United States
Environmental Protection
Agency

Office of
Pesticides and Toxic Substances
Washington, DC 20460

January 1985

Pesticides

EPA

TPTH (Triphenyltin Hydroxide)
Special Review Position Document 1

TRIPHENYLTIN HYDROXIDE

POSITION DOCUMENT 1

U.S. Environmental Protection Agency

Office of Pesticides and Toxic Substances

Office of Pesticide Programs

401 M Street, S.W.

Washington, D.C.

6560-50

ENVIRONMENTAL PROTECTION AGENCY

[OPP-30000/42]

TRIPHENYLTIN HYDROXIDE

SPECIAL REVIEW OF CERTAIN PESTICIDE PRODUCTS

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: [This Notice announces that EPA is initiating a Special Review of all pesticide products containing the active ingredient triphenyltin hydroxide (TPTH)]. EPA has determined that TPTH which is registered as a fungicide and mite suppressant, produces teratogenic effects in laboratory rats and that sufficient exposure to applicators exists to meet the risk criterion described in 40 CFR 162.11. Accordingly, a Special Review of products containing TPTH has been initiated to determine whether additional regulatory actions, if any, are required. During the Special Review process, EPA will carefully examine the risks and benefits of using TPTH products.

DATE: Comments, evidence to rebut the presumptions in this Notice, and other relevant information must be received no later than 45 days from the date this notice is received or until (insert date 45 days after date of publication in the FEDERAL REGISTER) (whichever is later).

84P-4070

ADDRESS: Written comments identified as "OPP-30000/42" should be sent by mail to:

Information Services Section,
Program Management and Support Division (TS-757C),
Office of Pesticide Programs,
Environmental Protection Agency,
401 M St., SW.,
Washington, D.C. 20460.

In person, bring comments to:
Rm. 236, CM #2,
1921 Jefferson Davis Highway,
Arlington, VA.

Information submitted in any comment concerning this notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR Part 2. An edited copy of the comment containing material claimed to be CBI must be submitted (with the CBI portions deleted) for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice to the submitter. All non-CBI written comments will be available for public inspection in Rm. 236 at the Virginia address given above, from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays.

FOR FURTHER INFORMATION CONTACT: By mail:

Betty Shackleford,
Registration Division (TS-767C),
Office of Pesticide Programs,
Environmental Protection Agency,
401 M St., SW.,
Washington, D.C. 20460.
Office location and telephone number:
Rm. 717, CM #2,
1921 Jefferson Davis Highway,
Arlington, VA,
(703-557-7400).

SUPPLEMENTARY INFORMATION: The term "Special Review" is the name now being used by EPA for the process previously called the Rebuttable Presumption Against Registration (RPAR) process. Modifications in the process will be proposed in regulations in the near future. Until other applicable final regulations are adopted, the present Special Review will adhere to RPAR procedures now in effect and set forth in 40 CFR 162.11.

EPA has determined that a Special Review will be conducted for all pesticide products containing TPTH as an active ingredient. EPA has also determined that data necessary to conduct the Agency's risk assessment must be developed on an accelerated basis, and that precautionary labeling is required to reduce risk during the Special Review process.

Issuance of this Notice means that potential hazards associated with the use of TPTH have been identified. These

hazards will be examined further to determine the nature and extent of the risk, and considering the benefits of TPTH, whether such risks cause unreasonable adverse effects on the environment.

A document entitled "Guidance for the Interim Registration of Pesticide Products Containing TPTH" (Guidance Document) has been issued. (The Guidance Document is also referred to as a Registration Standard.) The Guidance Document is available to the public from the contact person named above. This Guidance Document explains the basis of EPA's decision to start a Special Review and also contains references, background information, data requirements, and other information pertinent to the continued registration of pesticides containing TPTH.

I. INITIATION OF A SPECIAL REVIEW

A. GENERAL

A pesticide product may be sold or distributed in the United States only if it is registered or exempt from registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136 *et seq.*). Before a product can be registered, it must be shown that it can be used without "unreasonable adverse effects on the environment" (FIFRA section 3(c)(5)), that is, without causing "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of the pesticide" (FIFRA section 2(bb)). The burden of proving that a pesticide meets this standard for registration is on the proponent of initial or continued registration. If at any

time the Agency determines that a pesticide no longer meets this standard for registration, the Administrator may cancel the registration under section 6 of FIFRA.

The Agency has created an administrative process for fully evaluating whether a pesticide satisfies or continues to satisfy the statutory standard for registration. This Special Review process provides an informal procedure through which EPA may gather and evaluate information about the risks and benefits of a pesticide's use. It also provides a means by which interested members of the public may comment on and participate in EPA's decision making process. The regulations governing this process are set forth at 40 CFR 162.11.

A Special Review is begun when EPA determines that a pesticide meets or exceeds one or more of the risk criteria set out in the regulations (40 CFR 162.11(a)(3)). The Agency generally announces the beginning of the Special Review by issuing a Position Document 1 (PD 1) which is published in the FEDERAL REGISTER. In addition, registrants of affected products will receive the PD 1 by certified mail. Registrants and other interested persons are invited to scrutinize the basis for the Agency's decision to initiate the Special Review and to submit data and information which rebuts or supports the Agency's determination of risk. Commenters may also suggest methods to reduce risks of use of the pesticide. In addition to addressing risk issues, commenters are encouraged to submit evidence and discussions of the biological, economic,

social, and environmental costs and benefits of use of the pesticide. The public participation stage is described in more detail in Unit IV. This Notice constitutes Position Document 1 for pesticide products containing TPTH.

If risk issues are not satisfactorily resolved, EPA will proceed to evaluate the risks and benefits of TPTH in order to determine whether to propose regulatory actions to reduce the risks. After providing an opportunity for comment by the Scientific Advisory Panel, the Secretary of Agriculture, registrants, and the public on those actions and the reasons for them, EPA will issue an appropriate final notice. If EPA determines that the risks of use exceed the benefits, EPA will issue a notice of intent to cancel the registration of products intended for such use. The notice may state athe intention to cancel registrations outright or may require certain changes in the composition, packaging, application methods and/or labeling of the product. These changes would be intended to reduce the risks to levels that when considered against the benefits will not pose unreasonable adverse effects to man or the environment.

A notice initiating a Special Review is not a notice of intent to cancel the registration of a pesticide, and a Special Review may or may not lead to cancellation. This notice initiating the Special Review for TPTH products is an announcement of EPA's concern about the safety of the pesticide's use, and only after carefully considering the risks and benefits of TPTH and determining that it appears to cause unreasonable adverse effects on the environment, would EPA issue a notice of intent to cancel.

B. PRESUMPTION

EPA has determined that the use of pesticide products containing TPTH has exceeded one of the risk criteria in 40 CFR 162.11(a)(3)(ii)(B) which provides that a Special Review shall be conducted if the use of a pesticide "produces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety." Studies submitted to the Agency in support of the continued registration of TPTH have shown that TPTH produces teratogenic effects in laboratory animals. Based on these data and on an evaluation of potential exposure of applicators to TPTH, the Agency concluded that TPTH has exceeded the risk criterion for initiation of a Special Review.

1. Toxicological concerns. As part of the data requirements necessary to maintain the continued registration of the pesticide, two independent laboratories conducted studies in Sprague-Dawley rats to ascertain the teratogenic potential of TPTH. In the first study, conducted in 1976 by Cannon Laboratories, Inc., varying dosage levels of technical grade TPTH were orally administered by gavage to pregnant rats on days 6 through 15 of gestation. Increases in the incidences of hydrocephalus (the abnormal accumulation of serous fluid within the cranium accompanied by enlargement of the head, prominence of the forehead, atrophy of the brain, mental weakness and,

convulsions) and hydronephrosis (distention of the pelvis and calyces of the kidney with urine, as a result of obstruction of the ureter with accompanying atrophy of the parenchyma of the organ) above the incidences in concurrent control animals were observed in the fetuses at all dosage levels tested.

A second teratogenicity study was performed by Battelle Columbus Laboratories and submitted to the Agency in 1981. In this study, rats were mated and dosed with TPTH on days 5 through 19 of gestation. Increased incidences of hydronephrosis above the incidence in the concurrent control fetuses were again observed at all dosage levels tested. Although hydrocephalus was seen in only one fetus, an increased incidence of hydroureter (abnormal distention of the ureter of the kidneys with urine or with a watery fluid) above the concurrent control incidence occurred at all dosage levels tested. Based on these studies, the Agency has determined that TPTH produces teratogenic effects in laboratory animals. A "no-observed-effect-level" (NOEL) for these teratogenic effects has not been determined because these lesions were observed at all dosage levels. The "lowest-observed-effect-level" (LOEL) was 1.0 mg/kg/day.

To clarify whether some or all of the effects observed in the teratogenicity studies are true developmental anomalies, delayed maturation, or the like, the Agency has required a "postnatal" teratology study. The Agency believes this study will elucidate the nature, severity, and/or reversibility of the teratogenic effects manifested in the two studies referred to above.

In the postnatal teratology study, twice the number of dams typically observed in a teratology study are to be used. One half of the dams are to be sacrificed near parturition and the remaining half of the animals are permitted to deliver normally with post-weaning sacrifice and examination of the pups. The specific test requirements are outlined in the Guidance Document. Results of the postnatal teratology study must be submitted to the Agency by December 7, 1985. In addition, the Agency is conducting a teratogenicity "screening test" at Research Triangle Park, N.C. This testing is being performed in two phases and is designed to provide insight into the severity of the observed teratogenic effects. Based on the results of these data, which will be available in March 1985, the Agency may initiate additional immediate regulatory actions.

2. Applicator risk assessment. The Agency has estimated potential applicator exposure to TPTH. Because most applicator exposure occurs by the dermal route, a risk assessment has been performed based on dermal exposure to TPTH resulting from the air blast application to pecan trees. The risk assessment was limited to this site and application method because 72 to 82 percent of the pesticidal use of TPTH is for controlling fungal diseases in pecan culture. TPTH is generally applied by air blast application in pecan culture, although it may be applied aerially.

In calculating the dermal exposure risk calculation for pecan tree applicators, the Agency made the following assumptions.

a. Applicators have an average body weight of 70 kg.

b. Mixing/loading and pesticide application are done by the same individual.

c. Potential inhalation exposure would be minimal when compared to potential dermal exposure.

d. It was estimated that 3,000 cm^2 of the skin surface area would be exposed during the pesticide application. This is equivalent to wearing a short-sleeved, open-necked shirt, long pants, and neither head covering nor gloves.

e. Exposure during mixing/loading assumes a worker handles a 50 percent wettable powder (WP) formulation packaged in conventional bags.

f. In the absence of empirical dermal absorption data, the Agency assumed dermal absorption would be 100 percent.

Unit dermal exposure (mg/kg body weight/day) (mg/kg/ bw/day) during application was calculated from the linear regression correlation derived from the Office of Pesticide Programs Exposure Assessment Branch data base for air blast application to orchards ($p < 0.01$). Exposure during mixing and loading of the wettable powder was calculated from the same data base. Application rates typically range from 1.5 to 18.4 oz active ingredient per acre (ai/A).

The Agency estimated a typical exposure value for a mixer/loader/applicator of 0.74 mg/kg/day, with a lowest value of 0.68 mg/kg/day and an upper value of 0.88 mg/kg/day. This range is derived from the range in application rates.

Because the teratogenic effects seen in the animal studies occurred at all test dosage levels, the Agency has been unable to determine "margins of safety" (MOS) (ratio of NOEL to exposure) from the available test results. Therefore, teratogenic "risk quotients" (ratio of LOEL to exposure) were calculated based on the LOEL.

The risk quotient determination for teratogenicity indicates that potential exposure of pesticide applicators in pecan culture to TPTH occurs at a level that is known to produce teratogenic effects in laboratory animals, thereby resulting in a highly significant teratogenic risk for pregnant women.

3. Dietary exposure. To assess potential teratogenic hazards that might be associated with dietary exposure to TPTH, the Agency has performed a risk assessment for the food commodities listed in 40 CFR 180.236. "Risk quotients" were again determined because a NOEL was not observed in the teratogenicity studies. The risk quotients are based on eating a single serving of the respective food items by a 60 kg pregnant woman. These data are presented in Table I.

TABLE I -- DIETARY RISK QUOTIENT DETERMINATION FOR TERATOGENICITY

Commodity	Estimated Serving Size	Weight (kg)[1/]	Tolerance (ppm)	TPTH mg/serving	TPTH mg/kg/body weight b.w.=60kg	"Risk Quotient" (LOEL of 1.0 mg/kg/day divided by mg/kg body weight)
Carrots						
raw	1 cup	0.11	0.10	0.011	0.00018	5,600
cooked	1 cup	0.15	0.10	0.015	0.00025	4,000
Sugar (beet)	1/2 cup[2/]	0.12	0.10	0.012	0.00020	5,000
Pecans	1/2 cup	0.06	0.05	0.003	0.00005	20,000
Peanuts	1/2 cup	0.07	0.05	0.0035	0.00006	16,700
Potatoes	1 cup	0.20	0.05	0.010	0.00017	5,900
Kidney	3 oz.	0.09	0.05	0.0045	0.00008	12,500
Liver	3 oz.	0.09	0.05	0.0045	0.00008	12,500

1/ From "Nutritive Value of American Foods," Agriculture Handbook No. 456, USDA, Washington, D.C., 1975.

2/ Estimated total daily intake

The risk quotients presented in Table I indicate that the existing tolerances provide a substantial or ample level of protection from potential teratogenic effects that may be associated with dietary exposure to the parent TPTH. Because the risk quotient determinations are based on a single serving of the respective food commodities, individual dietary practices may augment or lessen the risks accordingly. However, adequate protection exists even if multiple servings of the food commodities listed in Table I are consumed.

The Agency does not expect residues of the parent TPTH to exceed the current existing tolerance levels. However, there is significant concern about the potential toxicological activity of the mono- and diphenyltin metabolites of TPTH and their contribution to the total food residue. A reassessment of the existing tolerances will be made once the analytical methodology and residue data, including storage stability data, for TPTH and its mono- and diphenyltin metabolites are submitted for the plant commodities listed in 40 CFR 180.236. Similar residue data and storage stability studies for processed commodities derived from peanuts, potatoes, and sugarbeets are also needed. Studies on processed commodities must include data for tetraphenyltin in addition to data for TPTH and the mono- and diphenyltin metabolites. Residue data and analytical methodology for meat, milk, poultry, and eggs are also being required. The above information is being requested from the registrants in the Guidance Document.

The Agency is also aware that TPTH and its acetate and chloride analogues are used abroad. The treated commodities include dry beans (Bolivia), cocoa (Brazil), potatoes (Brazil, Cyprus, Ireland, Switzerland, and the United Kingdom), and rice (Brazil). The recommended international maximum residue limits for the triphenyltin derivatives do not include contributions that may be made by inorganic tin and di- and monophenyltin moieties. Subsequently, international commodities which do not have an existing tolerance listed in 40 CFR 180.236 may be subject to administrative action if found to contain TPTH residues.

C. ADDITIONAL EFFECTS OF CONCERN

Additional data submitted to the Agency in support of the continued registration of TPTH have precipitated further concerns about the safety of the pesticide. At this time, the available data on these effects are insufficient to determine whether a Special Review risk trigger has been met or exceeded. However, the Agency believes the effects described below merit additional investigation and has required data to delineate their exact nature and extent.

TPTH has produced immunotoxic effects in mice and guinea pigs. A 90-day subchronic study using guinea pigs indicated that the pesticide may inhibit lymphopoiesis and produce atrophy of lymphoid tissues. In this study, performed in 1960, leukocyte counts were depressed at the lowest dosage level tested (2.5 ppm or 0.1 mg/kg/day). Although the Agency has classified this study as minimally acceptable, the small number of animals used in each test group as well as the absence of

a NOEL for the observed effects have resulted in additional data requirements.

Exposure to TPTH also produced decreased testicular weights in rat pups in a three-generation reproduction study performed in 1967. In this study, the F_2b generation exhibited decreased testicular weights when compared to the concurrent controls at dosage levels of 1.0 ppm and above. A NOEL for the reproductive effects was estimated to be 0.025 mg/kg/day. This study has been classified as provisionally invalid because only summary data were submitted. Registrants should submit these supporting data, if available, to the Agency. In the event these data are not available, a new study as required in the Guidance Document must be submitted.

The oncogenic potential of TPTH cannot be determined at this time. In one study, female mice dosed with TPTH developed endometrial hyperplasia at the lowest dosage level tested, 1.05 mg/kg/day. The development of a test chemical-induced change in a reproductive organ is considered a serious adverse effect by the Agency and because of the low dosage at which the effect was observed it must be considered in the overall assessment of TPTH toxicity. Additional studies have been required on an expedited basis in the Guidance Document to clarify this concern.

The Agency has also performed a preliminary risk assessment, based on a 90-day inhalation study in rats and calculated applicator inhalation exposure at 0.0016 mg/kg/day, to determine potential risks to applicators by this exposure

route. A NOEL was not established for the effects observed in the rat study (ie., alopecia, nasal discharge, red ears, piloerection, etc.) and the resultant risk quotient (151) determination indicates it may be prudent to require respiratory protection since any "margin of safety" assessment would result in a lower safety factor. TPTH is in EPA Toxicity Category I (highest toxicity rating) by the inhalation exposure route.

Additional studies which have been submitted to support the continued registration of TPTH indicate the pesticide is highly toxic to aquatic invertebrates, warmwater fish and estuarine/ marine organisms and is moderately to highly toxic to birds. These studies suggest continued use of TPTH may have potentially deleterious effects on wildlife and aquatic organisms.

Data requirements are being mandated in the Guidance Document on an expedited basis to clarify the environmental fate of TPTH. These data include accumulation in rotational crops and fish, leaching, adsorption, desorption, aerobic and anaerobic soil metabolism, soil dissipation and photodegradation of the pesticide, re-entry data, avian reproduction and dietary studies, and a coldwater fish study.

Based on the evaluation of the results of the studies required above, the Agency will determine whether additional information and/or restrictions are necessary. Pivotal data requirements and an expedited submission schedule are summarized in Table II.

TABLE II -- DATA PIVOTAL TO THE SPECIAL REVIEW

Data Requirements	Submission Date
Studies Pivotal to Teratogenicity	
Teratogenicity	December 7, 1985
Postnatal Teratogenicity	" " "
Teratogenicity[1] (Dermal Exposure Route)	Reserved
Analytical Methodology for Plant and Animal Residues Including Metabolites and Tetraphenyltin Hydroxide	June 7, 1985
Residue Storage Stability Data	December 7, 1985
Crop and Processed Commodities Storage Stability Data Including Metabolites and Tetraphenyltin Hydroxide	June 7, 1986
Studies Pivotal to Additional Concerns	
Soil and water photodegradation	" " "
Mobility Studies	" " "
Soil Dissipation Studies	" " "
Immunotoxicity Studies	January 7, 1986
Dermal Penetration	" " "
General Metabolism	March 7, 1986
Residue Determination for Food Use Crops, Tobacco, Meat, Milk Poultry and Eggs	June 7, 1986
Reproduction 2-generation	September 7, 1986
Chronic Toxicity	December 7, 1988
Oncogenicity	" " "

1/ Contingent on the results of the postnatal and standard teratogenicity and dermal penetration studies.

D. CURRENT REGULATORY ACTIONS

Because the Agency has determined that TPTH produces teratogenic effects in laboratory animals at concentrations to which applicators may be exposed, the Guidance Document requires that a warning be added to the pesticide label stating that TPTH causes birth defects in laboratory animals and that exposure during pregnancy should be avoided. Additional label changes include the "Restricted Use" classification which limits the use of the pesticide to certified applicators or to persons directly under their supervision. Protective clothing including a long-sleeved shirt, long pants, impermeable gloves, hat, boots, and an approved pesticide respirator are also required.

In addition to the protective clothing described above, a face shield is required when the technical product is being handled. The Registration Standard also stipulates that no new permits will be issued for the experimental use of TPTH as an anti-fouling agent in marine paints, nor will any FIFRA section 3 registration applications be considered during the Special Review.

All currently registered TPTH products will remain registered while the Special Review is in progress. However, the Agency is deferring final decisions on the reregistration of any products containing TPTH as a sole active ingredient until the Special Review is concluded. No new uses for TPTH will be issued during this period. The Agency also will not approve pending requests for tolerances for TPTH on rice and soybeans or issue any new tolerances during the Special Review.

The Agency is also currently considering the issuance of a Data Call-in Notice pursuant to FIFRA section 3(c)2(B) in order to require registrants to submit specific information on the use, exposure potential, and benefits of TPTH.

E. COMMENTS ON THE INITIATION OF THE SPECIAL REVIEW

Prior to the initiation of a Special Review, technical registrants receive private notification of the Agency's determination that the criteria to initiate a Special Review may have been met. This notification includes information on the toxicity findings, route of exposure and related general information. Registrants then have 30 days following receipt of the notification to rebut the Agency's conclusions.

In response to the Agency's notification that a Special Review of TPTH was being considered, Uniroyal Corporation proposed amending their product label in an effort to reduce risks and obviate the Special Review of the pesticide. Uniroyal proposed classifying the pesticide as a restricted use chemical, a 24-hour reentry label statement, a prohibition for female applicators of childbearing age, and cancellation of all products except those packaged in water soluble bags.

The Agency believes the proposals submitted by Uniroyal are generally in agreement with the requirements stipulated in the Guidance Document. However, the Agency does not have the information necessary to determine if these and other measures will adequately reduce the risks from exposure to the pesticide to an acceptable level. This determination will be made through the Special Review of TPTH.

F. REBUTTAL CRITERIA

All registrants, applicants for registration, and other interested members of the public are invited to submit evidence either to support or to rebut the presumption that TPTH causes teratogenic effects in rats and may cause such effects in humans. Under 40 CFR 162.11(a)(4)(iii) the presumption initiating a Special Review must be rebutted by proving, in the case of acute and chronic toxicity criteria, "that the determination by the Agency that the pesticide meets or exceeds any of the criteria for risk was in error."

G. BENEFITS INFORMATION

The Agency will conduct a comprehensive benefits review and analysis for TPTH during the Special Review process and will consider that information in setting forth the Agency's proposed regulatory decision in the Position Document 2/3 (PD 2/3). A preliminary analysis of the benefits of TPTH has been performed and is presented here.

The major use of TPTH is on pecans. Over 72 percent of the pesticide used annually is applied to this crop. Georgia is the primary pecan-producing State accounting for between one third and one half of the total annual production of pecans in the United States. New Mexico, Texas, Alabama, and Louisiana make up the remaining major pecan-producing States. Any one of the following States, Arkansas, Florida, Mississippi, North Carolina, Oklahoma, and South Carolina generally account for less than 3 percent of the total national production. Most of the

TPTH applications occur in the Southeast because the environmental conditions are conducive to disease development.

Scab is the most important fungal disease in pecan culture both in the Southeast and Southwest. Preliminary data suggest that although TPTH is the pesticide most commonly used in pecan culture, registered alternatives are available for all pests with the exception of sooty mold which is of minor concern. It is estimated that without the use of any fungicide, there would be a substantial loss in the annual yield. Use of the alternative fungicide benomyl in pecan culture may reduce this loss significantly, although a major concern with the use of benomyl is the development of benomyl resistant strains of fungi. To date, fungal strains that attack pecans have not demonstrated a resistance to TPTH. For this reason, TPTH and benomyl are often used on an alternating schedule or applied in combination. The chemical cost per acre difference between benomyl and TPTH is minor.

TPTH is also registered for use in controlling fungal diseases in sugarbeets, peanuts, carrots, and potatoes. On peanuts, TPTH is used to control early leafspot and incidentally contributes to mite suppression. TPTH is also registered for use on potatoes in controlling late and early blight. Late blight is the more serious concern in potato culture, especially in the Northeast. Use of TPTH for control of diseases of carrots appears to be minor but important for the control of *Cercospora* leafspot of sugarbeets. Benomyl is often applied for control for *Cercospora*,

but TPTH is used where benomyl-resistant strains have developed. The efficacy and potential unreasonable adverse effects that may be associated with alternatives for TPTH such as benomyl, metiram, maneb, captafol, thiophanate-methyl, and others will be fully reviewed in Position Document 2/3.

In addition to submitting evidence to rebut the presumptions of risk in the Special Review, 40 CFR 162.11(a)(5)(iii) provides that a registrant or applicant "may submit evidence as to whether the economic, social and environmental benefits of the use of the pesticide subject to the presumption outweigh the risk of use." If the presumption of risk is not rebutted, the benefits evidence submitted by registrants, applicants, and other interested persons will be considered by the Agency when determining the appropriate regulatory action.

Registrants, applicants or other interested persons who desire to submit benefits information should consider submitting information on the following subjects along with any other relevant information they desire:

1. Identification of the biological and economic importance of TPTH uses.

2. Identification of alternative chemical and nonchemical methods of control and any associated health effects and potential for human exposure.

3. Determination of any change in costs to TPTH users for obtaining equivalent disease control with available substitute products or management techniques.

4. Assessment of the expected changes in the level of efficacy, crop yield, crop quality, crop injury, and environmental impacts associated with the use of alternative control measures.

5. Identification of increased or reduced risks associated with the mixing, loading, and applying of alternative chemicals, with their potential increase in use if TPTH were not available.

6. Identification of cultural and spray application practices, that impact on farmworker exposure to TPTH.

7. Identification of cultural or integrated pest management practices which are enhanced or limited by use of TPTH.

II. REBUTTAL SUBMISSION PROCEDURES

All registrants and applicants for registration are being notified by certified mail of the Special Review being initiated on their products containing TPTH.

The registrants and applicants for registration will have 45 days from the date this notice is received or until (insert date 45 days after date of publication in the FEDERAL REGISTER) (whichever is later) to submit evidence in rebuttal to the Agency's presumption. Other interested parties may submit comments during the same period.

III. DUTY TO SUBMIT INFORMATION ON ADVERSE EFFECTS

Registrants are required by section 6(a)(2) of FIFRA to submit any additional information regarding unreasonable adverse effects on man or the environment which comes to their attention at any time. Registrants of TPTH products must immediately

submit any published or unpublished information, studies, reports, analyses, or reanalyses regarding any TPTH effects in animal species or humans, and claimed or verified accidents to humans, domestic animals, or wildlife which have not been previously submitted to EPA. These data should be submitted with a cover letter specifically identifying the information as being submitted under section 6(a)(2) of FIFRA. Registrants should notify EPA of any studies on TPTH currently in progress, their purpose, the protocol, the approximate completion date, a summary of all results observed to date, the name and address of the laboratory performing the studies, and a statement as to whether these studies are being conducted in accordance with the Good Laboratory Practices specified in 40 CFR Part 160, published in the FEDERAL REGISTER of November 29, 1983 (48 FR 53946).

IV. PUBLIC COMMENT OPPORTUNITY

During the time allowed for submission of rebuttal evidence, specific comments are solicited on the presumptions set forth in this Notice and in the Registration Standard. In particular, any documented episodes of adverse effects on humans or domestic animals should be submitted to the Agency as soon as possible. Any information as to any laboratory studies in progress or completed should be submitted to the Agency as soon as possible with a statement as to whether those studies are in compliance with the Good Laboratory Practices specified in 40 CFR Part 160. Specifically, information on any adverse toxicological effects of TPTH, its

impurities, metabolites, and degradation products is solicited. Similarly, submission of any studies or comments on the benefits from the use of TPTH is requested. All comments and information and analyses, which come to the attention of EPA, may serve as a basis for final determination of regulatory action following the Special Review.

All comments and information should be sent to the address given above, preferably in triplicate, to facilitate the work of EPA and others interested in inspecting them. The comments and information should bear the identifying notation [OPP-30000/42].

During the comment period, interested members of the public or registrants may request a meeting to discuss the risk issues and methods of reducing risks. Any records pertaining to such meetings, including minutes, agendas, and comments received will be filed under docket number OPP-30000/42.

Dated: 12/17/84

Steven Schatzow

Director,
Office of Pesticide Programs.