guideline No. 133-3), are required to support the reregistration of the use of fonofos on residential and recreational area turfgrass. The two studies must be conducted concurrently and a correlation must be developed between the dislodgeable residue dissipation and dermal exposure data for the purpose of estimating exposure at various postapplication intervals. The registrant should submit a protocol for Agency approval prior to initiation of the study.

The applicator exposure monitoring study is unacceptable because the study measured only inhalation exposure to fonofos; dermal exposure monitoring was not performed. In addition, less than the required five application replicates were performed at each site. An additional study, monitoring dermal and inhalation exposure during mixing, loading, and band application at planting (Guideline Nos. 231 and 232), is required to support the reregistration of fonofos.

Additional Data Required to Support the Reregistration of Fonofos

Data Requirement	Test Substance	Crop/application method
158.390 Reentry Protection		
132-1 Foliar Dissipation	TEP[a]	turfgrass
133-3 Dermal Exposure	TEP[a]	turfgrass
Mixer/Loader/Applicator Exposure Monitoring		
231 Estimation of Dermal Exposure at Outdoor Sites	TEP[a]	soil - band application
232 Estimation of Inhalation Exposure at Outdoor Sites	TEP[a]	soil - band application

[a]Typical end-use product.

3.0 EVALUATION OF POSTAPPLICATION/REENTRY AND APPLICATOR EXPOSURE MONITORING STUDIES

Stauffer Chemical Company conducted three foliar dissipation studies, a soil dissipation study, each containing postapplication exposure estimates, and an applicator exposure monitoring study. Paladin Associates, Inc. reviewed the studies (Review and Evaluation of Individual Non-dietary Exposure Studies of Fonofos Applied to a Variety of Crops. Final Report, Dec. 21, 1990. USEPA Contract No. 68-D9-0166) for acceptability under the guidelines of Subdivisions K and U of the Pesticide Assessment Guidelines. The foliar dissipation studies on corn and sorghum and the soil dissipation study were considered acceptable; the the corresponding postapplication exposure data were considered supplementary with respect to the requirements of Subdivision K. The foliar dissipation study on turfgrass was also acceptable; however, the postapplication exposure estimates for turfgrass were considered unacceptable. In addition, the applicator exposure monitoring study was found to be unacceptable. The Paladin review is attached (Attachment 1).

4.0 POSTAPPLICATION EXPOSURE TO FONOFOS

Total toxic foliar dislodgeable residues were calculated by summing the foliar dislodgeable residue levels of fonofos and fonofos equivalent oxon. Fonofos oxon residues were converted to equivalent fonofos residues using the ratio of the LD_{50} values of the two compounds as follows:

fonofos LD_{50}/fonofos oxon LD_{50} = [16 mg/kg]/[2.7 mg/kg] = 5.93; fonofos oxon residues X 5.93 = fonofos equivalent oxon residues.

Foliar dislodgeable residue data and postapplication exposure to total toxic residues of fonofos and fonofos oxon on corn and sorghum are presented below in Tables 1 and 2, respectively. Soil residue data and postapplication dermal exposure to total toxic residues of fonofos and fonofos oxon in soil are presented in Table 3.

Table 1. Average foliar dislodgeable residues of and estimated total exposure to fonofos and fonofos oxon on corn following one foliar application of Dyfonate 20 G at 1.0 lb ai/A.

Day	FDR - fonofos + fonofos equiv. oxon (ng/cm^2)	Dermal exposure ($\mu g/day$)[a]	Inhalation exposure ($\mu g/day$)[b]	Total exposure/ 60 kg (mg/kg/day)
0	882.4	13412.5	33	0.2
1	357.4	5432.5	68	0.09
3	387.0	5882.4	42	0.1
5	21.4	325.3	27	0.006
7	24.4	371.0	22	0.007
10	6.3	96.0	11	0.002

[a]Calculated as follows: foliar dislodeable residues (ng/cm^2) X 1.9 $\mu g/hr/ng/cm^2$ (dermal transfer coefficient for peach harvesters, Poppendorf and Leffingwell, 1982). X 8 hours.

[b]Measured amounts of fonofos + fonofos equivalent oxon in 10 m^3 of air (amount of air inhaled during an 8-hour work day).

Table 2. Average foliar dislodgeable residues of and estimated total exposure to fonofos and fonofos oxon on sorghum following one foliar application of Dyfonate 4 EC at 1.0 lb ai/A.

Day	FDR - fonofos + fonofos equiv. oxon (ng/cm^2)	Dermal exposure[a] (μg/day)	Inhalation exposure[b] (μg/day)	Total exposure/ 60 kg (mg/kg/day)
0	319	4849	162	0.084
1	129	1961	41.5	0.033
3	65	988	23	0.017
6	6.3	96	23	0.002

[a]Calculated as follows: foliar dislodeable residues (ng/cm^2) X 1.9 $\mu g/hr/ng/cm^2$ (dermal transfer coefficient for peach harvesters, Poppendorf and Leffingwell, 1982) X 8 hours.

[b]Measured amounts of fonofos + fonofos equivalent oxon in 10 m^3 of air (amount of air inhaled during an 8-hour work day).

Table 3. Average soil residues of and estimated postapplication dermal exposure to fonofos and fonofos oxon following one preemergent soil-incorporated application each of Dyfonate 20 G and Dyfonate 4 EC at 1.0 and 4.0 lb ai/A, respectively, to a corn field.

Day	**Dyfonate 20G** Soil residues - fonofos + fonofos equiv. oxon ($\mu g/ft^2$)	Estimated dermal exposure[a] (mg/kg/day)	**Dyfonate 4EC** Soil residues - fonofos + fonofos equiv. oxon ($\mu g/ft^2$)	Estimated dermal exposure[a] (mg/kg/day)
0	199.8	0.00023	271.6	0.00032
1	160.2	0.00019	315.0	0.00037
3-28	209.2 - 6.3	0.00024 - 0.000007	236.6 - 9.6	0.00028 - 0.00001

[a]Calculated based on a body weight of 60 kg as follows: soil residues ($\mu g/ft^2$) X 0.07 μg/day/$\mu g/ft^2$ (Spear, 1977 correlation developed for estimating full day exposure to parathion and paraoxon residues in soil).

To determine reentry intervals, an Allowable Exposure Level (AEL) for postapplication exposure to fonofos and fonofos oxon on foliage and soil was calculated. OREB estimates the AEL to be 0.002 mg/kg/day based on a NOEL of 8 ppm from a subchronic dog feeding study (EPA Acc. No. 090678), which converts to a dose of 0.2 mg/kg/day, and a safety factor of 100. It should be noted that this AEL is equal to the EPA RfD and is based on a subchronic oral NOEL. The use of a subchronic dermal NOEL would be more appropriate in determining the AEL for postapplication exposure to residues on foliage and soil; however, data are not currently available on the subchronic dermal toxicity of fonofos.

Based on an AEL of 0.002 mg/kg/day, the total postapplication exposure data presented in Tables 1, 2, and 3 support the establishment of the following reentry intervals for fonofos:

Foliar applications

Corn (20 G formulation) - 10 days
Sorghum (4 EC formulation) - 6 days

Soil applications (preemergent, all crops)

20 G formulation - 0 days
4 EC formulation - 0 days

Attachment

cc: (without Attachment)
B. Lowery/SRRD (H7508C)
E. Saito/SACB (H7509C)
Fonofos File
Correspondence File
Circulation