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MEMORANDUM

SUBJECT: **TPTH (Triphenyltin Hydroxide)**: HED Risk Assessment for the Reregistration Eligibility Decision (RED) Document. Chemical No. 083601. Reregistration Case No. 0099. Case # 819289. Submission # S549772. DP Barcode D250103.

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Attached is the Health Effect Division's risk assessment for the fungicide Triphenyltin Hydroxide (TPTH) for purposes of issuing a Reregistration Eligibility Decision (RED) Document for this active ingredient. Cumulative risk assessment considering risks from other pesticides or chemical compounds having a common mechanism of toxicity is not addressed in this document. The disciplinary science chapters and other supporting documents for the TPTH RED are included as attachments as follows:

Report of the Hazard Identification Assessment Review Committee. Doherty/Rowland (11/13/98)
Report of the FQPA Safety Factor Committee. Brenda Tarplee (12/17/98)
Product and Residue Chemistry Chapter. Catherine Eiden (4/12/99; D255158)
Toxicology Chapter. John Doherty (3/22/99; D254359)
Occupational and Residential Exposure Assessment. Kelly O'Rourke (5/6/99; D250108)
Dietary Exposure and Risk Estimates for Reregistration. Sarah Law (4/13/99; D254712, D254713)
Incident Report. Jerome Blondell and Monica Spann (12/23/98; D251180)
Tier I Estimated Environmental Concentrations for Triphenyltin Hydroxide. D. Young (2/26/99, D250265)
TPTH Revised Q_1^* (3/4's Interspecies Scaling Factor). Bernice Fisher and Hugh Pettigrew (8/18/98)

RDI: BRSrSci: SKnizner

1.0 EXECUTIVE SUMMARY

The Health Effects Division (HED) has conducted a human health assessment for the active ingredient Triphenyltin Hydroxide (TPTH) for the purpose of making a Reregistration Eligibility Decision.

TPTH is a List A reregistration chemical and was the subject of a Registration Standard dated 4/11/84, its associated Guidance Document dated 9/84, and a Reregistration Standard Update dated 3/18/92. These documents summarized regulatory conclusions on the available data and specified that additional data were required for reregistration purposes. Several submissions of data have been received since the Update was issued. Special Review (RD1) was issued in 1985 (50 FR1107 on 1/9/85). Currently, TPTH is still in Special Review. In response to the PD1 and the data call in's (DCI's) (5/88, 9/90 and 7/93), the registrants developed data for the following uses and tolerances: pecans, potatoes and sugar beets (40 CFR §180.236). Tolerances and uses not supported by the registrants during this process are (cancellation was effective August 9, 1996; 61FR36298): carrots, peanuts and tobacco. The Special Review will be concluded with the issuance of this RED on the tolerances and uses currently being supported. Reregistration of TPTH is being supported only for agricultural uses; it is not supported for residential, aquatic or forestry uses.

TPTH is a fungicide registered for use on pecans, potatoes and sugar beets. TPTH is used to control early and late blight on potatoes; leaf spot on sugar beets, peanuts, scab and several other diseases on pecans. In addition to its fungicidical activity, TPTH exhibits antifeeding properties for surface-feeding insects. TPTH is manufactured by members of the TPTH Task Force (AgrEvo, Elf Atochem and Griffin) under the trade names Super Tin®, Pro-Tex®, Brestan®, and Photon®. TPTH is formulated both as a wettable powder in a water-soluble pack and as a flowable concentrate requiring a closed mixing/loading system. These products may be applied as broadcast foliar applications using ground or aerial equipment and by chemigation (potatoes only). A "closed system" is required for aerial applications. The closed system for mixing and/or loading this product must be capable of removing the pesticide from the shipping container, rinsing the container, and transferring the pesticide and rinsate into mixing tanks and/or application equipment. TPTH products also require a "mechanical transfer system" which is a mechanism capable of removing the pesticide from the shipping container and transferring the pesticide into mixing tanks and/or application equipment to prevent worker exposure to the pesticide. The maximum application rate for pecans is 0.375 lb ai/acre; the maximum number of applications to pecans per season is 10, with an interval range of 14-28 days. The maximum application rate for potatoes is 0.1875 lb ai/acre; TPTH can be applied to potatoes up to 6 times per season, at 7-day intervals. The maximum application rate applied to sugar beets is 0.25 lb ai/acre; TPTH labels state that applications to sugar beets may be made at 10 to 14-day intervals, for a maximum of four times per season. However, an increase to five times per season is planned by the registrant. TPTH is a restricted use pesticide.

HED evaluated the toxicology, residue chemistry and exposure data bases for TPTH and determined that the data are adequate to support a reregistration eligibility decision. However, there are toxicological data gaps for an acute and subchronic neurotoxicity screen and a developmental immunotoxicity screen The following three dietary exposure and risk assessments were conducted for TPTH for the general population: acute dietary, chronic dietary, and cancer dietary. HED also considered occupational dermal and inhalation exposure for pesticide handlers, mixers, loaders, applicators and postapplication workers during harvesting activities. Occupational exposure and risk assessments were conducted for TPTH based on the following occupational exposure durational/routes: short- and intermediate-term dermal and inhalation (for any time period). Long-term worker exposure is not expected.

The aggregate risk assessment for the general population and specific subgroups addressed food and water exposures only because TPTH has no registered uses in residential settings.

HAZARD IDENTIFICATION

The toxicity database indicates that TPTH is highly toxic via the oral, dermal, inhalation routes (Toxicity Category II , II, and I respectively).

TPTH belongs to a class of chemicals (organotins) known to be immunotoxic. The primary treatment related effects via oral exposures are immunotoxicity as indicated by decreases in lymphocytes and immunoglobulins in rats and mice, following both sub-chronic and chronic exposures. TPTH is carcinogenic both in the rat (inducing pituitary and testicular tumors) and in the mouse (inducing liver tumors). The low dose linear approach (Q_1^*) was used for human characterization and was based on the pituitary tumors observed in rats. The Q_1^* is 1.83×10^0 $(mg/kg/day)^{-1}$. This Q_1^* will be used for assessing cancer risk for all routes of exposure (oral, dermal and inhalation). The Q_1^* derived from the oral studies is used as a default for the dermal and inhalation routes since dermal and inhalation carcinogenicity studies are not required according to Subdivision F based on the use pattern of this chemical.

In developmental toxicity studies, TPTH causes resorptions in pregnant rabbits at dose levels only slightly higher than it caused maternal effects on body weight. There was no evidence of increased susceptibility to fetuses noted in the available rat or rabbit developmental toxicity studies. The slope of the dose response curve in the rabbit developmental toxicity study is considered steep. In the rat multi-generation reproductive toxicity study increased susceptibility to the offspring was demonstrated (offspring toxicity [decreased litter size, liver and spleen weight] was seen at a dose lower than parental toxicity [decreased body weight gain]). Because of the immunotoxic potential of TPTH, a special study for developmental immunotoxicity (consult with Agency on protocol) is required.

The FQPA Safety Factor Committee recommended two different safety factors for acute and chronic dietary risk assessment. The FQPA Safety Factor was reduced to 3x for acute dietary risk assessment because of the need for a developmental immunotoxicity study in rats (i.e., data

gap). Increased susceptibility was seen only in the offspring of parental animals receiving repeated oral exposures (i.e., only a concern for chronic dietary exposures). The 10x FQPA Safety Factor for chronic dietary risk assessment was retained because increased susceptibility was noted in the rat multi-generation reproduction study.

TOXICITY DOSES AND ENDPOINTS FOR RISK ASSESSMENT

For the acute dietary exposure and risk assessment, the dose selected was the no observed adverse effect level (NOAEL) of 0.3 mg/kg/day based on increased incidents of hyoid body and/or arches unossified in rabbit fetuses from an oral developmental toxicity study in rabbits at the lowest observed adverse effect level (LOAEL) of 0.9 mg/kg/day. These fetal malformations are presumed to occur following a single exposure (dose) and therefore, are considered to be appropriate for this risk assessment. Since this is an *in utero* effect, this endpoint is applicable to the subpopulation females 13+ years old only. A dose and endpoint were not selected for the general population (including infants and children) because there were no effects attributable to a single dose (exposure) observed in oral toxicology studies, including maternal toxicity in the rat and rabbit developmental toxicity studies, that are appropriate for extrapolation. Therefore, an acute dietary risk assessment for the general population (including infants and children) is not required. The uncertainty factor used in this assessment was 100 which includes a 10x for inter-species extrapolation and a 10x for intra-species variation. The acute Reference Dose (RfD) is 0.003 mg/kg. The FQPA Safety Factor Committee determined that the 10x FQPA Safety Factor be reduced to 3x for acute dietary risk assessment. Application of the 3x FQPA Safety Factor resulted in the acute population adjusted dose (aPAD) of 0.001 mg/kg for acute dietary risk assessment.

For the chronic (non-cancer) dietary exposure and risk assessment, the dose selected was the NOAEL of 0.1 mg/kg/day based on decreased white blood cells from a rat chronic feeding study with a LOAEL of 0.25 mg/kg/day. The uncertainty factor used in this assessment was 300 which includes a 10x for inter-species extrapolation, a 10x for intra-species variation and an additional 3x for instability of the test material in the diet and potential for increased mortality near the LOAEL. The Chronic RfD is 0.0003 mg/kg/day. The FQPA Safety Factor Committee recommended that the 10x FQPA Safety Factor be retained for chronic dietary risk assessment for all populations. Application of the 10x FQPA Safety Factor resulted in the chronic PAD (cPAD) of 0.00003 mg/kg/day for chronic dietary risk assessment.

TPTH is considered a B_2 carcinogen. The revised unit risk, Q_1^* $(mg/kg/day)^{-1}$ of TPTH, based upon fatal pituitary gland adenoma tumor rates in female rats is 1.83×10^{0} in human equivalents (converted from animals to human by use of the 3/4's scaling factor - 1993, Tox_Risk, 3.5- K. Crump). For the conversion to human equivalents, weights of 0.35 kg for the rats, 70 kg for humans and the 3/4's scaling factor were used. It is to be noted that Q_1^* $(mg/kg/day)^{-1}$ is an estimate of the upper bound on risk and that (as stated in the EPA Risk Assessment Guidelines) "the true value of the risk is unknown, and may be as low as zero." This Q_1^* will be used for assessing cancer risk toxicity for all routes of exposure (oral, dermal and inhalation).

Short-term (1-7 days) and intermediate-term (7 days to several months) dermal risk assessments were required. The doses and endpoints for both risk assessments are >3.0 mg/kg/day based on lack of maternal or developmental toxicities. A long-term (several months to life-time) non-cancer dermal risk assessment was not required. However, a dermal cancer risk assessment was required and a dermal absorption factor of 10% was used for this risk assessment. A short- and intermediate- term inhalation exposure risk assessment was required. The dose and endpoint selected for risk assessment is a NOAEL = 0.00034 mg/L based on clinical signs (labored breathing, males) and inflammatory lesions in the lungs and deaths at 0.002 mg/L (LOAEL).

Separate risk assessments were conducted for dermal and inhalation routes because there were different endpoint effects; therefore an aggregate risk assessment was not conducted.

NON-OCCUPATIONAL EXPOSURE AND RISK ASSESSMENTS (GENERAL POPULATION)

HED conducted acute and chronic dietary (food) exposure analyses using the Dietary Exposure Evaluation Model (DEEM™). In the acute dietary assessment, exposure was compared to the acute Population Adjusted Dose (aPAD) based on the acute reference dose (RfD) reflecting retention of a 3x FQPA Safety Factor. In the chronic dietary assessment, exposure was compared to the chronic PAD based on the chronic RfD reflecting retention of a 10x FQPA Safety Factor. HED considers dietary residue contributions greater than 100% of the PAD to be of concern. The acute and chronic analyses (Tier 3 for each analysis) are refined estimates using anticipated residues from field trial data, processing factors and percent of crop treated data from Biological Economic Analysis Division (BEAD). No monitoring data from USDA's Pesticide Data Program (PDP) or FDA's Surveillance Monitoring program were available for TPTH.

Both acute and chronic (non-cancer and cancer) risk estimates exceed HED's level of concern. **Acute dietary** exposure at the 99.9th percentile comprised 306% of the aPAD for Females 13+ (13-50 years old), the population subgroup of concern. **Chronic (non-cancer) dietary** exposure comprised 279% of the cPAD for the general population and 596% of the cPAD for the most highly exposed subgroup, children (1-6 years). The cancer risk estimate for the U.S. population is 1.5×10^{-4}. This cancer risk estimate exceeds the level the Agency generally considers negligible (10^{-6}) for excess lifetime cancer risk. As noted above, the dietary exposure estimates have been refined as much as possible based on available data.

The available environmental fate data suggest that TPTH will not leach to ground water in most use environments. However, although monitoring data for TPTH are not available, water quality models using conservative assumptions suggest it may reach surface waters. HED's drinking water level of comparison (DWLOC) is effectively zero because acute and chronic dietary (food) exposure alone exceeds HED's level of concern.

In the case of TPTH, chronic (non-cancer and cancer) aggregate risk estimates include exposure through food and water only because there are no residential uses. At this point, we have

presented risk estimates for food alone because, risk estimates associated with consumption of TPTH and its toxicological residues exceed HED's levels of concern based on estimates of dietary (food) exposure alone. Therefore, any exposure from TPTH via drinking water would only cause HED's risk estimates to further exceed levels of concern.

OCCUPATIONAL EXPOSURE AND RISK ASSESSMENT

There are **no residential** or non-occupational uses for TPTH; therefore exposures are not likely, nor are residential postapplication exposures expected. There is potential for spray drift during aerial application, however, HED does not currently have an approved method of assessing this scenario. Incident data do not indicate that spray drift is a problem.

Occupational exposure to TPTH residues via dermal and inhalation routes can occur during handling, mixing, loading, applying, and reentry activities. Based on toxicological criteria and potential for exposure, HED has conducted dermal and inhalation exposure assessments for the occupational handler and postapplication worker. Because different endpoint effects were selected for the assessment of dermal and inhalation risks, separate risk assessments were conducted for dermal and inhalation exposures. The duration of exposure is expected to be short- and intermediate-term for the occupational handler. Exposures were evaluated for both commercial applicators and private growers using TPTH. Private growers are expected to have short-term exposure (i.e., it is assumed that they treat only their own field), while commercial applicators are likely to have both short- and intermediate-term exposure to TPTH (i.e., it is assumed that several fields are treated). The cancer risk assessment was conducted using the sum of dermal and inhalation exposures combined with an oral Q_1^*. Separate cancer risks were calculated, where applicable, for commercial applicators and private growers because, in several cases, the number of days these two types of workers are exposed is significantly different.

Occupational risk estimates exceed HED's level of concern. Several of the occupational **handler** scenarios exceed HED's level of concern defined by target MOEs of 100 for short- and intermediate-term dermal risk estimates, 100 for inhalation risk estimates, and by cancer risk estimates that exceed 1.0E-4.

MOEs for **short- and intermediate-term dermal** risk estimates at baseline ranged from 33 to 50 for the scenario involving the application of sprays to orchards with an airblast sprayer at maximum and typical application rates. PPE (personal protective equipment) did not mitigate these risk estimates, but engineering controls reduced exposure resulting in MOEs of 630 and 950, which are substantially below HED's level of concern. Seven scenarios required engineering controls by default because unit exposure data for baseline and PPE are either not applicable or not available. The engineering control scenario for mixing and loading wettable powder in water-soluble bags for aerial/chemigation application yielded MOEs that ranged from 21 to 31 even when typical application rates, rather than maximum rates, were used. The engineering control scenarios for mixing and loading liquids for aerial/chemigation application and for mixing and loading and applying wettable powder in water-soluble bags with a

groundboom sprayer had MOEs of 84 and 94, respectively, when the maximum application rate was used. These MOEs were mitigated to 170 and 190, respectively, with the use of the typical application rate.

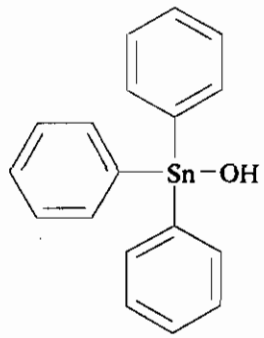
The MOE for **inhalation** risk estimate was 95 for the scenario involving the application of sprays to orchards with an airblast sprayer at the maximum application rate. This risk estimate was mitigated to an MOE of 140 with the use of the typical application rate, and an MOE of 480 with PPE.

The **cancer** risk estimate at baseline was 1.4E-4 for the scenario involving the commercial application of sprays with a groundboom sprayer, while for the private grower, the cancer risk estimate was 4.3E-6. As mentioned previously, seven scenarios require engineering controls by default. Of these, the scenarios for mixing and loading wettable powder in water-soluble bags for aerial/chemigation application and for groundboom application yielded cancer risk estimates ranging from 1.8E-4 to 3.1E-4 for the commercial applicator. For the private grower, the cancer risk estimates for these same scenarios ranged from 7.3E-6 to 1.9E-4.

The **postapplication** assessment indicates that for pecan harvesting, MOEs exceed 100 on day zero after application, while cancer risk estimates are greater than 1.0E-4 until 7 days after the last application at the Georgia site, and between 21 and 30 days after the last application at the Texas site. MOEs for maintenance activities are $\geq$100 on day zero after application for potatoes, and on the second day after application for sugar beets. The cancer risk estimate for maintenance activities was found to be less than 1.0E-4 on the second day after application for both potatoes and sugar beets. The MOE and cancer risk estimate for potato harvesting do not exceed HEDs level of concern on any day after application. The current reentry interval (REI) is 48 hours for all crops. TPTH has the potential to be a primary eye irritant (toxicity category I), which triggers the worker protection standard's (WPS) default REI of 48 hours.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

TPTH (triphenyltin hydroxide) is a fungicide registered for use on pecans, potatoes and sugar beets.



Empirical Formula:	$C_{18}H_{16}OSn$
Molecular Weight:	366.7
CAS Registry No.:	76-87-9
PC Code:	083601

TPTH is a fine white powder with a melting point of 118-120 C, bulk density of 0.2758 g/mL at 25 C, octanol/water partition coefficient (log Kow) of 3.268, and vapor pressure of $< 1x10^{-7}$ torr at 25 C. TPTH is practically insoluble in water (8 ppm), and is moderately soluble in most organic solvents (acetone 70 g/L; benzene 41 g/L; 1,2-dichloromethane 74 g/L; ether 28 g/L; ethanol 10 g/L; and methylene chloride 171 g/L).

3.0 HAZARD CHARACTERIZATION

3.1 Acute Toxicity

Table 1. Acute Toxicity of Triphenyltin Hydroxide.

Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-1	Acute Oral-rat	071364 252512	LD_{50} = 165 mg/kg ♂ 156 mg/kg ♀	II
81-2	Acute Dermal-rat	071364	LD_{50} = 1600 mg/kg	II
81-3	Acute Inhalation-rat	071364	LC_{50} =60.3 μg/L	I
81-4	Primary Eye Irritation	071364	Corrosive	I
81-5	Primary Skin Irritation	071364	PIS = 2.8	III

Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-6	Dermal Sensitization	Several Studies	Not sensitized in the Buehler assay.	Not considered a sensitizer.

3.2 Hazard Profile

Table 2. Toxicity Profile of Triphenyltin Hydroxide[1].

Study Type	MRID No.:	Results
21-day dermal - rats (1985)	00142880 258230 (Accession Number)	Systemic: NOAEL > 20 mg/kg/day. No systemic effects at highest dose tested. Systemic: NOAEL < 5 mg/kg/day. Local irritation.
Subchronic feeding - rats (1986)	00157771 261754 (Accession Number)	NOAEL < 0.33 mg/kg/day: decreased IgG antibodies. At 7.63 mg/kg/day: decreased body weight and gain and food consumption.
Subchronic feeding -mouse (1986)	00157952 261753 (Accession Number)	< 0.75 mg/kg/day (lowest dose tested): decreases in IgA and IgM antibodies. At 3.78 mg/kg/day: decreased adrenal weight and at 19.46 mg/kg/day: decreased ovary weight and increased liver weight.
Subchronic feeding - guinea pig (1960)	00086467	NOAEL < 2.5 ppm (estimated 0.1 mg/kg/day) (lowest dose tested): decreased leucocyte counts.
Subchronic feeding -dog		No valid study. Refer to chronic feeding study below.
Subchronic inhalation - rats (1989)	41017701	NOAEL = 0.00034 mg/L. LOAEL = 0.002 mg/L: deaths and lung and respiratory irritation and edema.
Chronic feeding - dog (1987)	40285501	NOAEL and LOAEL > 0.562 ♂ and 0.624 ♀ mg/kg/day. No effects at the highest dose tested.

[1]All studies classified as ACCEPTABLE or otherwise determined to contain useful data.

Study Type	MRID No.:	Results
Chronic feeding - rat (1970)	00080390 099050 (Accession Number)	NOAEL = 0.1 mg/kg/day; LOAEL = 0.25 mg/kg/day: decreased leucocyte counts.
Chronic/carcinogenicity -rat (1989)	41085702	NOAEL < 0.3 mg/kg/day (lowest dose tested) in ♂ and 0.4 in ♀ mg/kg/day: deaths in females and decreases in immunoglobulin. **Positive for pituitary and testicular tumors.** Dose levels considered adequate.
Carcinogenicity -mouse (1989)	41087501	NOAEL < 0.85 mg/kg/day (lowest dose tested) based on decreased in immunoglobulins. Particularly IgA and IgM in either males or females. **Positive for hepatocellular adenomas and carcinomas.** Dose levels considered adequate.
Developmental toxicity - (1985) rat representative study, one of several studies	257402 (Accession number)	Maternal toxicity: NOAEL = 1 mg/kg/day; LOAEL = 2.8 mg/kg/day: decreased body weight and food consumption. Developmental toxicity: NOAEL = 2.8 mg/kg/day; LOAEL = 8 mg/kg/day: decreased fetal weight and increased sternebrae unossified. (Typical response at this dose level.) At 8 mg/kg/day may have smaller litter size and less viable fetuses in other studies or poor pup survival.
Developmental toxicity - rabbit/oral (1987)	40104801	Maternal toxicity: NOAEL = 0.1 mg/kg/day; LOAEL = 0.3 mg/kg/day: decreased body weight gain. Developmental toxicity: NOAEL = 0.3 mg/kg/day; LOAEL = 0.9 mg/kg/day: lower fetal body weight and increased incidents of hyoid body and/or arches unossified.
Developmental toxicity - rabbit/dermal (1993) (dermal)	42909101	Maternal and developmental toxicity: NOAEL and LOAEL > 3 mg/kg/day. No effects at highest dose tested.

Study Type	MRID No.:	Results
Reproductive toxicity - rat (1986)	264667 to 2254676 (Accession number)	Parental toxicity: NOAEL = 0.925 mg/kg/day; LOAEL = 2.5 mg/kg/day decreased body weight. Developmental toxicity: NOAEL = 0.25 mg/kg/day; LOAEL = 0.925 mg/kg/day: decreased litter size, liver and spleen weights.
Gene Mutation-Ames test (1981)	00125264	Not mutagenic in *S. tymphimurium* or *E. Coli* ± metabolic activation.
Mouse lymphoma assay (1985)	00152226	Borderline positive in the presence of S-9 mix but negative in absence of S-9.
Cytogenetics - human chromosome aberrations (1985)	00152223	Positive for inducing chromosome aberrations in presence of metabolic activation (± S-9). Study demonstrates clastogenic property of TPTH.
Recombinant assay (Convers) (1985)	00155521	Negative in *Sacc. Cerevisiae* ± S-9 metabolic activation.
Bone marrow cells *in vivo* (1987)	40377102	No effect on bone marrow cells.
Micronucleus assay *in vivo* (1985)	00152225	Negative at 140 mg/kg but study did not demonstrate that TPTH went to the bone marrow.
Dominant lethal assay (1978)	00125265	Negative at up to 38 mg/kg/day. At 150 mg/kg/day, high rate of deaths.
Gene mutation (1985)	00152224	Not mutagenic ± metabolic activation in Schizosaccharomyces.
Unscheduled DNA synthesis (1985)	00155522	Negative up to cytotoxic dose levels.

Study Type	MRID No.:	Results
General metabolism (several studies 1986 to 1989)	41309102 40029406 40029405 40029407 41387201 41309101	The contributions from six studies combine to meet the general metabolism requirement for TPTH. The ^{14}C studies are confounded by the fact that the labeled phenyl group splits off and the fate of the parent compound is not followed. Thus, the labeled phenyl may be excreted in the urine but this does not represent excretion of intact TPTH. The ^{113}Sn labeled TPTH studies follow the fate of the tin although this may be as triphenyl, diphenyl or monophenyl or as tin itself. The biliary route is the most important in excretion of ^{113}Sn from TPTH. Most of the label (80-100% in several studies) is recovered in the feces. Little remains in tissues (for example, 0.5%). After 24 hours, the kidneys, liver epididymis and brain had the most label. After 7 days, little remained in the tissues.
Dermal penetration (1986 and 1987)	00156684 40198301 40073001	Studies demonstrate that TPTH adheres to the skin and only a small percentage (<1%) is absorbed in 10 hours. The TPTH remaining on the skin can potentially be absorbed over time. Because of complications involved with adherence to the skin, a dermal absorption factor of 10% was derived by comparing the oral and dermal developmental toxicity studies.
Special Immunotoxicity (Several studies 1982 to 1990	41518200 40303701 00124218 00124217 00141313	<u>In rats (41518200):</u> NOAEL = 1.82 mg/kg/day; LOAEL = 3.4 mg/kg/day: decreases in IgG. At higher doses: decreased spleen weight and white blood cells and circulating lymphocytes. <u>In mice (41518200):</u> NOAEL = 0.23 mg/kg/day, LOAEL = 1.15 mg/kg/day: decreased spleen weight absolute and relative. At higher doses: decreased IgM, WBC, neutrophils and circulating lymphocytes. <u>Immunosuppression: (40303701):</u> No evidence of increased susceptibility to *trichinella spiralia* at 2.5 mg/kg/day.

Currently there are **data gaps** for the following studies:

81-8 (870.6200). Acute Neurotoxicity screen
82-7 (870.6200). Subchronic Neurotoxicity screen
Special Study. Developmental Immunotoxicity screen (consult with Agency on protocol).

Quality and completeness of the database. The existing toxicity database for TPTH has been developing since the 1960's. Nearly all of the earlier studies have been replaced by studies conducted in the mid to late 1980's and have been classified to be acceptable using review criteria in effect in the late 1980s and early 1990s. In general, there is a high degree of confidence in the existing toxicity database especially for the studies used in assessing developmental toxicity and carcinogenicity. TPTH is considered to be an agent that may cause immunotoxicity. The chronic dietary RfD is based on decreases in white blood cells and both the rat and mouse chronic feeding and/or oncogenicity studies indicate decreases in immunoglobins. There is a high degree of confidence that the dose levels selected for the chronic RfD are appropriate in that there would not be significant decreases in leucocytes or immunoglobulins at lower doses than 0.1 mg/kg/day. Although the available toxicity database for TPTH is adequate to define the potential toxicity of TPTH, there are questions remaining concerning the potential for neurotoxicity and immunotoxicity. There are data gaps for acute and subchronic neurotoxicity. Immunotoxicity is considered a more significant effect of concern for TPTH than neurotoxicity and the developmental neurotoxicity study is not designed to evaluate immunotoxicity. Therefore, a developmental immunotoxicity study is required for TPTH. Additional data to define the potential for TPTH to cause true immunotoxicity is required.

Toxicity in rats. The toxicologically significant effects of TPTH *in rats* include decreases in leucocytes and immunoglobulins at dose levels as low as 0.25 or 0.33 mg/kg/day which are considered potential indicators of immunotoxicity. Following chronic feeding, deaths result at doses as low as 0.4 mg/kg/day in females, probably related to pituitary tumors. In subchronic and chronic studies, decreases in body weight and food consumption result at approximately 1.3 to 1.6 mg/kg/day. Other systemic effects include decreased liver weight, bile duct hyperplasia and portal sclerosis as well as increases in serum enzyme activity (ASAT, ALP and ALAT). The pituitary displayed hyperplasia in the pars intermedia and the testis displayed Leydig cell hyperplasia and tubular atrophy and the testis also had increases in Leydig cell tumors.

In several developmental toxicity studies in rats, maternal toxicity consisted of lower body weight and food consumption at approximately 2.8 mg/kg/day and developmental toxicity at approximately 8 mg/kg/day consisted of lower fetal weight, smaller litter size and some decreases in ossification. An initial concern for hydronephrosis and hydroureter observed in an earlier study was removed by subsequent studies that did not demonstrate this effect. There was an indication that the fetuses may be more sensitive than adults in the multi generation reproduction study since at 0.925 mg/kg/day the fetuses were lower in weight and appeared smaller in size and also their liver and spleen weights were decreased. Parental toxicity was

noted at 2.5 mg/kg/day and consisted mainly of a body weight decreases.

Toxicity in dogs. Dogs were assessed at a dose level of 18 ppm (equivalent to approximately 0.562 and 0.624 mg/kg/day in males and females, respectively) in a chronic study but there were no systemic effects noted in either sex.

Toxicity in mice. In both the subchronic dose range finding study and the carcinogenicity study, mice showed decreases in immunoglobulins. In the subchronic study, there was slightly increased initial body weight, decreased adrenal and ovary weight in females without pathological changes and increased liver weight. In the carcinogenicity study, there were decreases in kidney weight (without associated pathology), liver weight decreases and at higher doses body weight decreases and deaths. The mouse study was considered positive for liver tumors.

Toxicity in rabbits. In the oral developmental toxicity studies with *rabbits*, TPTH resulted in decreases in body weight at doses as low as 0.3 mg/kg/day. At higher doses such as 2 mg/kg/day, poor general condition and resorptions in the pregnant does result. Developmental toxicity was noted at 0.9 mg/kg/day as lower fetal weight and a slight increase in unossified hyoid. A developmental toxicity study by the dermal route demonstrated a NOAEL and LOAEL of > 3 mg/kg/day for both maternal and developmental toxicity since there were no effects at 3 mg/kg/day, the highest dose tested.

Immunotoxicity. Substituted organotins are also known to be immunotoxic. The chronic RfD is based on decreased leucocytes in a rat chronic toxicity study. Both the rat and mouse toxicity studies consistently showed decreases in certain antibodies. Decreases in leucocytes were noted in the guinea pig subchronic and toxicity study (at approximately 0.1 mg/kg/day). Decreased immunoglobulins were noted in the mouse study at 0.75 mg/kg/day. Subacute dosing verified that the rat at 3.4 mg/kg/day and mouse at 1.15 mg/kg/day have decreased white blood cells and spleen size. A special immunotoxicity study with TPTH, however, did not indicate that TPTH is specifically immunotoxic since the rats dosed at 2.5 mg/kg/day for 10 days were not more susceptible to opportunistic infections. In order to further assess for potential immunotoxicity, the rat series 83-6 developmental toxicity study must include, in addition to the neurotoxicity parameters, special provisions to assess for the function of the immune system in the neonate and weaned offspring. It is strongly advised that the protocol for this study be submitted to the Agency for review prior to initiating the study.

Endocrine disruption. There are several indications that imply that TPTH may cause endocrine disruption. In rats, testicular and pituitary tumors were a marked feature in the carcinogenicity study. In the mouse there were changes in adrenal and ovary weights. There were no specific assays for blood levels of hormones in the studies submitted to further assess for possible endocrine disruption. There has been discussion between the registrants and the Agency regarding the design of some special studies to assess the potential for TPTH to affect the hormone levels in an attempt to demonstrate and characterize the possible relationship between

TPTH, hormonal effects and the development of pituitary and testicular tumors. These studies have not been submitted to the Agency as of March 1999.

Carcinogenicity. TPTH is classified as a B2: probable human carcinogen based on evidence of carcinogenicity in mice (liver tumors) and rats (pituitary and testicular tumors) at dose levels that were adequate for assessment of carcinogenicity. The low dose linear approach (Q_1*) was used for human characterization and was based on the pituitary tumors observed in rats. The Q_1* is 1.83×10^0 $(mg/kg/day)^{-1}$. This Q_1* will be used for assessing cancer risk for all routes of exposure (oral, dermal and inhalation). The Q_1* derived from the oral studies is used as a default for the dermal and inhalation routes since dermal and inhalation carcinogenicity studies are not required according to Subdivision F based on the use pattern of this chemical.

Mutagenicity. TPTH is not considered to have a mutagenicity/genetic toxicity concern. Most studies are negative for mutagenic/genetic toxicity effects. Although there were some apparent positive responses, other tests, particularly *in vivo*, conducted to verify the significance of the apparent positive studies *in vitro* were negative.

General metabolism. There are several studies which define the metabolism of TPTH using either ^{14}C or ^{113}Sn labeled TPTH. The contributions from six studies combined to meet the general metabolism requirement for TPTH. The ^{14}C studies are confounded by the fact that the labeled phenyl groups split off and the fate of the parent compound is not followed. Thus, the labeled phenyl may be excreted in the urine but this does not represent the excretion on intact TPTH. The ^{113}Sn labeled TPTH studies follow the fate of the tin although this may be as triphenyl, diphenyl or monophenyl or tin itself. The biliary route is important in excretion of ^{113}Sn. Most of the label (80-100% in several studies) is recovered in the feces. Little remains in the tissues (for example, 0.5%). After 24 hours, the kidneys, liver, epididymis and brain had the most label. After 7 days very little labeled chemical remained in the tissues.

Metabolites. There are no known special toxicity problems or issues associated with the metabolites of TPTH. It appears that all plant metabolites are also animal metabolites. TPTH is serially metabolized to diphenyl and monophenyl tin and excreted.

Dermal absorption. There are several studies to assess for dermal absorption. However, the high affinity that TPTH has for the skin confounds assessing for the potential for TPTH to be absorbed dermally. A dermal absorption factor of 10% was extrapolated based on the comparison of the LOAELs of the oral and dermal developmental toxicity studies in rabbits.

3.3. FQPA Considerations.

3.3.a. *Neurotoxicity.* TPTH belongs to a class of chemicals called substituted organotins. This class includes trimethyl and triethyl tin which are noted for their neurotoxic effects and serve as positive controls in neurotoxicity studies. TPTH did not demonstrate obvious neurotoxicity in either the rat, rabbit or dog studies. This may be because the larger and bulkier phenyl groups

prevent TPTH from reaching the nervous tissue at sufficiently high concentrations. Neurotoxicity assessment, however, is not considered complete for TPTH and the series 81-8, 82-7 and 83-6 acute, subchronic and developmental neurotoxicity studies are being requested. The series 83-6 developmental toxicity study will require a special protocol (refer to paragraph on immunotoxicity below).

3.3.b. *Increased susceptibility.* There were no indications of increased susceptibility in either the rat or rabbit prenatal developmental toxicity studies. The rat multigeneration reproduction study, however, did indicate toxicity increased susceptibility (based on decreases in liver and spleen weight and a decease in live litter size in offspring) at a dose (0.9 mg/kg/day) lower than the dose causing parental toxicity (2.5 mg/kg/day).

3.3.c. *Data gaps for assessment of potential hazard to infants and children.* HIARC required a developmental toxicity study that evaluates immunotoxicity, a potential toxic effect of TPTH to which fetuses and neonates may be specially susceptible, in place of a developmental neurotoxicity study. It is recommended that the protocol for this study be submitted to OPP prior to initiating the study.

3.3.d. *Status of the 10 x FQPA Safety Factor.* TPTH was discussed by the FQPA Safety Factor Committee on November 30, 1998. The committee recommended two different factors: a 3x for acute and a 10x for chronic dietary risk assessments. There are no registered residential uses at the present time.

3.3.e. *Application of the 10x Safety Factor.* The following is an excerpt for the FQPA Safety Committee report dated December 17, 1998.

1. FQPA Safety Factor Recommendation

The Committee recommended two different FQPA Safety Factors: **3x for acute** dietary risk assessments and **10x for chronic** dietary assessments.

2. Rationale for the FQPA Safety Factor

The Committee made these recommendations for the FQPA Safety Factor for TPTH because:

1. There was evidence of increased susceptibility to the offspring following pre- and/or postnatal exposure in the two-generation reproduction study in rats. Offspring toxicity was observed at a dose lower than parental systemic toxicity.

2. TPTH is considered to affect the endocrine system and there is concern for the possible relationship between TPTH, hormonal effects, and the development of pituitary and testicular tumors.

3. TPTH is considered as an agent that may cause immunotoxicity. The chronic dietary RfD is based on decreases in white blood cells and both the rat and mouse chronic feeding and/or oncogenicity studies indicate decreases in immunoglobulins.

4. HIARC required a developmental toxicity study that evaluates immunotoxicity, a potential toxic effect of TPTH to which fetuses and neonates may be especially susceptible, in place of a developmental neurotoxicity study.

3. Population Subgroups for Application of the Safety Factor

Acute Dietary Assessment: The Committee determined that the FQPA Safety Factor can be **reduced to 3x** for acute dietary risk assessment for the **subpopulation Females 13+ only** because the increased susceptibility was seen only in the offspring of parental animals receiving repeated oral exposures (two-generation reproduction toxicity study) and not seen following *in utero* exposures (developmental studies). Thus, the increased susceptibility concern was for chronic dietary exposure. The application of the 3x safety factor to the acute dietary exposure assessment is based on the concern for the potential immunotoxic effects which resulted in the requirement for a developmental neurotoxicity with special inclusions for immunotoxicity assessment (data gap).

Chronic Dietary Assessment: The Committee determined that the FQPA Safety Factor should be **retained (10x)** for chronic dietary risk assessment for **All Populations which include Infants and Children** because increased susceptibility to the offspring was seen following repeated oral exposures in the two generation reproduction study in rats.

Residential Assessment: There are no registered uses of TPTH that would result in residential exposure at this present time.

3.4. Endpoint Selection

Table 3 provides a summary of toxicological endpoints for use in human risk assessment. A detailed description of the rationale for selection of the selected doses and endpoints can be found in the attached HIARC report.

Table 3. Summary of Toxicological Endpoints for Use in Human Risk Assessment.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL = 0.3 mg/kg/day (100 UF) (3x FQPA)	Increased incidents of hyoid body and/or arches unossified in rabbit fetuses.	Oral Developmental toxicity -Rabbit (MRID No.: 40104801)
	Acute PAD = 0.001 mg/kg for Females 13+		
	No acute oral endpoint identified for general population; risk assessment not required.		
Chronic Dietary	NOAEL = 0.1 mg/kg/day (300 UF) (10x FQPA)	Decreased white blood cells.	Chronic feeding study -Rat (Accession No.: 099050)
	Chronic PAD = 0.00003 mg/kg/day		
	Risk assessment required for general population including infants and children.		
Carcinogenicity (oral/dermal/ inhalation)	Oral Q1* 1.83 $(mg/kg/day)^{-1}$	TPTH is classified as a B2 Carcinogen - probable human carcinogen based on pituitary and testicular tumors in rats and liver tumors in mice. A dermal absorption of 10% should be used for this risk assessment. An inhalation absorption of 100% should be used for this risk assessment.	
Short-Term (Dermal)	Dermal NOAEL = 3 mg/kg/day (MOE: 100)[1]	No effects at the highest dose tested.	Dermal Developmental toxicity - Rabbit (MRID No.: 42909101)
Intermediate-Term (Dermal)	Dermal NOAEL = 3 mg/kg/day (MOE: 100)[1]	No effects at the highest dose tested.	Dermal Developmental toxicity - Rabbit (MRID No.: 42909101)
Long-Term Non-cancer (Dermal)	None	Use pattern does not indicate exposure will be for this interval.	
Inhalation (Any Time Period)	0.00034 mg/L (100 UF) (MOE: 100)[1] (0.092 mg/kg/day)[2]	Deaths following lung lesions.	Subchronic Inhalation toxicity -Rat (MRID No.: 41017701)

[1] MOE is only for occupational exposure; there is no residential exposure.

[2] Inhalation dose in mg/L was converted to mg/kg/day using the following equation:
Dose (mg/kg/day) = (NOAEL (0.00034 mg/L) * Respiration rate of a young adult Wistar rat (8.46 L/hr) * Study daily exposure duration (6 hr/day)) / Body weight of a young adult Wistar rat (0.187 kg)

The endpoints selected for the acute dietary, chronic dietary, short, intermediate and long term exposure scenarios are listed in Table 3 above. A more detailed discussion of the selection of these endpoints can be found in the HIARC report dated December 17, 1998.

The slope of the doses selected for these exposure endpoints is considered steep. The oral developmental toxicity study in rabbits assessed doses as close as 0.1, 0.3, 0.9 and 1, 2, 4, and 8 mg/kg/day. At doses above 1 mg/kg/day, the general condition of the rabbits and the incidence of resorptions changed dramatically with an increase in dose over this narrow dose range. In the chronic study in rats, the dose levels varied from approximately 0.25 to 4.0 mg/kg/day and there were marked increases in deaths over this narrow range of doses.

3.5 Endocrine Disrupter Effects

The Food Quality Protection Act (FQPA; 1996) requires that EPA develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect...." The Agency is currently working with interested stake holders, including other government agencies, public interest groups, and industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (that is, until 8/3/99) to implement this program. At that time, EPA may require further testing of TPTH for endocrine effects.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Registered Uses

There are no registered residential uses of TPTH. TPTH is a restricted use pesticide.

TPTH is a fungicide registered for use on pecans, potatoes and sugar beets. TPTH is used to control early and late blight on potatoes; leaf spot on sugar beets, peanuts, scab and several other diseases on pecans. In addition to its fungicidical activity, TPTH exhibits antifeeding properties for surface-feeding insects. TPTH is manufactured by members of the TPTH Task Force (AgrEvo, Elf Atochem and Griffin) under the trade names Super Tin®, Pro-Tex®, Brestan®, and Photon®. TPTH is formulated both as a wettable powder in a water-soluble pack and as a flowable concentrate requiring a closed mixing/loading system. These products may be applied as broadcast foliar applications using ground or aerial equipment and by chemigation (potatoes only). The maximum application rate for pecans is 0.375 lb ai/acre; the maximum number of applications to pecans per season is 10, with an interval range of 14-28 days. The maximum application rate for potatoes is 0.1875 lb ai/acre; TPTH can be applied to potatoes up to 6 times per season, at 7-day intervals. The maximum application rate applied to sugar beets is 0.25 lb ai/acre; TPTH labels state that applications to sugar beets may be made at 10 to 14-day intervals, for a maximum of four times per season. However, an increase to five times per season is planned by the registrant. TPTH is a restricted use pesticide.

4.2 Dietary Exposure

Tolerances have been established at 0.05 ppm for residues of TPTH *per se* in/on pecans, potatoes, sugar beet roots, and kidney and liver of cattle, goats, hogs, horses, and sheep [40 CFR §180.236]. No tolerances for residues of TPTH have been established for processed food/feed commodities.

OPPTS GLN 860.1300: Nature of the Residue in Plants and Livestock

The qualitative nature of TPTH in plants and animals is adequately understood based on potato, soybean, and rice metabolism studies, and acceptable ruminant and poultry metabolism studies. HED has previously concluded [(J. Doherty, PP#F2823/FAF#3H5384, 10/28/83) and the Residue Chemistry Chapter of the TPTH Update (March 1992)] that the residues to be regulated in plants and livestock are parent TPTH and its diphenyltin hydroxide (DPTH) and monophenyltin hydroxide (MPTH), or oxide, metabolites.

OPPTS GLN 860.1340: Residue Analytical Methods

The available methods for tolerance enforcement, listed in the Pesticide Analytical Manual (PAM), Vol. II, as Methods I-IV, are colorimetric methods that measure TPTH *per se*. A new tolerance enforcement method was required for TPTH residues as the Agency no longer considers colorimetric methods to be adequate for enforcing tolerances and because the tolerance expression for TPTH is being revised to include DPTH and MPTH.

A proposed GC/flame photometric detection (FPD) enforcement method (Method AL007/91-0), which determines TPTH and its metabolites, DPTH and MPTH, has undergone successful independent laboratory validation using sugar beet and potato matrices (D228535, 1/24/97, L. Cheng), and has been submitted for an Agency tolerance method validation (TMV) (D252196, 1/15/99, S. Law).

Residue data on crop plants and processed commodities have been collected using methods which sequentially screen for total extractable organotin using graphite furnace atomic absorption spectroscopy and analyze for individual phenyltin analytes by GC/FPD or HPLC. These methods are similar to the method described above with minor modifications involving changes in solvents and cleanup procedures.

In conjunction with the ruminant feeding study (DP Barcode D239451, J. Punzi, 4/2/98), the registrants provided data validating a GC/FPD method for determining residues of TPTH and its metabolites DPTH and MPTH in animal commodities. The method is similar to the proposed enforcement for plant commodities described above. The LOQ for each analyte is 0.02 ppm in milk, cream, and muscle, and 0.1 ppm in kidney, liver, and fat. However, HED has previously concluded that the method must be modified to include a base hydrolysis step to release conjugated residues. Alternatively, the registrants must provide data indicating that base hydrolysis is unnecessary for adequate recovery of the total toxic residue.

An independent laboratory validation (ILV) of this method has also been conducted and the method is currently undergoing an Agency Tolerance Method Validation (TMV) by the Biological and Economic Analysis Division (BEAD) Laboratory.

The Agency's review of the registrant's response to the Reregistrations Standard Update (L. Cheng, 11/23/93) required that, "... representative samples from the plant and animal metabolism studies be analyzed using the proposed enforcement method in order to ascertain that these methods are capable of recovering all residues of concern. If analysis of samples from previously accepted metabolism studies is impractical, the registrant must provide data from other sources to demonstrate the adequate recovery of the total toxic residue." These data remain outstanding, but are considered confirmatory.

OPPTS GLN 860.1360: Multiresidue Method Testing

The registrants have not provided recovery data for TPTH and its metabolites using FDA multiresidue methods. This represents a data-gap. The registrants are referred to OPPTS GLN 860.1360 for details concerning multiresidue method testing.

OPPTS GLN 860.1380: Storage Stability Data

The requirements for supporting storage stability data are tentatively satisfied for the purposes of reregistration. To support the residue field trial data for pecans, data depicting the storage stability of TPTH and its metabolites in pecans held in frozen storage for up to 261 days (~9 months) must be provided. Currently available data indicate residues of TPTH are stable in sugar beet leaf tops from zero to 7 months and from 2 to 4 years. The registrants have advised the Agency that the required 2-year storage stability study on sugar beets is continuing. The Agency considers these data confirmatory.

The available storage stability data indicate that residues of TPTH, MPTH and DPTH are stable at -20 C for 14-16 weeks in potatoes, sugar beet roots, refined sugar and sugar beet molasses.

Samples of cow tissue and milk were analyzed within 30 days of collection in the ruminant feeding study. Therefore, storage stability data on residues of TPTH in animal commodities are not required.

OPPTS GLN 860.1500: Magnitude of the Residue in Crop Plants

For purposes of reregistration, the requirements for magnitude of the residue data in/on plants are fulfilled for the following crops pending adequate resolution of storage stability issues: pecans, potatoes, and sugar beets. Adequate field trial data depicting TPTH residues of concern in/on these crops following applications made according to the maximum or proposed use patterns have been submitted. Geographical representation is adequate and a sufficient number of trials reflecting representative formulation classes were conducted.

The registrants need to propose a tolerance for residues of TPTH and its metabolites in/on sugar

beet tops. Residue field trial data are available indicating that the combined residues of TPTH and its regulable metabolites in/on sugar beet tops were 2.5-9.7 ppm harvested 21 days following treatment at 1x. These data are supported by the available storage stability data. Additional storage stability data are being collected and considered confirmatory. For the purposes of this RED, the estimated tolerance for TPTH residues in/on sugar beet tops is 10 ppm.

Existing tolerances for pecans (0.05 ppm), potatoes (0.05 ppm), and sugar beets (0.05 ppm) are adequate. These tolerances are based on non-detectable residues in field trial samples and limits of quantitation (LOQ) of 0.1 ppm for each metabolite: MPTH, DPTH, and TPTH.

OPPTS GLN 860.1520: Magnitude of the Residue in Processed Food/Feed

The reregistration requirements for magnitude of the residue in processed food/feed commodities are fulfilled for potatoes and sugar beets.

The available potato processing studies indicate that TPTH residues do not concentrate in chips or granules, but concentrate by 3x in wet peel. Based upon this concentration factor and the current residue data (D250912-17, 1/14/99, S. Law), showing 28 potato samples with non-detectable residues and a LOQ of 0.01 ppm for each of the TPTH regulable residues, an appropriate tolerance for TPTH residues in wet peel is 0.1 ppm. This tolerance is based on the addition of the LOQ (0.01 ppm) for each compound of toxicological concern (MPTH, DPTH, and TPTH) multiplied by the concentration factor (3x).

Data from sugar beet processing studies also indicate that TPTH residues do not concentrate in refined sugar, but concentrate by 22x in dehydrated pulp and approximately 3x in molasses. Based upon these concentration factors and the HAFT residues of 0.015 ppm in/on sugar beet roots, a tolerance of 0.5 ppm for TPTH residues in dehydrated pulp should be established; the established tolerance for residues of TPTH in/on sugar beet root (0.05 ppm) will cover residues in molasses derived from processing sugar beets treated with TPTH.

OPPTS GLN 860.1480: Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

Reregistration requirements for magnitude of the residue in meat, milk, poultry and eggs are fulfilled. A tolerance of 0.05 ppm has been established for residues of TPTH *per se* in liver and kidney of cattle, goats, sheep, hogs and horses. Currently, there are no TPTH uses on poultry feed items.

The available data indicate that the established tolerances for residues of TPTH in the kidney and liver of cattle, goats, horses, and sheep (0.05 ppm each) are too low. These tolerances were reassessed, in terms of the combined residues of TPTH, to 4.0 ppm in liver and 2.0 ppm in kidney of cattle, goats, horses, and sheep.

Residue data from the feeding study also indicate that tolerances for the combined residues of TPTH should be established in cattle, goats, horses, and sheep as follows: 0.5 ppm in meat; 0.2 ppm in fat; and 0.06 ppm in milk based on non-detectable levels (0.02 ppm) for each metabolite.

The low-dose group from the feeding study (7 ppm) is approximately 233.3x the theoretical dietary burden for swine. Using the results of the feeding study to reassess tolerances for swine, the data indicate that tolerances for residues of TPTH in hog kidney and liver should be revoked concomitant with establishing a separate tolerance of 0.3 ppm for residues in hog meat byproducts (the combined LOQ for TPTH residues in kidney, liver and fat). In addition, tolerances should also be established for residues of TPTH in hog fat at 0.3 ppm and in hog meat at 0.06 ppm (the combined LOQ for TPTH residues in meat).

OPPTS GLN 860.1400: Magnitude of the Residue in Water, Fish, Irrigated Crops

TPTH is not registered for use on potable water or aquatic food and feed crops; therefore, no residue chemistry data are required under these guideline topics.

OPPTS GLN 860.1460: Magnitude of the Residue in Food-Handling Establishments

TPTH is not registered for use in food-handling establishments; therefore, no residue chemistry data are required under these guideline topics.

OPPTS GLN 860.1850: Confined Accumulation in Rotational Crops

A confined rotational crop study was deemed adequate by EFED (E. Regelman, 2/22/91). Total radioactive residues (TRR) were 0.011-0.096 ppm in/on RACs of spinach, radish, carrots, and wheat planted 30 days following the last of six soil applications of ^{14}C-TPTH at 0.25 lb ai/A/application (totaling 1.5 lb ai/A/season; 2x). TRRs in rotational crop RACs were 0.024-0.066 ppm from the 120-day plant-back interval (PBI) and <0.008-0.017 ppm from the 365-day PBI. Analyses of spinach leaves, radish and carrot roots, and wheat grain from the 30- and 120-day PBIs indicated that total organotin compounds accounted for ≤0.005 ppm in each commodity and were comprised mainly of TPTH. These data indicate that accumulation of TPTH residues in rotational crops is limited. As TPTH residues of concern were <0.01 ppm at the 30-day PBI, limited field rotational crops studies are not required, and the registrants should amended all labels to include a 30-day rotational crop restriction.

OPPTS GLN 860.1900: Field Accumulation in Rotational Crops

Based on the results from the confined rotational study, limited field studies on TPTH residues in rotational crops are not required.

TOLERANCE REASSESSMENT SUMMARY

Tolerances for residues of TPTH are currently expressed in terms of TPTH *per se* (40 CFR §180.236). For purposes of tolerance enforcement, TPTH residues of concern in plant and animal commodities have been determined to include TPTH and its metabolites, MPTH and DPTH. Accordingly, the tolerance definition for TPTH residues should also be changed to read as follows:

Tolerances are established for the combined residues of the fungicide triphenyltin hydroxide and its monophenyltin (MPTH) and diphenyltin (DPTH) hydroxide and oxide metabolites, expressed in terms of parent TPTH, in/on the following raw agricultural commodities:

A summary of the TPTH tolerance reassessment for the animal and crop commodities and recommended modifications in commodity definitions are presented in Table 6.

Tolerances Listed Under 40 CFR §180.236:

Sufficient data are available to reassess tolerances for the combined residues of TPTH in/on pecans, potatoes, sugar beets, and livestock commodities.

The available residue data indicate that the established tolerances for TPTH residues in/on pecans, potatoes and sugar beet roots are adequate provided that use directions are amended as required, and the storage stability data are provided for residues in pecans and confirmatory data for sugar beet tops.

The available data indicate that the established tolerances for residues of TPTH in the kidney and liver of cattle, goats, horses, and sheep (0.05 ppm each) are too low. These tolerances should be reassessed, in terms of the combined residues of TPTH, to 4.0 ppm in liver and 2.0 ppm in kidney of cattle, goats, horses, and sheep.

Residue data indicate that tolerances for residues of TPTH in hog kidney and liver should be revoked concomitant with establishing a separate tolerance of 0.3 ppm for residues in hog meat byproducts.

Tolerances Needed Under 40 CFR §180.236:

Based on the available residue data, a tolerance of 10.0 ppm should be established for TPTH residues in/on sugar beet tops.

Separate tolerances are also required for residues of TPTH in the following processed commodities: potato, wet peel (0.1 ppm), and in sugar beet, dried pulp (0.5 ppm).

For livestock commodities, new tolerances for the combined residues of TPTH in cattle, goat, horse, and sheep commodities should be established at 0.5 ppm in meat, 0.2 ppm in fat, and 0.06 ppm in milk. New tolerances are needed for residues in hog meat and fat (at 0.06 and 0.3 ppm, respectively). In addition, the separate tolerances for residues in hog kidney and liver should be revoked concomitant to establishing a separate tolerance for residues in hog meat byproducts at 0.3 ppm.

Table 6. Tolerance Reassessment Summary for Triphenyltin Hydroxide (Table C from Chemistry Chapter).

Commodity	Current Tolerance (ppm)[a]	Tolerance Reassessment (ppm)[b]	Comment/*Correct Commodity Definition*
Tolerances listed under 40 CFR §180.236:			
Pecans	0.05	0.05	
Potatoes	0.05	0.05	
Sugar beet, roots	0.05	0.05	*Beets, sugar, roots*
Liver and kidney of cattle, goats, horses, and sheep	0.05	4.0	The available data from the ruminant feeding study support increasing the tolerance on liver.
		2.0	The available data from the ruminant feeding study support increasing the tolerance on kidney.
Liver and kidney of hogs		Revoke	The tolerance should be revoked concomitant with establishing a separate 0.3 ppm tolerance for residues in *meat byproducts* of hogs.
Tolerances needed under 40 CFR §180.236:			
Beets, sugar, tops (leaves)	None	10.0	Based on the available field trial data on sugar beet tops.
Beet, sugar, pulp, dried	None	0.5	Based on a concentration factor of 22x and HAFT residues of 0.016 ppm
Potato, peel, wet	None	0.1	Calculated with a concentration factor of 3x and HAFT residues of 0.03 ppm based on non-detectable residues and a LOQ of 0.01 ppm for each metabolite.
Meat of cattle, goats, horses, and sheep	None	0.5	Based on data from the ruminant feeding study.
Fat of cattle, goats, horses, and sheep	None	0.2	
Hog, fat	None	0.3	
Hog, meat	None	0.06	
Hog, *meat byproducts*	None	0.3	A tolerance of 0.3 ppm for residues in mbyp should be established to replace separate tolerances for residues in kidney and liver
Milk	None	0.06	Based on non-detectable residues and a LOQ of 0.02 ppm for each metabolite.

[a] Expressed in terms of TPTH *per se*.

[b] Expressed in terms of the combined residues of TPTH, and its metabolites MPTH and DPTH.

CODEX HARMONIZATION

There are currently no Codex Maximum Residue Limits (MRLs) established for residues of TPTH in/on plant or animal commodities (electronic correspondence from S. Funk, 10/15/98).

4.3 Dietary Exposure (Food Source)

The acute and chronic (non-cancer and cancer) dietary exposure assessments were conducted using the Dietary Exposure and Evaluation Model (DEEM™) system. DEEM™ can be used to estimate exposure from constituents in foods comprising the diets of the U.S. population, including all population subgroups. The software contains food consumption data from the USDA Continuing Survey of Food Intake by Individuals (CFSII) from 1989-1992.

The tolerances published for TPTH under 40 CFR §180.236 have been reassessed. However, TPTH inputs to the DEEM™ for a Tier 3 acute and chronic analysis included anticipated residues from field trials, processing factors (where applicable) and %CT (BEAD Quantitative Usage Analysis for TPTH, electronic correspondence, 4/22/99, J. Faulkner) for pecans, potatoes, sugar beets, milk and meat. Dietary refinements, such as anticipated residues, are a way to estimate actual exposures, as opposed to high-end estimates (See Table 7). No monitoring data for TPTH were available from USDA's PDP or FDA's Surveillance Monitoring Program.

For the acute assessment, the anticipated residues for sugar beets and potatoes were calculated based on the addition of ½ the sum of LOQs (0.01 ppm) for the parent and each regulable metabolite for samples with non-detectable residues. For potatoes and sugar beets roots, all field trial samples had non-detectable residues. For pecans, the distribution of field trial results, corrected for %CT was used (value for pecans was based on the total tin method - i.e., TPTH and its regulable metabolites plus any other form(s) of tin).

For the chronic assessment, the anticipated residues for sugar beets and potatoes were calculated based on the addition of ½ the LOQ of 0.01 ppm for each regulable metabolite for samples with non-detectable residues. For potatoes and sugar beets roots, all field trial samples had non-detectable residues. The sugar beet value was further corrected for an exaggerated application rate. For pecans, the average residue value from the field trial results was used (value for pecans is based on total tin method) and corrected for %CT.

Data from processing studies indicate that residues of TPTH and its metabolites do not concentrate in the processed fractions of potato chips or potato granules. However, data indicate that residues of TPTH and its metabolites do concentrate in sugar beet molasses (3x) and reduce in sugar beet refined sugar (0.02x), baked potatoes (0.03x), boiled potatoes (0.04x) and wet potato peel (3x). These commodities' processing factors were adjusted accordingly in the acute and chronic (non-cancer and cancer) dietary exposure analyses; otherwise DEEM™ default processing factors were used.

Table 7. Anticipated Residues (AR) for Dietary Risk Assessment (Does not Include % CT [6]).

Commodity	Acute AR (ppm)[1]	Chronic AR (ppm)[2]
Sugar beets	0.015	0.004[3]
Sugar beet, refined sugar[3]	0.0003	0.00008
Molasses[3]	0.045	0.012
Pecan	Distribution of field trial data.	0.005
Potato	0.015	0.015
Potato, chips[4]	0.015	0.015
Potato, baked[4]	0.00045	0.00045
Potato, boiled[4]	0.0006	0.0006
Potato, granules[4]	0.015	0.015
Muscle[5]	0.30	0.049
Kidney[5]	1.0	0.17
Liver[5]	3.16	0.53
Fat[5]	0.12	0.021
Milk	0.006	0.0016
Cream	0.026	0.008
Skim Milk	0.004	0.0013

[1] AR calculated based on the addition of ½ the sum of LOQs (0.01 ppm) for each metabolite (TPTH, DPTH, and MPTH) for samples with non-detectable residues or based on the highest of measured field trial results (value for pecans is based on total tin method - i.e., TPTH and its regulable metabolites plus any other form(s) of tin) multiplied by a processing factor, where applicable.

[2] AR calculated based on the addition of ½ the LOQ of 0.01 ppm for each metabolite or average of field trial results, multiplied by processing factor, where applicable. If field trials were conducted at an exaggerated rate, the residue values were corrected for a 1x rate of application. For sugar beets, the rate of treatment was 2.9 lbs ai/A or 3.86x of the maximum labeled rate (0.75 lbs ai/A). For potatoes the treatment rate was the maximum labeled rate of 0.75 lbs ai/A (1x). For pecans the rate of treatment was 4.125 lbs ai/A or approximately 1x; the maximum labeled rate is 3.8 lbs ai/A (See Table A).

[3] AR based on reduction or concentration factor (refined sugar 0.02X, molasses 3X).

[4] Residues do not concentrate in chips or granules. Reduction factor for baked potatoes is 0.03X ; for boiled potatoes it is 0.04X; concentration factor for wet potato peel is 3x.

[5] AR based on combined regulable residues of TPTH in cattle, goats, sheep, hogs and horses.

[6] %CT information: Acute Estimated Maximum: 44% for sugar beets, 23% for potatoes and 56% for pecans. Chronic Weighted Average: 35% for sugar beets, 13% for potatoes and 35% for pecans.

The Reference Dose (RfD) is derived from an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control, along with the application of uncertainty factors. The percent of the RfD is calculated as the ratio of the exposure value to the RfD (exposure/RfD x 100 = % RfD). The population adjusted dose (PAD) is the adjusted RfD reflecting the retention or reduction of the FQPA safety factor for all populations which include infants and children. For TPTH, the population adjusted doses pertaining to acute and chronic dietary exposure are 0.001 mg/kg/day and 0.00003 mg/kg/day, respectively.

4.3.1 Acute Dietary Exposure Assessment

For the Tier 3 probabilistic (Monte Carlo) acute dietary exposure analysis of TPTH, exposure (consumption x residue concentration) was compared to an acute PAD of 0.001 mg/kg/day (FQPA Safety Factor Committee Report, 12/17/98). The input values for the analysis include anticipated residues, processing factors (where applicable) and percent %CT from BEAD. The respective estimated maximum of percent crop treated was used for each crop: pecans (56%), potatoes (23%) and sugar beets (44%). The acute dietary risk analysis estimates the distribution of single day exposures for the overall U.S. population and certain subgroups. The analysis evaluates exposure to the chemical for each food commodity and assumes uniform distribution of TPTH in the food supply. HED considers dietary residue contributions greater than 100% of the PAD to be of concern.

Sugar beet and potato ARs were based on the addition of ½ the sum of the limit of quantitation (LOQ) (0.01 ppm) for each regulable metabolite (TPTH-parent, MPTH and DPTH) for samples with non-detectable residues. For pecans, the distribution of field trial results, corrected for %CT was used (value for pecans is based on total tin method - i.e., TPTH and its regulable metabolites plus any other form(s) of tin). Processing factors were used in the DEEM™ adjustment factor #1 column where data were available (refined sugar = 0.02x, molasses = 3x, baked potatoes = 0.03x, boiled potatoes = 0.04x and potato wet peel = 3x). To further refine the residues, the boiled potato processing factor (0.04x) was used for potato uncooked, cooked, canned and frozen food forms because data were not available for these food forms (personal communication with C. Swartz, 3/25/99). The DEEM™ default processing factor of 1.92 was used for dried meat. The estimated maximum of %CT for pecans, sugar beets and potatoes was used.

Meat and milk anticipated residues were calculated; the values were inserted probabilistically into this assessment as follows: assumed that the resulting concentration in milk (or meat) applies only to that percentage of milk (or meat) corresponding to the highest %CT for any one feed item for that chemical. For example, the %CT for potatoes and sugar beets (feed items) are 23% and 44%; assume that 44% of the milk contains residues corresponding to the maximum theoretical dietary burden (MTDB) and the remaining 56% of milk are residue free. This is inserted into the Monte Carlo assessment by including the appropriate number of zeroes in an RDF file such that there is only a 44% probability of encountering a residue corresponding to the MTDB and an 56% probability of encountering a zero value (Guidance for Submission of Probabilistic Human Health Exposure Assessments to OPP, 11/5/99).

DEEM™ has consumption data for five subgroups of females in the category "females 13+ years old": females 13+ years old, pregnant, not-nursing; females 13+ years old nursing; females 13-19 years old, not pregnant, not nursing; 20+ years old, not pregnant, not nursing, and females 13-50 years old. For probabilistic assessments, HED policy is to regulate at the 99.9th percentile. As shown in Table 8, the acute dietary residue contribution at the 99.9th percentile (and at the 99th percentile) occupied more than 100% (306%) of the PAD for females 13+ years old, the population subgroup of concern for acute oral exposure, and therefore exceeds HED's level of concern. No acute dietary risk assessment is required for the general population (no acute toxicity endpoint identified). This Tier 3 acute analysis for TPTH is a refined estimate with all

input residues equal to the respective anticipated residue value, processing factor (where applicable), and %CT.

Table 8. Summary of Acute Dietary Exposure From TPTH.

Subgroups	95th Percentile Exposure (mg/kg/day) |% acute PAD|	99th Percentile Exposure (mg/kg/day) |% acute PAD|	99.9th Percentile Exposure (mg/kg/day) |% acute PAD|
Females (20+ years old/not pregnant/ not nursing)	0.000647 [65%]	0.001150 [11%]	0.003613 [361%]
Females (13-19 years old/ not pregnant/not nursing)	0.000762 [76%]	0.001402 [140%]	0.002729 [273%]
Females (13+/pregnant/not nursing)	0.000676 [67]	0.001215 [121]	0.003091 [309]
Females (13+ years old, nursing)	0.000692 [69%]	0.001275 [127%]	0.003452 [345%]
Females (13-50 years old)	0.000688 [69%]	0.001226 [122%]	0.003062 [306%]

4.3.2 Chronic Dietary Exposure Assessment

A chronic (non-cancer and cancer) exposure analysis was performed using the DEEM™ exposure modeling software. The input values for the Tier 3 analysis include anticipated residues and incorporated processing factors and percent of the crop treated information from BEAD. The respective weighted average of percent crop treated was used for each crop: pecans (35%), potatoes (13%) and sugar beets (35%). Exposure (consumption) was compared to the chronic PAD of 0.00003 mg/kg/day (FQPA Safety Factor Committee Report, 12/17/98).

The chronic ARs were calculated for potatoes and sugar beets based on the addition of ½ the limit of quantitation (LOQ) of 0.01 ppm for each regulable metabolite (TPTH-parent, MPTH and DPTH) for samples with non-detectable residues. The sugar beet value was further corrected for an exaggerated application rate. For pecans, the average residue value from the field trial results was used (value for pecans is based on total tin method) and corrected for %CT. Processing factors were used in the DEEM™ adjustment factor #1 column where data were available (refined sugar = 0.02x, molasses = 3x, baked potatoes = 0.03x, boiled potatoes = 0.04x and potato wet peel = 3x). The DEEM™ default processing factor of 1.92 was used for dried meat. The weighted average of %CT for pecans, sugar beets and potatoes was used.

As shown in Table 9, the chronic dietary residue contribution occupies more than 100% of the PAD for all population subgroups and therefore does exceed HED's level of concern. Chronic dietary exposure comprised 279% of the PAD for the U.S. population and for the most highly exposed subgroup, children 1-6, the residue contribution occupies 596% of the chronic PAD.

This Tier 3 chronic analysis for TPTH is a refined estimate where anticipated residues from crop field trials, processing factors (where data were available) and %CT were used as inputs.

Table 9. Summary of Chronic Dietary Exposure From TPTH.

Subgroups	Total Chronic Dietary Exposure (mg/kg/day)	Percent of Chronic PAD (%cPAD)
U.S. Population	0.000084	279
All Infants (<1 year old)	0.000042	140
Nursing Infants (<1 year old)	0.000021	70
Non-nursing Infants (<1 year old)	0.000051	170
Children (1-6 years old)	0.000179	596
Females (13+ ys. old/preg./nn)	0.000067	222

4.3.3 Cancer Dietary Exposure Assessment

The cancer risk estimate for the U.S. population is 1.53×10^{-4}; this risk is based on a conservative 70 year exposure estimate for the U.S. population. This estimate is **excess the level** the Agency generally considers negligible for excess lifetime cancer risk.

4.3.4 Dietary Exposure (Drinking Water Source)

A Drinking Water Level of Comparison (DWLOC) is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. OPP uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. DWLOC values are not regulatory standards for drinking water. They do have an indirect regulatory impact through aggregate exposure and risk assessments. OPP compares the DWLOC value calculated for each type of risk assessment to the appropriate concentration estimate in surface and ground water. If the DWLOC value is greater than the estimated surface and ground water concentration, OPP believes there is no drinking water concern.

In the case of TPTH, because the estimated exposures to TPTH in food alone exceed HED's levels of concern for each risk assessment conducted (acute, chronic, and cancer) any exposure to TPTH in drinking water would only add to a dietary exposure that already exceeds HED's levels of concern. **Effectively, the DWLOCs for acute, chronic, and cancer risk estimates for all subpopulations are zero until dietary exposure estimates can be refined and the dietary risk estimates reduced.** Therefore, acute, chronic and cancer DWLOCs were not calculated for

TPTH.

Based on a Tier 1 assessment using water quality models and conservative assumptions, estimated concentrations of TPTH in ground water are 0.03 ppb. TPTH partitions to a high degree to soils and is not expected to leach to groundwater. Estimated concentrations of TPTH in surface water range from an average of about 1 ppb to a maximum of 13 ppb. The primary means of transport of TPTH to surface water is by spray drift and soil erosion.

The model used to estimate the groundwater concentrations was SCI-GROW. SCI-GROW is an empirical model that provides a groundwater screening exposure value for use in determining the potential risk to human health from drinking groundwater contaminated with pesticides. SCI-GROW estimates ground water concentrations for pesticides applied at the maximum allowable rate in areas where ground water is vulnerable to contamination. Actual concentrations observed in groundwater may be higher or lower than those derived using SCI-GROW, and actual monitoring data should be used to estimate environmental concentrations when possible. The Environmental Fate and Effects Division (EFED) assumes that in a majority of cases ground water will be less vulnerable to contamination than the areas used to derive the empirical formula used in SCI-GROW. It should be noted the K_{oc} for TPTH (K_{oc}: 5700 ml/g) is out of the range of K_{oc}s (K_{oc}s: 32-180 ml/g) for which SCI-GROW was developed. In general, if the estimated concentration in ground water from SCI-GROW does not exceed the DWLOC, one can be reasonably confident that there is no drinking water concern.

The model used to estimate surface water concentrations was the Generic Estimated Environmental Concentration (GENEEC). Although GENEEC was not originally designed for use in drinking water risk assessments, it can provide a reasonable upper-bound estimate for screening purposes. Using GENEEC as a model for a drinking-water basin implies that the basin has all the characteristics of the "standard" pesticide-application scenario described above. In actuality, drinking-water basin conditions may vary from these conditions. For example, runoff from land that is not treated with pesticide will dilute the actual pesticide concentrations. On the other hand, pesticide-contaminated inflow from upstream sources may serve to increase actual concentrations (while uncontaminated inflow will reduce concentrations). Hydrologic models can rarely reliably predict contaminant concentrations; however, EFED believes that with a conservative choice of input parameters (see below) pesticide-concentration estimates from GENEEC will be high for drinking water basins. If the estimated concentration in surface water from GENEEC does not exceed the DWLOC, one can be reasonably confident there is no drinking water concern.

4.4 Non-Dietary Exposure

Occupational exposure to TPTH residues via dermal and inhalation routes can occur during handling, mixing, loading, applying, and reentry activities. Based on toxicological criteria and potential for exposure, HED has conducted dermal and inhalation exposure assessments for the occupational handler and postapplication worker. Because different endpoint effects were selected for the assessment of dermal and inhalation risks, separate risk assessments were conducted for dermal and inhalation exposures. The duration of exposure is expected to be

short- and intermediate-term for the occupational handler. Exposures were evaluated for both commercial applicators and private growers using TPTH. Private growers are expected to have short-term exposure (i.e., it is assumed that they treat only their own field), while commercial applicators are likely to have both short- and intermediate-term exposure to TPTH (i.e., it is assumed that several fields are treated). The cancer risk assessment was conducted using the sum of dermal and inhalation exposures combined with an oral Q_1*. Separate cancer risks were calculated, where applicable, for commercial applicators and private growers because, in several cases, the number of days these two types of workers are exposed is significantly different.

4.4.1 Occupational Handler Exposure Scenarios

HED has identified 10 major exposure scenarios for which there is potential for occupational handler exposure during mixing, loading, and applying products containing TPTH to pecans, potatoes, and sugar beets. These occupational scenarios reflect mixing/loading and the use of aircraft (for pecans, potatoes, and sugar beets), groundboom sprayer (potatoes and sugar beets), airblast sprayer (pecans only), and chemigation (potatoes only) for application. The scenarios were classified as short-term (1-7 days) and intermediate-term (1 week to several months) based primarily on the frequency of exposure. A long term exposure duration is not expected. In general, the estimated exposures considered baseline protection (long pants and a long-sleeved shirt, no gloves, and an open cab or tractor), additional personal protective equipment (PPE, which includes a double layer of clothing and gloves and/or a dust/mist respirator), and engineering controls (water-soluble bags for wettable powder, closed mixing/loading systems for liquids, and enclosed cabs/trucks).

4.4.1.1 Occupational Handler Exposure Data Sources and Assumptions

The maximum and typical application rates used in the assessment are from TPTH labels and from information provided by BEAD. BEAD also provided the information concerning the acres treated per day based on equipment type.

The registrant submitted a monitoring study for mixing/loading TPTH wettable powder formulated in water-soluble bags (MRID# 43599401). HED found the data to be acceptable after certain adjustments were made and the surface area of the face used in the calculations was corrected from 500 cm^2 to 1,300 cm^2 (i.e., the registrant had used a protection factor to account for the wearing of a hat). The corrected mixing/loading unit exposures for dermal and inhalation used in this assessment are 0.046 mg/lb ai and 0.000071 mg/lb ai, respectively.

The registrant also submitted a monitoring study for the application of TPTH to pecan groves with an airblast sprayer (MRID# 40816901). HED found the data to be acceptable, but only applicable to exposure for an enclosed cab tractor. Although mixer/loader data were also submitted with this study, these data were not applicable because open pour practices are no longer used. The total dermal unit exposure was estimated to be 0.021 mg/lb ai; inhalation exposure was not measured.

It is the policy of HED to combine submitted chemical-specific data, when possible, with that

from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions. The data from the exposure study for wettable powder in water-soluble bags were not combined with PHED data, but instead were used solely to estimate unit exposure because the confidence in the PHED data for this scenario is low. The airblast sprayer exposure data were combined with PHED data for the enclosed cab scenario.

For scenarios that do not have chemical-specific data submissions, it is the policy of the HED to use data from PHED to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available. PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates). While data from PHED provides the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases.

4.4.1.2 Occupational Handler Risk Characterization

Because different endpoint effects were selected for the assessment of non-cancer dermal and inhalation risks, separate risk assessments were conducted for dermal and inhalation exposures. Both short- and intermediate-term MOEs for occupational handlers were derived based upon comparison of dermal exposure estimates against a NOAEL of 3 mg/kg/day from a dermal developmental study in the rabbit. Inhalation MOEs were derived based upon comparison of inhalation exposure estimates against a NOAEL of 0.00034 mg/m^3 which translates to 0.092 mg/kg/day. **The uncertainty factors and target MOEs for occupational workers are 100 for short- and intermediate-term dermal risk and inhalation risk. MOEs below this level would represent a risk concern for the Agency.** The cancer assessment used an oral Q_1* based on an oral rat and mouse studies. To calculate exposure, a 10 percent dermal absorption (based on camparison between rabbit oral and dermal studies) was used, while inhalation absorption was assumed to be 100 percent. The dermal and inhalation exposures were summed to calculate a total exposure, which was combined with the Q_1* to estimate cancer risk. **Cancer risk estimates greater that 1.0E-4 would represent a risk concern for the Agency.**

A summary of the short- and intermediate-term dermal and inhalation risk estimates for baseline, additional PPE, and engineering controls is presented in Appendix 3. A summary of the cancer risk estimates for baseline, additional PPE, and engineering controls is presented in Appendix 4. Baseline dermal unit exposure represents long pants, long sleeved shirt, no gloves, no respirator, and open cab tractor. Additional PPE includes double layer of clothing (50% protection factor for clothing), chemical-resistant gloves, and a dust/mist respirator. Depending on the scenario, engineering controls include closed mixing/loading or water-soluble bag, single layer clothing, chemical-resistant gloves (scenarios 1abc, 2abc, and 5 only), enclosed cab, enclosed cockpit, or enclosed truck (98% protection factor).

NOTE: Default PPE requirements based on the toxicity categories of TPTH technical material are as follows: Toxicity category II dermal requires a double layer of body protection (coverall worn over long pants and long sleeved shirt), shoes and socks and chemical-resistant gloves. Toxicity Category I inhalation requires a respiratory protective device.

Non-Cancer Risk Characterization: The estimates for short- and intermediate-term dermal and inhalation risks have not been combined because dermal and inhalation endpoint effects are different.

Dermal short- and intermediate-term risk at baseline ranged from 33 to 50 for scenario (5) application of sprays to orchards with an airblast sprayer at maximum and typical application rates. PPE (personal protective equipment) did not mitigate these risks, but engineering controls raised the MOEs to 630 and 950, which are substantially below HED's level of concern. Seven scenarios (1abc, 2abc, 3, 6, 7, 8 and 9) required engineering controls by default because unit exposure data for baseline and PPE are either not applicable or not available. The engineering control scenario (2a) mixing and loading wettable powder in water-soluble bags for aerial/chemigation application yielded MOEs that ranged from 21 to 31 even when typical application rates, rather than maximum rates, were used. The engineering control scenarios (1a) mixing and loading liquids for aerial/chemigation application and for mixing and loading and (8) applying wettable powder in water-soluble bags with a groundboom sprayer had MOEs of 84 and 94, respectively, when the maximum application rate was used. These MOEs were mitigated to 170 and 190, respectively, with the use of the typical application rate.

For scenario 2a, engineering controls (plus chemical-resistant gloves) in conjunction with the use of typical application rates, rather than maximum application rates, are not adequate to mitigate dermal risks to an MOE of 100 or more.

The **inhalation** risk estimate at baseline was 95 for scenario (5) application of sprays to orchards with an airblast sprayer at the maximum application rate. This risk estimate was mitigated to an MOE of 140 with the use of the typical application rate, and an MOE of 480 with PPE.

Cancer Risk Estimate Characterization: The estimates for dermal and inhalation exposures (including the appropriate absorption factors) have been combined to a total dose because an oral Q_1^* was used.

The **cancer** risk estimate at baseline was 1.4E-4 for scenario (4) commercial application of sprays with a groundboom sprayer, while for the private grower, the cancer risk was 4.3E-6. As mentioned previously, seven scenarios (1abc, 2abc, 3, 6, 7, 8 and 9) require engineering controls by default. Of these, the scenarios (2ab) mixing and loading wettable powder in water-soluble bags for aerial/chemigation application and for groundboom application yielded cancer risks ranging from 1.8E-4 to 3.1E-4 for the commercial applicator. For the private grower, the cancer risk estimates for these same scenarios ranged from 7.3E-6 to 1.9E-4.

For scenario 2ab, engineering controls (plus chemical-resistant gloves) in conjunction with the use of typical application rates are not adequate to mitigate cancer risk estimates to below 1.0E-4.

A number of issues must be considered when interpreting the results of the occupational risk assessment:

- Daily acres to be treated in each scenario. These are based on use information gathered by the Biological and Economic Analysis Division (BEAD). The typical daily acres treated are as follows: 40 acres for airblast application to pecan orchards, 150 acres for groundboom application to potatoes and sugar beets, 1,000 acres for aerial application to potatoes and sugar beets, and 400 acres for aerial application to pecan orchards (this is rarely done). Specific data were not available for private growers using chemigation for potatoes, or for flaggers during aerial application; therefore, the Exposure Science Advisory Council estimate of 350 acres (for aerial and chemigation applications in agricultural settings) was used as a default. Although a typical aerial application of TPTH treats 1,000 acres, it is likely that an automated means of flagging, rather than human flaggers, would be employed for applications to greater than 350 acres.

- For the non-cancer assessment, calculations were completed using the maximum application rates for specific crops recommended by the available TPTH labels. "Typical" application rates were also used in the calculations in cases where maximum rates yielded risks that exceed the appropriate level of concern (i.e., MOE < 100 or Cancer risk > 1E-4). Typical application rates were used in the calculations for the cancer assessment.

- Due to a lack of scenario-specific data, HED often must calculate unit exposure values using generic protection factors (PF) to represent various risk mitigation options (i.e., the use of personal protective equipment (PPE) and engineering controls). PPE protection factors include those representing a double layer of clothing (50 percent PF for body exposure), chemical resistant gloves (90 percent PF for hand exposure), and respiratory protection (80 percent PF for use of dust/mist mask).

- Surrogate PHED data were used to assess exposure for all but two of the major exposure scenarios (2abc - mixing/loading wettable powder in water-soluble bags, and 5 - applying sprays to orchards with an airblast sprayer). Surrogate PHED unit exposure values generally fall between the geometric mean and the median of the data set used to calculate the value.

- The majority of the samples from the study for mixing/loading wettable powder in water-soluble bags (scenario 2abc) had levels reported at less than the LOD. One-half the LOD was used to calculate the unit exposure (consistent with current HED policy) which may overestimate exposure. However, because such a small amount of material was handled during the study (one water-soluble bag per 500 gallon tank, per replicate), the exposure may actually be underestimated. It should be noted that if the PHED dermal

unit exposure (0.021 mg/lb ai) for this scenario was used instead of the study dermal unit exposure (0.046mg/lb ai), most of the risks that currently exceed HED's level of concern would remain a concern.

- Several handler assessments were completed using "low quality" PHED data due to the lack of a more acceptable data set (see Table 3 for the specific scenarios where only "low quality" data were available).

Incident Reports

HED has reviewed the OPP Incident Data System (IDS), the Poison Control Center, the California Department of Food and Agriculture (replaced by the Department of Pesticide Regulation in 1991), and the National Pesticide Telecommunications Network (NPTN) databases for reported incident information for TPTH. No data were reported from PCC or California Department of Food and Agriculture. From the NPTN, TPTH was not reported to be involved in human incidents out of the list of the top 200 chemicals for which MPTN received calls from 1984-1991. Seven cases were submitted to the IDS; however, the cases from the IDS do not have documentation confirming exposure or health effects unless otherwise noted. HED concluded that relatively few incidents of illness from exposure to TPTH have been reported. No recommendations can be made based on the few incident reports available (See memo, J. Blondell/M. Spann, D251180).

4.4.2 Occupational Postapplication Exposure

HED has determined that there are potential postapplication exposures to individuals entering treated areas for the purpose of:

- Harvesting pecans (although this is done mechanically, it is a very dusty operation);
- Scouting and moving hand-set irrigation pipes for potatoes and sugar beets; and
- Harvesting, sorting/packing, and brushing/washing potatoes and sugar beets. Although this is usually done mechanically for potatoes, there may be some farms at which these activities are performed by hand. For sugar beets, these activities are done almost exclusively by mechanical means and, therefore, were not assessed. However, in the case that hand methods are used for sugar beet harvesting, the exposures are not expected to exceed those encountered during potato-harvesting activities.

None of these crop activities have been identified as scenarios yielding potential chronic exposure (i.e., ≥ 180 days of exposure/year) concern.

4.4.2.1 Data Sources and Assumptions for Postapplication Exposure Calculations

The registrant submitted a reentry study of pecan workers operating windrowing equipment as part of pecan harvesting activities (MRID# 43557401). Both dermal and inhalation exposure monitoring were conducted. In addition, soil and thatch samples were collected fro the dripline beneath the treated pecan trees. HED found the data to be acceptable. The geometric means of the monitoring data, as well as the soil/thatch residue levels, were used in the assessment.

The registrant also submitted soil and foliar dissipation data that were collected following applications of TPTH to potatoes and peanuts (MRID# 42507801). HED found the data acceptable and deemed the potato data useful for the sugar beet assessment because they both have similar application rates and cultural techniques. TPTH did not appear to dissipate in the soil; therefore, the highest daily mean level (1.36 parts per billion TPTH) at one day post application was used in the assessment. The soil level was used in conjunction with a soil/dermal transfer coefficient of 3.9 ng/ppb/hr. The foliar dissipation curve is (log Y = -0.0573X + -0.498), from the TPTH foliar dissipation study accepted by EPA in 1986 (Y = the dislodgeable foliar residue in $\mu g/cm^2$ and X = the number of days after the application).

The assumptions used in the calculations for occupational postapplication risks include the following items:

- Application rates used for the calculations were derived using the following strategy:

  -- Harvesting pecans = not applicable, study provides exposure values (µg/kg/hr), therefore the calculation using application rate is not necessary (incidentally, the application rate was 0.375 lb ai/acre)
  -- Harvesting and maintenance activities for potatoes (non-cancer) = 0.1875 lb ai/acre
  -- Maintenance activities for sugar beets (non-cancer) = 0.25 lb ai/acre
  -- Harvesting and maintenance activities for potatoes or sugar beets (cancer) = 0.125 lb ai/acre

- Transfer coefficients (Tc) are not necessary for pecan harvesting estimates because the study provides exposure values (µg/kg/hr). For potato harvesting, a soil/dermal transfer coefficient of 3.9 ng/ppb/hr was used, based on the "Youth in Agriculture" study mentioned previously. For maintenance activities associated with potatoes and sugar beets, the transfer coefficient was assumed to be 2,500 cm2/hr.

- Daily exposure is assumed to occur for 8 hours per day.

- The average body weight of 60 kg is used in the non-cancer risk estimates (due to a developmental endpoint), while for cancer estimates, 70 kg is used, representing a typical adult.

- Exposure frequency is estimated to be 40 days/year for pecan harvesting, and 30 days/year for potato and sugar beet maintenance activities and harvesting.

- Exposure duration is assumed to be 35 years. This represents a typical working lifetime.

- Lifetime is assumed to be 70 years.

- Dermal absorption is assumed to be 10 percent for cancer estimates because the Q1* is not based on a dermal study, as in the handler assessment.

- The Q1* used in the cancer assessment is 1.83E+00 mg/kg/day -1.

4.4.2.2 Occupational Postapplication Risk Characterization

The postapplication risks are summarized in Appendices 5 through 7 . The postapplication assessment indicates that for pecan harvesting, MOEs exceed 100 on day zero after application, while cancer risk estimates are greater than 1.0E-4 until 7 days after the last application at the Georgia site, and between 21 and 30 days after the last application at the Texas site. MOEs for maintenance activities are ≥100 on day zero after application for potatoes, and on the second day after application for sugar beets. The cancer risk estimate for maintenance activities was found to be less than 1.0E-4 on the second day after application for both potatoes and sugar beets. The MOE and cancer risk estimate for potato harvesting do not exceed HEDs level of concern on any day after application.

The current reentry interval (REI) is 48 hours for all crops. TPTH has the potential to be a primary eye irritant (toxicity category I), which triggers the worker protection standard's (WPS) default REI of 48 hours.

The following issues must be considered when interpreting the results of the postapplication occupational risk assessment:

- Chemical-specific exposure and transferable residue data were used to complete this assessment. Most of these data have undergone at least primary review and have been considered acceptable, however, the studies are several years old and may require a more recent evaluation to ensure that adjustments were made according to our current policies.

- For the maintenance activities assessment, the non-cancer calculations were completed using the maximum application rates for specific crops recommended by the available TPTH labels. Typical application rates were used in the calculations for the cancer assessment.

- Factors used to calculate postapplication risks (e.g., hours exposure per day or days worked) are based on best professional judgment due to lack of data specific

to each crop/activity combination.

4.5 Residential Exposure

There are no residential or non-occupational uses for TPTH; therefore exposures are not likely, nor are postapplication exposures expected. There is potential for spray drift during aerial application, however, HED does not currently have an approved method of assessing this scenario. Incident data does not indicate that spray drift is a problem.

4.5.1 Cumulative Exposure

For risk assessment purposes, HED has not assumed that TPTH has a common mechanism of toxicity with any other chemicals.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

5.1 Acute Aggregate Risk Estimate

The acute aggregate risk assessment for TPTH includes risk estimates associated with dietary exposure through food and water, only. Because exposure to TPTH from food sources alone exceed HED's level of concern for acute dietary risk, any additional exposure through drinking water would lead to risk estimates that further exceed HED's level of concern. HED defers a calculation of aggregate risk as a result of exposures to TPTH in food and water until estimates of exposure through food alone have been reduced to an acceptable level. At that time, the OPP can reconsider the extent of the contribution, if any, of TPTH residues in drinking water to the acute exposure and aggregate risk estimates.

5.2 Short- and Intermediate-Term Aggregate Risk Estimates

Short- and Intermediate-Term aggregate risk estimates are not required because there are no residential uses.

5.3 Chronic (Non-Cancer) Aggregate Risk Estimate

The chronic aggregate risk assessment for TPTH includes risk estimates associated with dietary exposure through food and water, only. Because exposure to TPTH from food sources alone exceed HED's level of concern for chronic dietary risk, any additional exposure through drinking water would lead to risk estimates that further exceed HED's level of concern. HED defers a calculation of aggregate risk as a result of chronic exposures to TPTH in food and water until estimates of exposure through food alone have been reduced to an acceptable level. At that time, the OPP can reconsider the extent of the contribution, if any, of TPTH residues in drinking water to the chronic exposure and aggregate risk estimates.

5.4 Cancer Aggregate Risk

The cancer aggregate risk assessment for TPTH includes risk estimates associated with dietary exposure through food and water, only. (There are no registered residential uses of TPTH.) Because exposure to TPTH from food sources alone exceed HED's level of concern for cancer

dietary risk estimates, any additional exposure through drinking water would lead to risk estimates that further exceed HED's level of concern. HED defers a calculation of aggregate risk as a result of exposures to TPTH in food and water until estimates of exposure through food alone have been reduced to an acceptable level. At that time, the OPP can reconsider the extent of the contribution, if any, of TPTH residues in drinking water to the cancer exposure and aggregate risk estimates.

6.0 DATA NEEDS

Additional data requirements have been identified in the attached Science Chapters and are summarized here.

Toxicology Data for OPPTS Guidelines:

81-8 (870.6200). Acute Neurotoxicity screen
82-7 (870.6200). Subchronic Neurotoxicity screen
Special Study. Developmental Immunotoxicity screen (consult with Agency on protocol).

Product and Residue Chemistry Data for OPPTS Guidelines:

Pertinent product chemistry data requirements remain unfulfilled for all of the registered 96% T/TGAIs.
(i). 830.7050. Griffin 96% T.
(ii). 830.1550, 1700, 1750, 1800, 6314, 6316, 7050 and 7370. Elf Atochem 96% T.
(iii). 830.1550 and 7050. AgrEvo 96% T.
(iv). 830.1550, 1750, 6314, 6316, 6317, 6320 and 7050. Agtrol 96% T.
(v). 860.1340 Method: Independent Laboratory Validation (for animal method) and Radiovalidation (plant and animal methods).
(vi). 860.1360. Multiresidue Testing.
(vii). 860.1380 Storage Stability.

Occupational Exposure Data for OPPTS Guidelines:

- Factors used to calculate postapplication risks (e.g., hours exposure per day or days worked) are based on best professional judgment due to lack of data specific to each crop/activity combination.

APPENDICES

Appendix 1: Food/Feed Use Patterns Subject To Reregistration for Triphenyltin Hydroxide.

Appendix 2: Summary of Occupational Handler Dermal and Inhalation Non-Cancer Risk Estimates for TPTH at Baseline, with PPE, and Engineering Controls.

Appendix 3: Summary of Occupational Handler Cancer Risk Estimates for TPTH at Baseline, with PPE, and Engineering Controls.

Appendix 4: Summary of Estimated Postapplication Risk Estimates Based on Residue Ratios During Pecan Harvesting.

Appendix 5: Summary of Postapplication Risk Estimates from TPTH During Maintenance Activities.

Appendix 6: Summary of Postapplication Risk Estimates from TPTH During Potato Harvesting.

Appendix 7: Residue Chemistry Science Assessments for Reregistration of Triphenyltin Hydroxide.

ATTACHMENTS (083601)

Report of the Hazard Identification Assessment Review Committee. Doherty/Rowland (11/13/98)
Report of the FQPA Safety Factor Committee. Brenda Tarplee (12/17/98)
Product and Residue Chemistry Chapter. Catherine Eiden (04/12/99; D255158)
Toxicology Chapter. John Doherty (03/22/99; D254359)
Occupational and Residential Exposure Assessment. Kelly O'Rourke (5/6/99; D250108)
Dietary Exposure and Risk Estimates for Reregistration. Sarah Law (04/13/99; D254712, D254713)
Incident Report. Jerome Blondell and Monica Spann (12/23/98; D251180)
Tier I Estimated Environmental Concentrations for Triphenyltin Hydroxide. D. Young (02/26/99, D250265)
TPTH Revised Q_1^* (3/4's Interspecies Scaling Factor). Bernice Fisher and Hugh Pettigrew (08/18/98)

cc: Without Attachments: P. Deschamp, Caswell File

APPENDIX 1

Food/Feed Use Patterns Subject To Reregistration for Triphenyltin Hydroxide (Case 0099).

Site Application Type Application Timing Application Equipment [a]	Formulation [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)	Max. # Apps./season	Minimum Retreatment Interval (Days)	Use Limitations [b]
Sugar beets					
Broadcast foliar applications Aerial or ground equipment	4 lb/gal FlC [1812-244] [45639-186] 80% WP [1812-350] 0.5 lb/gal EC [1812-351] 47.5% WP [45639-170]	0.25	3	10	The labels specify a maximum rate of 0.75 lb ai/A/season. The minimum volume for aerial and ground applications is 5 and 15 gal/A, respectively. The label prohibits the grazing or feeding of sugar beet tops to livestock. A 21-day PHI is specified except on the 47.5% WP label which specifies a 14-day PHI.
Potatoes					
Broadcast foliar application Aerial, ground or chemigation equipment	4 lb/gal FlC [1812-244] [45639-186] 80% WP [1812-350] 0.5 lb/gal EC [1812-351]	0.19	4	7 [c]	The label specifies a maximum rate of 0.75 lb ai/A/season. The minimum volume for aerial applications is 3 gal/A. A 21-day PHI is specified.
	47.5% WP [45639-170]	0.24	3	7	The label allows a maximum rate of 0.71 lb ai/A/season. The minimum volume for aerial applications is 3 gal/A. A 7-day PHI is specified.

Appendix 1 continued.

Site Application Type Application Timing Application Equipment [a]	Formulation [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)	Max. # Apps./season	Minimum Retreatment Interval (Days)	Use Limitations [b]
Pecans					
Broadcast foliar applications Aerial or ground equipment	4 lb/gal FlC [1812-244] 80% WP [1812-350] 47.5% WP [45639-170]	0.38	10	14	The label allows a maximum of 3.8 lb ai/A/season. The minimum volume for aerial applications is 20 gal/A. The label prohibits applications after shucks have started to open; a PHI is not specified.

[a] The labels prohibit application through any type of irrigation system except on potatoes. Chemigation of potatoes through any irrigation system other than the following is prohibited: sprinkler including center pivot, lateral move, end tow, side (wheel) roll, traveler, big gun, solid set, or hand move irrigation systems.

[b] The labels specify a 48-hour restricted entry interval (REI) for all crops with the exception of labels for the 47.5% WP (EPA Reg. No. 45639-170) and a 4 lb/gal FlC (EPA Reg. No. 45639-186) which specify a 24-hour REI.

[c] Use directions for potatoes on the 4 lb/gal FlC labels (EPA Reg Nos. 1812-244 and 45639-186) do not indicate a RTI. These labels state that applications to potatoes "should begin with the appearance of blight weather conditions and continue as needed."

APPENDIX 2

Summary of Occupational Handler Dermal and Inhalation Non-Cancer Risk Estimate for TPTH at Baseline, with PPE, and Engineering Controls.

Exposure Scenario (Scenario #)	Crop	Application Rate (lb ai /A)	Dermal Short- and Intermediate-Term MOE = 100			Inhalation MOE = 100			Input Parameters and Potential Mitigation Measures
			Baseline	PPE	Engineering Controls	Baseline	PPE	Engineering Controls	
MIXER/LOADER RISK									
Mixing/Loading Liquids for Aerial/Chemigation Application (1a)	Pecans	0.375	See Eng. Control	See Eng. Control	140	See Eng. Control	See Eng. Control	520	
	Potatoes	0.1875			110			410	
	Sugar beets	0.25			84			310	The maximum application rate is driving this risk.
	Sugar beets	0.125 (Typ)			170			N/A[2]	
Mixing/Loading Liquids for Groundboom Application (1b)	Potatoes	0.1875			740			2,800	
	Sugar beets	0.25			560			2,100	
Mixing/Loading Liquid for Orchard Airblast Sprayer Application (1c)	Pecans	0.375			1,400			5,200	
Mixing/Loading Wettable Powder (WSB) for Aerial/Chemigation Application (2a)	Pecans	0.375	See Eng. Control	See Eng. Control	26	See Eng. Control	See Eng. Control	600	Both the activity (i.e., the unit exposure) and the number of acres treated per day (1,000) are driving these risks.
	Pecans	0.25 (Typ)			39			N/A[2]	
	Potatoes	0.1875			21			480	
	Potatoes	0.125 (Typ)			31			N/A[2]	
	Sugar beets	0.25			16			360	
	Sugar beets	0.125 (Typ)			31			N/A[2]	
Mixing/Loading Wettable Powder (WSB) for Groundboom Application (2b)	Potatoes	0.1875			140			3,200	
	Sugar beets	0.25			100			2,400	
Mixing/Loading Wettable Powder (WSB) for Orchard Airblast Sprayer Application (2c)	Pecans	0.375			260			6,000	

Summary of Occupational Handler Dermal and Inhalation Non-Cancer Risk Estimate for TPTH at Baseline, with PPE, and Engineering Controls.

Exposure Scenario (Scenario #)	Crop	Application Rate (lb ai /A)	Dermal Short- and Intermediate-Term MOE = 100			Inhalation MOE = 100			Input Parameters and Potential Mitigation Measures
			Baseline	PPE	Engineering Controls	Baseline	PPE	Engineering Controls	
APPLICATOR RISK									
Applying Sprays with a Fixed-Wing Aircraft (3)	Pecans	0.375	No Data See Eng. Cont.	No Data See Eng. Cont.	240	No Data See Eng. Cont.	No Data See Eng. Cont.	630	
	Potatoes	0.1875			190			510	
	Sugar beets	0.25			140			380	
Applying Sprays with a Groundboom Sprayer (4)	Potatoes	0.1875	460	580	1,300	310	1,500	5,300	
	Sugar beets	0.25	340	440	960	230	1,100	4,000	
Applying Sprays to Orchards with an Airblast Sprayer (5)	Pecans	0.375	33	55	630	95	480	950	Both the maximum application rate and the activity (i.e., unit exposure) are driving this risk.
	Pecans	0.25 (Typ)	50	82	950	140	720	1,400	The activity (i.e., unit exposure) is driving this risk.
MIXER/LOADER/APPLICATOR RISK									
Mixing/Loading Liquids and Applying Sprays with a Groundboom Sprayer (6)	Potatoes	0.1875	N/A[1]	N/A[1]	470	N/A[1]	N/A[1]	1,800	
	Sugar beets	0.25			350			1,400	
Mixing/Loading Liquids and Applying Sprays to Orchards with an Airblast Sprayer (7)	Pecans	0.375	N/A[1]	N/A[1]	430	N/A[1]	N/A[1]	810	
Mixing/Loading Wettable Powder (WSB) and Applying Sprays with a Groundboom Sprayer (8)	Potatoes	0.1875	N/A[1]	N/A[1]	130	N/A[1]	N/A[1]	2,000	
	Sugar beets	0.25			94			1,500	The maximum application rate is driving this risk.
	Sugar beets	0.125 (Typ)			190			N/A[2]	
Mixing/Loading Wettable Powder (WSB) and Applying Sprays to Orchards with an Airblast Sprayer (9)	Pecans	0.375	N/A[1]	N/A[1]	180	N/A[1]	N/A[1]	820	

Summary of Occupational Handler Dermal and Inhalation Non-Cancer Risk Estimate for TPTH at Baseline, with PPE, and Engineering Controls.

Exposure Scenario (Scenario #)	Crop	Application Rate (lb ai /A)	Dermal Short- and Intermediate-Term MOE = 100			Inhalation MOE = 100			Input Parameters and Potential Mitigation Measures
			Baseline	PPE	Engineering Controls	Baseline	PPE	Engineering Controls	
FLAGGER RISK									
Flagging Spray Applications (10)	Pecans	0.375	120	140	6.,200	140	700	7,000	
	Potatoes	0.1875	250	270	12,000	280	1,400	14,000	
	Sugar beets	0.25	190	210	9,400	210	1,100	11,000	

N/A[1] - There is no unit exposure for mixer/loader to add to the applying unit exposure until engineering controls.
N/A[2] - Inhalation MOE is not of concern at the maximum application rate; therefore, an assessment of the typical application was not necessary.

Baseline unit exposure represents long pants, long sleeved shirt, no gloves, open cab tractor, and no respirator. Additional PPE includes double layer of clothing (50% protection factor for clothing), chemical resistant gloves, and a dust/mist respirator. Engineering controls include closed mixing/loading or water-soluble bag, single layer clothing, chemical resistant gloves (scenarios 1abc, 2abc, and 5 only), enclosed cab, enclosed cockpit, or enclosed truck (98% protection factor). Application rates are based on the maximum application rates listed on the TPTH labels, and on typical application rates reported by BEAD. Acres treated per day are from BEAD reports of the acres treated in one work day.

Two scenarios (4 and 10) do not require additional PPE or engineering controls to mitigate dermal (short- and intermediate-term) or inhalation concerns. Seven scenarios (1abc, 2abc, 3, 6, 7, 8 and 9) require engineering controls by default because unit exposures for baseline and PPE are either not applicable or not available. Scenario 5 requires engineering controls to mitigate dermal risks from applying TPTH-containing products.

Please note that for scenario 2abc, engineering controls (plus chemical-resistant gloves) in conjunction with the use of typical application rates, rather than maximum application rates, are not adequate for mitigation of dermal risks.

APPENDIX 3

Summary of Occupational Handler Cancer Risk Estimate for TPTH at Baseline, with PPE, and Engineering Controls.

Exposure Scenario (Scenario #)	Crop	Application Rate (lb ai /A)	Cancer Risk Estimate			Input Parameters and Potential Mitigation Measures
			Baseline	PPE	Engineering Controls	
MIXER/LOADER RISK						
Mixing/Loading Liquids for Aerial/Chemigation Application (1a)	Pecans	0.25	See Eng. Control	See Eng. Control	3.4E-6	
	Potatoes	0.125			6.3E-5 / 1.5E-6	
	Sugar beets	0.125			3.8E-5	
Mixing/Loading Liquids for Groundboom Application (1b)	Potatoes	0.125			6.1E-5 / 1.9E-6	
	Sugar beets	0.125			3.7E-5 / 1.9E-6	
Mixing/Loading Liquid for Orchard Airblast Sprayer Application (1c)	Pecans	0.25			1.0E-6	
Mixing/Loading Wettable Powder (WSB) for Aerial/Chemigation Application (2a)	Pecans	0.25	See Eng. Control	See Eng. Control	1.7E-5	
	Potatoes	0.125			3.1E-4 / 7.3E-6	Both the activity (i.e., the unit exposure) and the number of acres treated per day (1,000) are driving these risks.
	Sugar beets	0.125			1.9E-4	
Mixing/Loading Wettable Powder (WSB) for Groundboom Application (2b)	Potatoes	0.125			3.0E-4 / 9.4E-6	
	Sugar beets	0.125			1.8E-4 / 9.4E-6	
Mixing/Loading Wettable Powder (WSB) for Orchard Airblast Sprayer Application (2c)	Pecans	0.25			5.0E-6	
APPLICATOR RISK						
Applying Sprays with a Fixed-Wing Aircraft (3)	Pecans	0.25	No Data See Eng. Cont.	No Data See Eng. Cont.	2.0E-6	
	Potatoes	0.125			3.8E-5	
	Sugar beets	0.125			2.3E-5	
Applying Sprays with a Groundboom Sprayer (4)	Potatoes	0.125	1.4E-4 / 4.3E-6	8.1E-5 / 2.5E-6	3.5E-5 / 1.1E-6	The number of acres treated per day (150) is driving this risk.
	Sugar beets	0.125	8.3E-5 /	4.9E-5 /	2.1E-5 / 1.1E-6	

Summary of Occupational Handler Cancer Risk for TPTH at Baseline, with PPE, and Engineering Controls

Exposure Scenario (Scenario #)	Crop	Application Rate (lb ai /A)	Cancer Risk Estimate			Input Parameters and Potential Mitigation Measures
			Baseline	PPE	Engineering Controls	
Applying Sprays to Orchards with an Airblast Sprayer (5)	Pecans	0.25	4.4E-5	2.5E-5	2.5E-6	
MIXER/LOADER/APPLICATOR RISK						
Mixing/Loading Liquids and Applying Sprays with a Groundboom Sprayer (6)	Potatoes	0.125	N/A	N/A	3.0E-6	
	Sugar beets	0.125			3.0E-6	
Mixing/Loading Liquids and Applying Sprays to Orchards with an Airblast Sprayer (7)	Pecans	0.25	N/A	N/A	3.5E-6	
Mixing/Loading Wettable Powder (WSB) and Applying Sprays with a Groundboom Sprayer (8)	Potatoes	0.125	N/A	N/A	1.1E-5	
	Sugar beets	0.125			1.1E-5	
Mixing/Loading Wettable Powder (WSB) and Applying Sprays to Orchards with an Airblast Sprayer (9)	Pecans	0.25	N/A	N/A	7.5E-6	
FLAGGER RISK						
Flagging Spray Applications (10)	Pecans	0.25	4.5E-6	3.4E-6	9.1E-8	
	Potatoes	0.125	3.4E-5	2.5E-5	6.8E-7	
	Sugar beets	0.125	2.0E-5	1.5E-5	4.1E-7	

N/A - There is no unit exposure for mixer/loader to add to the applying unit exposure until engineering controls.

Baseline unit exposure represents long pants, long sleeved shirt, no gloves, open cab tractor, and no respirator. Additional PPE includes double layer of clothing (50% protection factor for clothing), chemical resistant gloves, and a dust/mist respirator. Engineering controls include closed mixing/loading or water-soluble bag, single layer clothing, chemical resistant gloves (scenarios 1abc, 2abc, and 5 only), enclosed cab, *enclosed cockpit, or enclosed truck* (98% protection factor). Application rates are based on the maximum application rates listed on the TPTH labels, and on typical application rates reported by BEAD. Acres treated per day and number of exposures per year are based on data from BEAD. In the cases where the number of acres treated or the number of exposures per year are different for commercial applicator and private grower, both estimates are presented, separated by a "/" in the following manner: commercial value / private grower value.

Two scenarios (5 and 10) do not require additional PPE or engineering controls to mitigate risk. Seven scenarios (1abc, 2abc, 3, 6, 7, 8 and 9) require engineering *controls by default because unit* exposures for baseline and PPE are either not applicable or not available. Scenario 4 requires additional PPE to mitigate cancer risk for commercial applicators when applying TPTH-containing products.

Please note that for scenario 2ab, engineering controls (plus chemical-resistant gloves) in conjunction with the use of typical application rates *are not adequate for mitigation of cancer risks.*

APPENDIX 4

Summary of Estimated Postapplication Risk Estimates Based on Residue Ratios During Pecan Harvesting.

Days After Last Treatment	Soil/Thatch Residue (ug/g)[a]	Residue Ratio[b]	MOE		Cancer Risk Estimate
			Dermal	Inhalation	
Georgia					
0	42.9	4.0	170	480	1.9E-04
1	23.3	2.2	320	890	1.1E-04
3	27	2.5	270	770	1.2E-04
7	10.8	1.0	680	1900	4.9E-05
14	11.7	1.1	630	1800	5.3E-05
21	18	1.7	410	1200	8.1E-05
30	18.4	1.7	400	1100	8.3E-05
60	10.7	0.99	690	1900	4.8E-05
90	10.9	1.01	680	1900	4.9E-05
120	3.5	0.32	2100	5900	1.6E-05
Texas					
0	7.2	1.76	220	1100	1.4E-04
1	7.4	1.80	220	1100	1.5E-04
3	3.8	0.93	420	2100	7.6E-05
7	6.4	1.56	250	1200	1.3E-04
14	9.2	2.24	170	850	1.8E-04
21	6.2	1.51	260	1300	1.2E-04
30	4.2	1.02	380	1900	8.4E-05
60	4.0	0.98	400	2000	8.0E-05
90	3.1	0.76	520	2500	6.2E-05
120	4.8	1.17	330	1600	9.6E-05

a Soil/thatch residues from pecan harvester exposure study (MRID# 43557401).

b Residue ratios calculated by dividing the residue level on a given day by the residue level on the day exposure samples were collected (assumed to be 10.8 µg/g for GA and 4.1 µg/g for TX).

APPENDIX 5

Summary of Postapplication Risk Estimates from TPTH During Maintenance Activities.

Days After Last Treatment	Potatoes Non-cancer[a] App. Rate: 0.1875 lb ai/A		Sugar beets Non-cancer[a] App. Rate: 0.25 lb ai/A		Potatoes and Sugar beets Cancer[a] App. Rate: 0.125 lb ai/A	
	DFR[b] (ug/cm2)	MOE	DFR[b] (ug/cm2)	MOE	DFR[b] (ug/cm2)	Cancer Risk Estimate
0	0.084	100	0.112	80	0.056	1.2E-04
1	0.074	120	0.099	91	0.049	1.1E-04
2	0.065	140	0.087	100	0.043	9.3E-05

a The maximum application rates (0.1875 lb ai/A and 0.25 lb ai/A) were used for non-cancer assessment of potatoes and sugar beets, respectively. The typical application rate (0.125 lb ai/A) for both potatoes and sugar beets was used to estimate cancer risk.

b Dislodgeable foliar residue. Based on regression equation from study (MRID# 42507801) and using application rate indicated above, initial DFR of 4%, and a dissipation rate of 12% per day.

APPENDIX 6

Summary of Postapplication Risk Estimates from TPTH During Potato Harvesting.

Days After Last Treatment[a]	Non-cance		Cance	
	TR[b] (ppb TPTH)	MOE	TR[b] (ppb TPTH)	Cancer Risk
Any Day	1.36	4,300,000	1.36	4.5E-9

a TPTH was not found to dissipate appreciably in soil; therefore, the above risks are applicable for any day after treatment.

b The transferrable residue was based on the highest daily average residue measured.

Please note that although, in some cases, risks do not exceed HED's level of concern on day zero after application in the above two tables, the MOEs are based on a dermal endpoint, and the cancer risks are based on an oral Q_1^*. TPTH has the potential to be a primary eye irritant (toxicity category I), thus invoking the worker protection standard (WPS) default REI of 48 hours. The 48-hour REI is consistent with the current label; entry prior to this requires PPE as outlined in the WPS.

APPENDIX 7

Residue Chemistry Science Assessments for Reregistration of Triphenyltin Hydroxide.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
860.1200: Directions for Use	N/A	Yes[2]	See Table A.
860.1300: Plant Metabolism	N/A	No	**00030252 00030253 00030254 00030309 00030310 00030311 00086459 00086493 00086494 00124220**
860.1300: Animal Metabolism	N/A	No	**00030250 00030251 00030313 00030315 00030316 00080381 00086552 00086553 00086554 00124220**
860.1340: Residue Analytical Methods			
- Plant commodities	N/A	Yes[3]	**00029834 00029835 00030259 00030272 00036021 00036027 00036029 00080387 00086450 00086452 00086472 00086473 00086534 00086545 00086561 00086569 00086571 00086601 00086603 00124220** *00156382 00160465 00160466 00160467 00160468 00160469 00165010 00165025 40149301 40149302 40149303 40149304 40149305 40149401 40149402 41556601 41556602 41785201 41785202 41785203 41785204* 42806101[4] 43617901[5] 43635501[6] 43838801[7] 43838802[7] 43855301[8] 43855302[8] 43855303[8] 43874701[9] 43874702[9] 44066301[10] 44066302[10]

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
- Animal commodities	N/A	Yes [11]	43808101[12] 43808102[12] 44334401[13] 44334402[13]
860.1360: Multiresidue Methods	N/A	Yes [14]	
860.1380: Storage Stability Data	N/A	Yes [15]	*41556601 41556602 41785201 41785202* 42564801[16] 42806101[4] 42965101[17]
860.1500: Crop Field Trials			
Root and Tuber Vegetables Group			
- Potatoes	0.05 [§180.236]	No	**00086492 00086494** *00160466 40149401 40149304 41556602* 44667001[18]
- Sugar beets, roots	0.05 [§180.236]	No	**00086560** *00160468 40149302 40149401 41556601*
Leaves of Root and Tuber Vegetables Group			
- Sugar beets, tops	0.05 [§180.236]	No	43836601[19]
Tree Nuts Group			
- Pecans	0.05 [§180.236]	No	**00086600** *00165025 40149303 41267101*[20]
860.1520: Processed Food/Feed			
- Sugar beet	None	No	*41785201 41785203*
- Potatoes	None	No	*41785202 41785204*
860.1480: Meat, Milk, Poultry, and Eggs			
- Liver and kidney of cattle, goats, hogs, horses, and sheep	0.05 [§180.236]	No	**00053415 00080381** 44334401[13] 44334402[13]
860.1400: Water Fish and Irrigated Crops	None	N/A	
860.1460: Food Handling	None	N/A	

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
860.1850: Confined Rotational Crops	None	No	41512701[21]
860.1900: Field Rotational Crops	None	No	

1. **Bolded** references were reviewed in the Residue Chemistry Chapter of the Triphenyltin Hydroxide Reregistration Standard dated 4/11/84, and *italicized* references were reviewed in the Residue Chemistry Chapter of the Triphenyltin Hydroxide Reregistration Standard Update dated 3/18/92. All other references were reviewed as noted.

2. Based upon the available residue data and/or changes in data requirements, the Agency is recommending changes to use directions. The recommended label amendments are listed in the SUMMARY OF SCIENCE FINDINGS, under Directions for Use.

3. The proposed enforcement method for plants must be validated by the Agency prior to publication in the Pesticide Analytical Manual, Volume II. The method has been submitted for an Agency tolerance method validation. Radiovalidation of the method is also required.

4. DP Barcode D192579, L Cheng, 11/23/93.

5. DP Barcode D215273, L. Cheng, 6/27/95.

6. DP Barcode D216970, L. Cheng, 7/25/95.

7. DP Barcode D221155, L Cheng, 2/23/96.

8. DP Barcode D222076, L Cheng, 1/24/97.

9. DP Barcode D222078, L Cheng, 2/23/96.

10. DP Barcode D228535, L Cheng, 1/24/97.

11. The GC/FPD method used to determine TPTH residues in the ruminant feeding study is adequate for data collection. However, HED has previously concluded that the method must be modified to include a base hydrolysis step to release conjugated residues. Alternatively, the registrants must provide data indicating that base hydrolysis is unnecessary for adequate recovery of the total toxic residue (radiovalidation data). If the registrants wish to propose the GC/FPD method as an enforcement method for animal commodities, then an ILV of the method should be conducted in accordance with PR Notice 96-1.

12. DP Barcode D220557, L. Cheng, 2/23/96.

13. DP Barcode D239451, J. Punzi, 4/2/98.

14. The registrants need to provide recovery data for TPTH and its metabolites using FDA multiresidue methods. The registrants are referred to OPPTS GLN 860.1360 for details concerning multiresidue method testing.

15. Data are required depicting the storage stability of TPTH and its metabolites in pecans held in frozen storage for up to 9 months. Data are also required depicting the storage stability of TPTH residues in sugar beet tops stored frozen for up to 2 years. The registrants have informed the Agency that the required 2-year study on sugar beets is underway.

16. DP Barcode D185360, L. Cheng, 3/10/93.

17. DP Barcode D196286 and D211111, L. Cheng, 7/12/94 and 4/18/95.

18. DP Barcodes D250912, D250915, D250917, S. Law, 1/14/99

19. DP Barcode D221156, D226002, and D234680, L. Cheng, 2/23/96, 1/24/97 and 7/28/97.

20. No DP Barcode, R. Perfetti, 5/6/94.

21. EFGWB, E. Regelman, 2/22/91.