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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

August 20, 1999

MEMORANDUM

SUBJECT: **Review of Registrant Submitted Monte Carlo (Probabilistic) Acute and Chronic (Non-Cancer and Cancer) Dietary Exposure Analyses for TPTH Residues in Pecans, Potatoes, Sugar Beets, Meat and Milk.** PC Code: 083601. Reregistration Case No. 0099. MRID 44852101. DP Barcode D257154.

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I. INTRODUCTION

In anticipation of HED's preliminary human health risk assessment for triphenyltin hydroxide (TPTH) (S. Law, 5/14/99, D250103), the TPTH Task Force submitted acute probabilistic (Monte Carlo) and chronic (non-cancer and cancer) dietary exposure analyses for TPTH on foods (MRID 44852101). The analyses were performed by Novigen Sciences, Inc., using Dietary Exposure Evaluation Model (DEEM™), the software currently used in HED for conducting dietary exposure and risk analyses. Summaries of the residue data used were provided. The TPTH Task Force dietary analyses were submitted subsequent and independent of HED's in-house acute probabilistic Monte Carlo and chronic (non-cancer and cancer) dietary analyses (S. Law, 4/13/99, D254712 and D254713). HED's analyses used the TPTH anticipated residues (ARs) from the Residue Chemistry Chapter for the TPTH RED (C. Eiden, 4/12/99, D255118). HED's ARs have undergone secondary review in ChemSAC (3/24/99); the acute probabilistic and chronic dietary

exposure analyses have undergone secondary review in Dietary Exposure (DE) SAC (4/6/99).

This review evaluates and compares the TPTH Task Force's acute probabilistic and chronic dietary analyses to HED's acute probabilistic and chronic dietary analyses (i.e., adequacy of the input parameters for food residues, adjustment factors, percent crop treated (%CT) data used, etc.) with respect to HED's current policies. Forthcoming are revised HED acute and chronic analyses (S. Levy, DRAFT, D258010) in concurrence from the review of this MRID (44852101) and a revised HED Residue Chemistry Chapter (C. Eiden, D258541) for the TPTH RED.

II. CONSUMPTION DATA

HED and Novigen both used the DEEM™ software to evaluate the dietary exposure based on individual consumption data from USDA's Nationwide Continuing Surveys of Food Intake by Individulas (CSFII). However, HED used the 1989-1992 CSFII data; Novigen used the 1994-1996 CSFII data. The Agency currently has not completed validation of recipe translations for the 1994-1996 consumption data, therefore it is HED's current policy to use the 1989-1992 CSFII data for analyses. Therefore, the registrant submission cannot be accepted because they did not use the 1989-1992 CSFII consumption data, as per HED policy.

III. DIETARY EXPOSURE MODELS

HED and Novigen both used the tiered approach to select the most appropriate residue value for both the acute and chronic analyses. For the acute and chronic analyses, HED and Novigen both performed Tier III analyses, using field trial residue values (as monitoring data are not available for TPTH or its regulable metabolites). [HED has previously concluded that the residues to be regulated in plants and livestock are parent TPTH and its diphenyltin hydroxide (DPTH) and monophenyltin hydroxide (MPTH), or oxide, metabolies.] Both HED and Novigen performed dietary cancer risk estimates.

IV. TOXICOLOGY

A. Acute

The HED FQPA Safety Factor Assessment Review Committee has determined that the 10x FQPA Safety Factor should be **reduced to 3x** for acute dietary risk assessment for all populations that include infants and children (See FQPA Document, 12/17/98).

Table #1. Acute TPTH Toxicity Assumptions.

NOVIGEN	HED	HED's RESPONSE
HED and Novigen both derived their acute reference doses (RfD's) from a no observed adverse effect level (NOAEL) (Novigen used NOEL) of 0.3 mg/kg based on increased incidents of hyoid body and/or arches unossified in rabbit fetuses.		No Response.
HED and Novigen both used an uncertainty factor (UF) of 100 (10x for inter-species and 10x for intra-species variation), as required by HED's Hazard Identification Assessment Review Committee (HIARC) (11/13/98). HED also determined that the acute risk assessment is required for Females 13+ years old only.		No Response.
Novigen reported MOE's for acute dietary exposure using the NOAEL of 0.3 mg/kg/day and an acceptable margin of exposure (MOE) of 300.	HED compared acute dietary exposure against an acute Population Adjusted Dose (aPAD) of 0.001 mg/kg/day (this is the equivalent of a MOE = 300), as required by the FQPA Safety Factor Committee (12/17/98).	Novigen and HED used the same NOAEL and UF, but reported the results differently (MOE vs. %aPAD). HED's current policy is to report dietary results in terms of %PAD. However, for the purposes of this acute assessment, the registrant's use of MOE is deemed acceptable.

B. Chronic

The HED FQPA Safety Factor Assessment Review Committee determined that the additional **10x factor should be retained** for all populations which include infants and children (See FQPA Document, 12/17/98).

Table #2. Chronic TPTH Toxicity Assumptions.

NOVIGEN	HED	HED's RESPONSE
HED and Novigen both derived their reference doses (RfD's) from a no observed adverse effect level (NOAEL) (Novigen used NOEL) of 0.1 mg/kg/day based on decreased white blood cells in a chronic rat feeding study.		No Response.
HED and Novigen both used an uncertainty factor (UF) of 300 (10x for inter-species and 10x for intra-species variations and an extra 3 fold for instability of the test material in the diet and potential for increased mortality near the LOAEL for a total of 300), as required by HED's HIARC (11/13/98).		No Response.

Novigen performed two chronic assessments: 1) compared chronic exposure against a chronic RfD of 0.0003 mg/kg/day and 2) compared chronic exposure against the chronic Population Adjusted Dose (cPAD) of 0.00003 mg/kg/day.	HED compared chronic exposure against a cPAD of 0.00003 mg/kg/day, as required by the FQPA Safety Factor Committee (12/17/98).	No Response.

C. Cancer

Table #3. Cancer TPTH Assumptions.

NOVIGEN	HED	HED's RESPONSE
HED and Novigen both used a Q_1^* approach to assess cancer risk for TPTH; the value used by both HED and Novigen was $Q_1^* = 1.83$ mg/kg/day^{-1} (8/18/98).		No Response.

V. RESIDUE DATA

A. Field Trial Data

Table #4. TPTH Field Trial Data Assumptions.

PECAN		
NOVIGEN	HED	HED's RESPONSE
Novigen used 57% of crop treated (%CT) for both the acute and chronic analyses.	For the acute analysis, HED used a residue distribution file (RDF) which incorporated the distribution of field trial results, corrected for the estimated maximum %CT (= 56%). For the chronic analysis, HED used 35% (weighted average) of crop treated.	As current policy dictates, HED used the estimated maximum of %CT for the acute analysis and the weighted average of %CT for the chronic analysis. %CT numbers were given to HED by OPP's Biological Economic and Analysis Division (BEAD) based on data from 1988-1998. %CT values were given to Novigen by Landis; no citations were reported. **The registrant's use of the same %CT values for both the acute and chronic analyses are not supported.**

For the acute and chronic analyses, Novigen used pecan field trial residues from MRID# 41267101 as a point estimate. Novigen stated that "to account for all three organotins analyzed, all values below the limit of detection were divided by three and then half the limit of detection (LOD) divided by 3 was used in the analyses."	For the acute analysis, HED used a distribution of field trial residues from MRID# 41267101 as a residue distribution file (RDF file), corrected for %CT. For non-detectable residues, ½ the limit of quantitation (LOQ) was assumed. The LOQ accounts for all organotins, since the method measured total tin - i.e., TPTH and its regulable metabolites plus any other form (s) of tin. For the chronic analysis, HED used the average of field trial residues from MRID# 41267101 as a point estimate.	Novigen is correct in noting that the sum of TPTH and its metabolites should be accounted for. Because the analytical method measured total tin, ½ the LOQ should have been used by Novigen as the AR for non-detectable residues, not 1/6 the LOQ. Furthermore, current HED policy dictates that pecans are considered to be partially blended, rather than blended commodities. Novigen's application of %CT as adjustment factor 2 in the DEEM™ acute analysis is inappropriate for this commodity; an RDF should have been used instead. **Therefore, the registrant's use of %CT in the analysis is unacceptable.**
POTATO		
NOVIGEN	HED	HED's RESPONSE
Novigen used 14% of crop treated (%CT) for both the acute and chronic analyses.	For the acute analysis, HED used a residue distribution file (RDF) which incorporated the potato anticipated residue from field trial results, corrected for the estimated maximum %CT (= 23%). HED used 13% (weighted average) of crop treated for the chronic analysis.	As current policy dictates, HED used the weighted average of %CT for the chronic analysis; the estimated maximum of %CT was used for the acute analysis. %CT numbers were given to HED by OPP's Biological Economic and Analysis Division (BEAD) based on data from 1988-1998. %CT values were given to Novigen by Landis; no citations were reported. **The registrant's use of the same %CT values for both the acute and chronic analyses are not supported.**

For the acute and chronic analyses, Novigen used field trial results from MRID# 44254601. Novigen stated that "to account for all three organotins analyzed, all values below the limit of detection were divided by three and then half the LOD divided by 3 was used in the analyses."	The acute and chronic ARs were calculated based on the addition of ½ the sum of LOQs (LOQ = 0.01 ppm) for each regulable metabolite (TPTH, MPTH and DPTH) from MRID# 44254601. All samples had non-detectable residues. For example, ½ LOQ = 0.005 ppm; the sum for TPTH, DPTH and MPTH = 0.005 ppm + 0.005 ppm + 0.005 ppm = 0.015 ppm. In the acute analysis, the ARs were put into RDFs, except for potatoes/white-dry, which is considered a "blended" commodity. In this case, a point estimate was used.	Novigen is correct in noting that the sum of TPTH and its metabolites should be accounted for. However, Novigen should have taken ½ of the sum of LOQs for TPTH and its metabolites, not 1/6 of the sum. MRID # 44254601 states that for potatoes, "The Limit of Quantitation (LOQ) was 0.01 ppm for TPTH and each metabolite, 0.03 ppm total TPTH equivalents." Furthermore, Novigen reported residue values below the LOQ (what they called LOD) and for TPTH only. The LOD was not reported in the original data submission. **Therefore, the registrant's potato AR value is unacceptable.**
SUGAR BEET		
Novigen used 41% of crop treated (%CT) for both the acute and chronic analyses.	HED used 44% (estimated maximum) for the acute analysis and 35% (weighted average) of crop treated for the chronic analysis and.	As current policy dictates, HED used the weighted average of %CT for the chronic analysis; the estimated maximum of %CT was used for the acute analysis. %CT numbers were given to HED by OPP's Biological Economic and Analysis Division (BEAD) based on data from 1988-1998. %CT values were given to Novigen by Landis; no citations were reported. **The registrant's use of the same %CT values for both the acute and chronic analyses are not supported.**

For the acute and chronic analyses, Novigen used field trial results from MRID# 41556601. Novigen stated that "to account for all three organotins analyzed, all values below the limit of detection were divided by three and then half the LOD divided by 3 was used in the analyses."	The acute and chronic ARs were calculated based on the addition of ½ the sum of LOQs (LOQ = 0.01 ppm) for each regulable metabolite (TPTH, MPTH and DPTH) from MRID# 41556601, extrapolated back to the 1x feeding rate for the chronic analysis. For the acute analysis, the value was not extrapolated to a 1x feeding rate. All samples had non-detectable residues. All sugar beet commodities (i.e., sugar beet sugar and molasses) are considered to be "blended" commodities. Therefore, point estimates were used.	HED assumed an LOQ of 0.01 ppm, analogous to potatoes, taking ½ the LOQ for TPTH, DPTH and MPTH; summing this value and extrapolating to a 1x rate gives a chronic AR of 0.004 ppm. HED notes that this AR value of 0.004 ppm should have been used in the acute assessment as well. Novigen is correct in noting that the sum of TPTH and its metabolites should be accounted for. However, Novigen should have taken ½ of the sum of LOQs for TPTH and its metabolites, not 1/6 of the sum. MRID# 41556601 states that "the Method Detection Limit (MDL) for TPTH is not quantified due to the unstable nature of this compound in the extraction procedure..." **Therefore, the registrant's sugar beet AR value is not supported by the data reported in MRID# 41556601.**

B. Processing Studies

The registrant cited and discussed specific processing studies for potatoes and sugar beets for the analyses. These processing studies were evaluated in previous Agency memoranda (C. Eiden, 4/12/99, D255158). The potato processing study was deemed acceptable (MRID# 41785204). Results for fried potatoes and chips were not reported. However, in re-evaluation of the data, the sugar beet processing study (MRID# 41785203) was deemed unacceptable (1991 Reregistration Standard Update) and a new study was required. Nonetheless, the data on phenyltins indicate that residues reduce 0.14X for molasses and reduce by 0.20X for refined sugar beet sugar during processing. A new confirmatory study will be required.

Table 5. Processing Factors used in Dietary Analyses.

NOVIGEN	HED	HED's RESPONSE
In both the acute and chronic analyses, HED and Novigen both applied processing factors in adjustment factor 1 to the residue levels in the RAC from field trial studies.		No Response.

Novigen used a **Refined Beet Sugar** processing factor of 0.20X from MRID# 41785203.	HED used a **Refined Beet Sugar** processing factor of 0.02X from MRID# 41785203.	Re-evaluation of the data from MRID# 41785203 indicates that a processing factor of **0.20X** is appropriate for **Refined Beet Sugar**. This processing factor will be used in forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010).
Novigen used a **Sugar Beet Molasses** processing factor of 0.14X from MRID# 41785203.	HED used a **Sugar Beet Molasses** processing factor of 3X from MRID# 41785203.	Re-evaluation of the data from MRID# 41785203 indicates that a processing factor of **0.14X** is appropriate for **Sugar Beet Molasses**. This processing factor will be used in forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010).
Novigen used a **Dehydrated Sugar Beet Pulp** processing factor of 1.00X from MRID# 41785203.	**Dehydrated Sugar Beet Pulp** is not a human consumption item; therefore, not in DEEM™.	No Response.
Novigen used a **Peeled Potato** processing factor of 0.009X from MRID# 41785204. Novigen stated that "processing factors were calculated using data for TPTH only."	HED used a cooking factor of 0.04X for **Boiled Potatoes** and 0.03X for **Baked Potatoes** from MRID# 41785204 for **Peeled Potatoes**. These processing factors are based on total regulable TPTH residues.	From MRID# 41785204, HED's re-evaluation of the data indicate that a processing factor of **0.004X** is appropriate for **Boiled Peeled Potato** (**Baked Peeled Potato** data were not given). This processing factor will be used in forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010). Processing factors should be calculated for TPTH and its regulable metabolites MPTH and DPTH. **The registrant calculated processing factors for TPTH only, therefore their processing factors do not account for all regulable metabolites.**

Novigen used a **Potato Granules** processing factor of 0.009X from MRID# 41785204. Novigen stated that "processing factors were calculated using data for TPTH only."	HED used the cooking factors of 0.04X for **Boiled Potatoes** and 0.03X for **Baked Potatoes** from MRID# 41785204 for the applicable **Potato Granules** food forms (Potatoes/white-dry in DEEM™).	Upon re-evaluation of MRID# 41785204, HED re-calculated a potato granules processing factor of **0.004X.** This processing factor will be used for **Potato/white-dry** in forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010). Furthermore, all processing factors should be calculated for TPTH and its regulable metabolites MPTH and DPTH. **The registrant calculated processing factors for TPTH only, therefore their processing factors do not account for all regulable metabolites.**
Novigen used a **Boiled Potato with Peel** processing factor of 0.17X from MRID# 41785204. Novigen stated that "processing factors were calculated using data for TPTH only."	HED used a cooking factor of 0.04X for **Boiled Potatoes** from MRID# 41785204.	Upon re-evaluation of MRID# 41785204, HED re-calculated a **Boiled with Peel** potato cooking factor of **0.17X.** This processing factor will be used for all **Boiled Potato with Peel** food forms in forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010). Furthermore, all processing factors should be calculated for TPTH and its regulable metabolites MPTH and DPTH. **The registrant calculated processing factors for TPTH only, therefore their processing factors do not account for all regulable metabolites.**

Novigen used a **Baked Potato with Peel** processing factor of 0.18X from MRID# 41785204. Novigen stated that "processing factors were calculated using data for TPTH only."	HED used a Cooking Factor and 0.03X for **Baked Potatoes** from MRID# 41785204.	Upon re-evaluation of MRID# 41785204, HED re-calculated a **Baked Potato with Peel** potato cooking factor of **0.12X.** This processing factor will be used for all **Baked Potato with Peel** food forms in forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010). Furthermore, all processing factors should be calculated for TPTH and its regulable metabolites MPTH and DPTH. **The registrant calculated processing factors for TPTH only, therefore their processing factors do not account for all regulable metabolites.**
Novigen did not use a processing factor for **Potato Peel** from MRID# 41785204. Novigen stated that "processing factors were calculated using data for TPTH only."	HED used a **Potato Peel** processing factor of 3x from MRID# 41785204.	Upon re-evaluation of MRID# 41785201, HED cannot confirm if residues in **Potato Peel** concentrate or reduce. Therefore, a default value of **1X** will be used for the **Potato Peel, Only** baked or fried food forms in forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010). The registrant did not calculate a **Potato Peel** processing factor for TPTH.

C. Secondary Residues

Table #6. Residues Used in Livestock Commodities.

NOVIGEN	HED	HED's RESPONSE
Novigen stated that tissue-to-feed ratios (the coefficient which indicates the proportion of residues in feed that are transferred through the animal to the tissues) used for meat and milk were provided by Landis.	HED extrapolated meat and milk residues from feeding levels closest to the calculated dietary burden (MRID# 443344-01 and -02). For purposes of comparison, tissue-to-feed ratios have been calculated for each meat and milk commodity below.	HED recently evaluated an acceptable feeding study that was submitted to the Agency (J. Punzi, 4/2/98, D239451, MRID 44334401). Tissue-to-feed ratios were provided by Landis to Novigen; no references were provided.
TISSUE-TO-FEED RATIOS FOR AVERAGE RESIDUES OF TPTH BASED ON AN AVERAGE DIETARY BURDEN.		
Muscle: 0.002 Liver: 0.02 Kidney: 0.006 Fat: 0.001 Milk: 0.001	Muscle: @ 21 ppm: 0.033 @ 7 ppm: 0.036 Liver: @ 21 ppm: 0.35 @ 7 ppm: 0.39 Kidney: @ 21 ppm: 0.11 @ 7 ppm: 0.12 Fat: @ 21 ppm: 0.013 @ 7 ppm: 0.016 Milk: @ 21 ppm: 0.002 @ 7 ppm: 0.003 Skimmed Milk: @ 21 ppm: 0.001 @ 7 ppm: 0.003 Cream: @ 21 ppm: 0.011 @ 7 ppm: 0.013	The HED tissue-to-feed ratios are supported by MRID# 44334401. These tissue-to-feed ratios were calculated for purposes of this memo for comparison to the registrant's values. No basis for the registrant tissue-to-feed ratios were reported.

Table 7: Chronic and Acute Dietary Burdens and Anticipated Residues for Meat/Milk.

	Novigen	HED	HED's RESPONSE
CHRONIC			
Dietary Burden	Beef Cattle: 0.0458 ppm Dairy Cattle: 0.0011 ppm Swine: 0.00028 ppm	Beef Cattle: 1.35 ppm Dairy Cattle: 0.68 ppm Swine: 0.008 ppm	As per HED policy, the average theoretical dietary burden for livestock is based on the anticipated residue calculated from field trial data divided by % dry matter, (%DM) multiplied by % diet.
Anticipated Residues	*Cattle:* Muscle: 0.000011 ppm Kidney: 0.000111 ppm Liver: 0.000033 ppm Fat: 0.000006 ppm Milk: 0.000001 ppm *Swine:* Muscle: 0.0000006 ppm Kidney: 0.0000017 ppm Liver: 0.0000056 ppm Fat: 0.0000003 ppm	Muscle: 0.049 ppm Kidney: 0.17 ppm Liver: 0.53 ppm Fat: 0.018 ppm Milk: 0.0016 ppm Cream: 0.008 ppm Skim Milk: 0.0013 ppm	HED's meat, milk and meat by-product chronic ARs are significantly higher because of higher calculated chronic dietary burdens and higher tissue-to-feed ratios. Furthermore, the registrant's ARs are significantly lower than HED's because the Task Force factored in the percent of cattle that could feed on sugar beet tops, based on the temporal component of when the tops are available as a feed item during the year. HED considered this issue and agreed in principle, with some modifications, with the registrant's approach. This will be reflected in HED's forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010).
ACUTE			

Dietary Burden	Dairy Cattle: 0.008 ppm Swine: 0.0025 ppm	Beef Cattle: 8.4 ppm Dairy Cattle: 2.2 ppm	As per HED policy, the reasonable maximum theoretical dietary burden for livestock is based on the anticipated residue (highest average field trial residue [HAFT]) calculated from field trial data divided by %DM multiplied by % diet. For beef cattle, the AR for sugar beet tops calculated from the highest average field trial value of 2 samples from the field trial with the highest residues at a 21-day PHI (9.67 ppm). For dairy cattle, the average residue was used (5.05 ppm) (MRID# 43836601).
Anticipated Residues	*Dairy Cattle:* Milk: 0.000008 ppm *Swine:* Muscle: 0.0000050 ppm Fat: 0.0000025 ppm Liver: 0.0000500 ppm Kidney: 0.0000150 ppm	Muscle: 0.3 ppm Kidney: 1.0 ppm Liver: 3.16 ppm Fat: 0.12 ppm Milk: 0.006 ppm Cream: 0.026 ppm Skim Milk: 0.004 ppm	HED's meat, milk and meat by-product ARs are significantly higher because of higher calculated acute dietary burdens. Furthermore, the registrant's ARs are significantly lower than HED's because the registrant's factored in the percent of cattle that could feed on sugar beet tops, based on the temporal component of when the tops are available as a feed item during the year. HED considered this issue and agreed in principle, with some modifications, with the registrant's approach. This will be reflected in HED's forthcoming revised acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010).

VI. Results

Tables 9, 10 and 11 display the results of HED's (S. Law, 4/13/99, D254712, D254713) and the registrant's acute and chronic (non-cancer and cancer) dietary exposure analyses. HED's level of concern for acute and chronic dietary risk is greater than 100% acute PAD or chronic PAD, respectively. The level that the Agency generally considers negligible for excess lifetime cancer risk is 1.0×10^{-6}. Updated HED acute and chronic dietary exposure analyses (S. Levy, DRAFT, D258010) are being conducted in concurrence from the review of this MRID (44852101) and a revised HED Residue Chemistry Chapter (C. Eiden, D258541) for the TPTH RED.

Table 9. Acute Dietary Exposure Results for TPTH.

Subgroups	TPTH Task Force's Acute Total Exposure at 99.9th percentile (mg/kg/day)	TPTH Task Force's MOE[1]	HED's Acute Total Exposure at 99.9th percentile (mg/kg/day)[2]	HED's Acute Risk at the 99.9th percentile (% aPAD)[2]
U.S. Population (48 states)	0.000003	104226	0.005299	529.9 %
Females (20+ years old/np/nn)	Did not report.	Did not report.	0.003613	361.9 %
Females (13-19 years old/ np/nn)	0.000002	126203	0.002729	272.9 %
Females (13+ years old/ preg/nn)	Did not report.	Did not report.	0.003091	309.1 %
Females (13+ years old/nursing)	Did not report.	Did not report.	0.003452	345.2 %
Females (13-50 years old)	0.000002	126203	0.003062	306.2 %

[1] MOE is calculated as the NOAEL (0.3 mg/kg/day) divided by the exposure. An acceptable MOE is >300.

[2] A revised HED acute dietary exposure analysis is being conducted (S. Levy, DRAFT, D258010). HED's revised acute dietary total exposure and estimated risk percentiles should lower with the modifications discussed in this document.

The results of HED's acute analysis indicate that the acute dietary risk estimates associated with the proposed uses of TPTH are **above the Agency's level of concern** (> 100% acute PAD) for all U.S. sub-populations which include females 13+ years old, as required by the HIARC.

Table 10. Chronic (non-cancer) Dietary Exposure Results for TPTH.

Subgroups	TPTH Task Force's Chronic Total Exposure (mg/kg/day)	TPTH Task Force's Chronic Risk (% cPAD)[1]	HED's Chronic Total Exposure (mg/kg/day)[2]	HED's Chronic Risk (% cPAD)[2]
U.S. Population (48 states)	0.000000	0.6 %	0.000084	279.1 %
Non-nursing infants	0.000000	1.5 %	0.000051	170.2 %

Children (1-6 years old)	0.000000	1.3 %	0.000179	596.2 %
Children (7-12 years old)	0.000000	1.0 %	0.000123	408.5 %
Females (13-19 years old/np/nn)	0.000000	0.7 %	0.000073	244.2 %
Males (13-19 years old)	0.000000	0.9 %	0.000089	297.6 %

[1] Task Force states, "Percent of RfD including an additional FQPA uncertainty factor (RfD = 0.00003)."

[2] A revised HED chronic dietary exposure analysis is being conducted (S. Levy, DRAFT, D258010). HED's revised chronic dietary total exposure and estimated risk percentiles should lower with the modifications discussed in this document.

HED's results of the chronic (non-cancer) analysis indicate that the acute dietary risk estimates associated with the proposed uses of TPTH are **above the Agency's level of concern** (> 100% chronic PAD) for all populations.

Table 11. Cancer Dietary Risk Estimate (Q1* = 1.83).

Subgroup	TPTH Task Force's Cancer Risk Estimate	HED's Cancer Risk Estimate[1]
U.S. Population (48 states)	3.44×10^{-7}	1.53×10^{-4}

[1] A revised HED chronic (cancer) dietary exposure analysis is being conducted (S. Levy, DRAFT, D258010). HED's revised chronic (cancer) dietary risk estimate should lower with the modifications discussed in this document.

HED's cancer risk estimate for the U.S. population is 1.53×10^{-4}. This estimate is **above the level** the Agency generally considers negligible for excess lifetime cancer risk.

VII. Sugar Beet Industry Assumptions

The main livestock feed crop registered for TPTH is sugar beets. Sugar beet tops are removed from the root after harvesting and are left in the field until the field is plowed. During this time period, the sugar beet tops can be foraged by livestock.

The registrant responds that there is great disparity between HED's and NOVIGEN's dietary risk assessments. The preliminary judgement is that the greatest disparity between the two documents is not the toxicity endpoints used, but rather in how the feeding of sugar beet leaves is addressed. The registrant responds that it appears that HED's assessment assumes that all beet leaves are fed to beef and dairy cattle and that this occurs for twelve months of the year.

The registrant is making a concerted effort to provide documentation on sugar beet leaf feeding practices. To this end the registrant has re-contacted all of the sugar beet regions and have requested letters documenting the use of sugar beet leaves. The registrant will ultimately have letters covering all of the sugar beet regions, but to date have received 12 letters which were submtited to the Agency for reference. Approximately 12 additional letters are expected in the near future.

The Task Force states that...

"according to sugar beet industry experts, sugar beet tops are fed only to foraging beef cattle; and sugar beet tops are foraged only in a limited geographic area. In fact, Wyoming and Montana are the only sugar beet producing states which report that cattle are allowed to forage on sugar beet tops treated with TPTH. At this time, however, there are no TPTH-treated sugar beet tops which are foraged because there are feeding restrictions on all TPTH labels. Within Wyoming and Montana, only 2% of the total sugar beet crop is available for foraging in both states. Together Wyoming and Montana account for approximately 8% of the total harvested sugar beet acreage. Therefore, only 0.16% (8% of total harvest x 2% foraged) of the national sugar beet production could contain TPTH residues. Additionally, approximately 41% of the sugar beet crop is treated with TPTH; therefore, only 0.07% of the nationwide crop could potentially contain TPTH residues."

The Task Force incorporated the above stated information for percent of the crop treated for sugar beet tops into the calculations of secondary residues of beef cattle only (it was assumed that dairy cattle are not fed sugar beet tops) for both the acute and chronic analyses. 1% (conservative estimate from their calculation of <0.1%) of the crop treated was assumed for both analyses.

HED's RESPONSE

An HED Senior Plant Physiologist (Dr. Bernard Schneider) reviewed the TPTH Task Force response to use of sugar beet tops for livestock use, and contacted various USDA Extension Agents in cooperation with USDA-IR-4, performed a literature search, and contacted sugar beet equipment dealers. His conclusions are as follows:

(1) In general, HED agrees with the acreage estimates of sugar beet tops fed to livestock submitted by the TPTH Task Force. HED's estimates used a combination of new estimates and referenced sources from the TPTH Task Force submittal as noted in Table 1. HED estimate's that 0.8 % of the tops from the total sugar beet acreages are fed to beef cattle.

(2) HED finds no evidence that sugar beet tops are fed to dairy cattle.

(3) Sugar beet tops are not fed to beef cattle in MI, MN, OH, eastern ND, and CO.

(4) Sugar beet tops are fed to beef cattle in ID, southern NE, MT and WA. (Sugar beet

tops are fed in CA; however, TPTH is not registered for use in CA)

(5) The standard 'topping' practice for almost all sugar beet growing areas is to use a four to twelve row beet defoliator or toppers, which depending on the choice of flails or knives will cut the beet tops into finer pulverized shreds, that are usually incorporated into the soil as a source of organic matter.

(6) Proper adjustment of the defoliator is necessary to prevent yield and quality of the extractable sucrose.

Table #8 summarizes the TPTH Task Force acreage estimates and additional estimates from University Extension Agents and Sugar Beet Grower Associations that HED found (references are cited at the end of this report):

Table 8. Estimates of Sugar Beet Acres and Percent Grazed by Beef and Dairy Cattle per State.

STATE (Reference)	ESTIMATE OF SUGAR BEET ACRES (1998 harvested acres)	PERCENT GRAZED BY BEEF CATTLE	PERCENT GRAZED BY DAIRY CATTLE
MI (11)	173,000	0%	0%
MN (12)	458,000	0%	0%
ID (13)	197,000-203,300	1% (1970 A - 2033 A)	0%
NE (14)	47,400-52,000	5% (2370A - 2600A)	0%
MT (15)	48,000	6% (2880A)	0%
CO (16)	57,300	0%	0%
ND (11, 12)	242,600	0%	0%
WA (17)	12,300	8% (1000A)	0%
Northern WY (18)	10,600	10% (1060A)	0%
CA (13)	100,000	<5% (<5000A)	0%
TOTALS	1,256,800 A	9573 A (0.8 %)	0%

NOTES:

Dr's. Ensminger and Perry (10) reference on beef cattle states that large acreages of sugar beet

tops are grazed by cattle and sheep in the Western States. This is consistent with the finding of any sugar beet tops fed in the eastern most sugar beet growing regions.

In California (13) less than 5% of the sugar beet acres were estimated to have their tops fed, however, TPTH is not registered in California and this data is not for use in the TPTH analysis.

In cases where an estimate was not available, HED used the appropriate acreage estimates from the TPTH reports from either University Agricultural Extension Agents or Sugar Beet Grower Associations, and when acre estimates were higher HED used the TPTH reference.

From USDA's 1997 Agricultural Statistics book, the total number of cattle (beef) in the United States from 1988-1997 was 99,374,000 heads. The average number of cattle from 1996-1997 in the largest sugar beet production states are presented in Table #9.

Table 9. Calculation of Percentage of Sugar Beet Producing States that have Cattle/US Total.

5 Largest Sugar Beet Producing States (1996-1997)	Average Number of Cattle Heads per State in thousands (1996-1997)	Percentage of Cattle Heads per State/US Average Number of Cattle
ID	1,760	1.8 %
MI	1,150	1.2 %
MN	2,825	2.8 %
ND	1,910	1.9 %
MT	2,725	2.7 %
Total %		Approximately 12 %

Of the five largest sugar beet producing states, accounting for 80% of sugar beet production, approximately 12% of the total US cattle are raised in these states. Therefore, approximately 12% of all U.S. cattle could potentially graze on sugar beet tops. Note that dairy cattle are not fed sugar beet tops; therefore, the following approach and assumptions would not apply to dairy cattle (milk in DEEM™).

On July 21 and August 18, 1999 HED members met with ChemSAC and decided on the following approach:

HED concurs with the Task Force that sugar beet tops are not available for grazing 12 months of the year. It is more realistic for the **chronic** assessment to assume sugar beet tops would be available for grazing after harvest for up to one month before the field is plowed (1 month availability/12 months). Therefore, for the chronic dietary assessment (S. Levy, DRAFT,

D258010), the percent of sugar beet treated, the percent of cattle that could feed on sugar beet tops, the temporal component, and the percent of sugar beet tops fed will be incorporated as "percent of crop treated" in adjustment factor number 2 column in the chronic assessment:

% CT x % US cattle that could graze on sugar beet tops x (1 month availability/12 months) x % sugar beet tops fed =

0.35 (weighted average) x 0.12 x 0.08 x 0.8 = 0.003 %

However, for the **acute** assessment, it is not appropriate to take into account the temporal component or the % sugar beet tops fed because HED is concerned with dietary acute exposure over a short time period, not residues averaged out over a year.

Therefore, for the acute assessment (S. Levy, DRAFT, D258010), the %CT and the percent of cattle that could feed on sugar beet tops will be used probabilistically in all meat product residue distribution files in the acute assessment:

% CT x % US cattle that could graze on sugar beet tops =

0.44 (estimated maximum) x 0.12 = 0.05 %

If a Monte Carlo is necessary, then the RDF file for meat/milk thus will contain 95 zeros and 5values at the acute AR level (i.e., 95% probability of meat/milk not containing any TPTH regulable residues).

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cc: RF, SF, List A File, DE SAC (4/6/99, 7/27/99), ChemSAC (3/24/99, 7/7/99, 7/21/99, 8/18/99), S. Levy, S. Knizner
RDI: CM2, Room 821E, 703-305-0783, SJL 8/20/99, SAK 8/20/99

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Chemical:	**Fentin hydroxide**
PC Code:	***083601***
HED File Code	**31000 Monte Carlo**
Memo Date:	***08/20/99***
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