(12-15-97)

MEMORANDUM

SUBJECT: The Revised HED Chapter of the Reregistration Eligibility Decision (RED) Document for Chlorothalonil (case number 0097; chemical number 081901)

FROM: Mary Clock, Biologist
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THRU: Karen Whitby, Chief
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TO: Lois Rossi, Director
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Please find attached the revised Human Health Risk Assessment for the chlorothalonil Reregistration Eligibility Decision document (RED). This HED chapter includes the most recent Hazard Assessment from Alan Levy in RAB2 and Mike Ioannou in TB1, Product and Residue Chemistry Assessments from William Smith in CEB1, Occupational and Exposure Assessment from Al Nielsen in RRB2, and Dietary Exposure Analysis from Brian Steinwand in CEB1. The attached document is an updated version of the most recent chlorothalonil human health risk assessment (May 5, 1997) and includes a revised classification of the chlorothalonil carcinogenic potential and carcinogenic risk from chlorothalonil. If you have any questions, please call Mary Clock at 308-2718.

HED Chapter

CHLOROTHALONIL

In this document, which is for use in EPA's development of the chlorothalonil Reregistration Eligibility Decision Document (RED), HED presents the results of its risk assessment of the potential human health effects of dietary, drinking water, occupational and residential exposure to chlorothalonil. This risk assessment was harmonized with that of California's Department of Pesticide Regulation (CDPR) through the discussion and sharing of information on toxicity endpoints, uncertainty factors, worker exposure assumptions (such as the value for body weight) and numerous other data and issues involved in risk assessment. Included is a discussion of the product chemistry, toxicology, and residue chemistry data that have been submitted as well as HED's recommendations for risk reduction and mitigation.

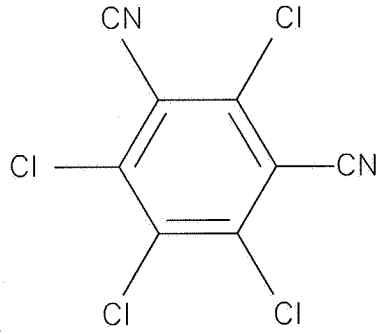
SCIENCE ASSESSMENT

A. PHYSICAL AND CHEMICAL PROPERTIES ASSESSMENT

Additional product chemistry data are required to support eleven Manufacturing-Use Products (MPs) registered to ISK Biosciences Corporation and one MP registered to Veterans Ilex, Incorporated. The outstanding product chemistry data requirements should not delay a reregistration eligibility decision for chlorothalonil, and HED has no objections to the reregistration of chlorothalonil with respect to the product chemistry data requirements.

1. Description of Chemical

Chlorothalonil (tetrachloroisophthalonitrile) is a broad spectrum non-systemic protectant fungicide for control of foliar diseases of vegetable and ornamental crops, and for mold/mildew control in paint films and wood.



Empirical Formula:	$C_8Cl_4N_2$
Molecular Weight:	265.9
CAS Registry No.:	1897-45-6
Shaughnessy No.:	081901

2. Identification of Active Ingredient

Technical chlorothalonil is a white crystalline solid with a melting point of 250-251° C. Chlorothalonil is practically insoluble in water at 25° C (ca. 0.6 ppm) and only slightly soluble in acetone, chloroform, ethanol, kerosene, methyl ethyl ketone, mineral oil, toluene, and xylene (≤8.0% by weight). The technical product is stable under normal storage temperatures, on exposure to ultraviolet radiation, and in moderate alkaline or acidic aqueous media.

3. Manufacturing-Use Products

The registrant, ISK Biosciences, asserts that there are 11 Manufacturing Use Products registered to ISK Biosciences Corporation and one MP registered to Veterans Ilex, Incorporated and three MPs registered to Sostram Corporation. A list of the chlorothalonil MPs subject to a reregistration eligibility decision is presented below in Table 1.

Table 1
Chlorothalonil Manufacturing-Use Products

Product (registration date)	HED Reg. No.	Registrant	Comments (i.e., transfers, label claim)
97% T (1/92)	50534-200	ISK Biosciences Corporation[a]	
96% T (9/83)	50534-7		Transferred (9/9/83) from Diamond Shamrock Corporation (HED Reg. No. 677-308).
97% T (10/83)	50534-24		Transferred (10/28/83) from Diamond Shamrock Corporation (HED Reg. No. 677-283).
96% T (4/84)	50534-117		
96% FI (4/84)	50534-114		Transferred (4/23/84) from Diamond Shamrock Corp. (HED Reg. No. 2204-12).
75% FI (10/83)	50534-29		Transferred (10/28/83) from Diamond Shamrock Corporation (HED Reg. No. 677-293).
75% FI (4/84)	50534-116		Identified in REFS as an end-use product; however, labeled for the manufacture of mildew-resistant cement grout only.
40.4% FI (10/83)	50534-34		Transferred (10/28/83) from Diamond Shamrock Corporation (HED Reg. No. 677-330).
40.4% FI (4/84)	50534-115		

30.8% FI (10/83)	50534-35		Identified in REFS as an end-use product; however, labeled for repackaging only.
29.6% FI (10/83)	50534-33		Transferred (10/28/83) from Diamond Shamrock Corporation (HED Reg. No. 677-326).
98% T (1/92)	60063-1	Sostram Corporation	*These "me-too" registrations are being addressed by RD and will not be considered further in the HED Chapter of the Chlorothalonil RED.*
40.4% FI (4/93)	60063-6		
	60063-8		
98% T (1/83)	61451-2	Veterans Ilex, Incorporated	Transferred (12/11/90) from Griffin Corp. (HED Reg. No. 1812-268)

[a] The name of the registrant has changed from SDS Biotech to Fermenta Plant Protection to Fermenta ASC Corp to ISK Biotech Corp. to ISK Biosciences Corp. without change in company number.

4. Regulatory Background

The regulatory background for chlorothalonil products in terms of comprehensive product chemistry reviews is presented below. The ISK Biosciences 96% Technicals (HED Reg. Nos. 50534-7, and 50534-117) were determined to be identical in the Chlorothalonil FRSTR; the registrant has subsequently confirmed that the 97% Technicals (HED Reg. Nos. 50534-24 and 50534-200) are essentially equivalent to these products.

Table 2
Regulatory Status of Chlorothalonil Registrations

Product (HED Reg. No.)	September 1984 Guidance Document [a]		March 1988 FRSTR	
	Data required	Data submitted in response	Data required	Data submitted in response
97% T* (50534-200)	Not Registered	N/A [b]	Not Registered	N/A
96% T (50534-7)	61-1,-2,-3, 62-1, -2,-3, 63-2 to -13	61-1,-2,-3, 62-1,-2,-3, 63-2 to -5,-7 to-14,-16 to-20	63-7,-12 to -14, -16,-17,-20	63-7,-12,-13
97% T (50534-24)	61-1 to -3, 62-1 to -3, 63-2 to -13	61-1 to -3, 62-1 to -3, 63-2 to -5, -7 to -14, -16 to -20	63-7,-12,-13, -14,-16,-17, -20	63-7, -12, -13

Product (HED Reg. No.)	September 1984 Guidance Document [a]		March 1988 FRSTR	
	Data required	Data submitted in response	Data required	Data submitted in response
96% T (50534-117)	61-1, -2, -3 62-1, -2, -3 63-2 through -13	61-1, -2, -3, 62-1,-2,-3, 63-2 to -5,-7 to-14, -16 to -20	63-7,-12, -13, -14,-16,-17,-20	63-7,-12,-13
96% FI* (50534-114)	61-1,-2,-3, 62-1,-2,-3, 63-2 to -13	61-1,-2, 62-2,-3, 63-7, 63-8	61-1,-3, 62-1[c], -2, 63-2,-3,-4, -7, -12,-14,-16, -17,-18,-20	None
75% FI (50534-29)	61-1,-2,-3, 62-1,-2,-3, 63-2 to -13	61-1,-2, 62-2,-3, 63-12, 63-13	61-1,-2,-3, 62-1[c],-2, 63-2,-3,-4,-7, -12,-14,-16, -17,-18,-20	None
75% FI (50534-116)	61-1,-2,-3, 62-1, -2,-3, 63-2 to-13	61-1,-2, 62-2,-3	61-1,-2,-3, 62- 1[c],-2, 63-2,-3, -4,-7,-12,-14, -16,-17,-18,-20	None
40.4% FI (50534-34)	61-1,-2,-3, 62-1,-2,-3, 63-2 to-13	61-1,-2, 62-2,-3, 63-7	61-1,-3, 62-1[c], -2, 63-2,-3,-4, -7, -12,-14,-16, -17,-18,-20	None
40.4% FI (50534-115)	61-1,-2,-3, 62-1,-2,-3, 63-2 to-13	61-2, 62-3	61-1,-3, 62-1[c], -2, 63-2,-3,-4, -7, -12,-14,-16, -17,-18,-20	None
30.8% FI (50534-35)	61-1,-2,-3, 62-1,-2,-3, 63-2 to-13	61-1,-2, 62-2,-3	61-1,-2,-3, 62-1[c],-2, 63-2,-3,-4,-7, -12,-14,-16, -17,-18,-20	None

Product (HED Reg. No.)	September 1984 Guidance Document [a]		March 1988 FRSTR	
	Data required	Data submitted in response	Data required	Data submitted in response
29.6% FI (50534-33)	61-1, -2, -3 62-1, -2, -3 63-2 to -13	61-1, -2 62-2, -3 63-7, -12	61-1, -3 62-1[c], -2 63-2,-3,-4,-7, -12,-14,-16, -17, -18, -20	None
98% T (61451-2)	61-1, -2, -3 62-1, -2, -3 63-2 to -13	61-1, -2, -3 62-1, -2, -3 63-2, -3, -4, -7 to -13, -17	61-1, -3 62-1, -2, -3 63-5, -7, -13, -14, -16, -17, -20	61-1, 61-2, -3 62-1, 62-2 63-5, -7, -13

* T=technical; FI=formulation intermediate

[a] The Guidance Document did not address physical/chemical data requirements for GLNs 63-14 through 63-20.

[b] N/A = not applicable

[c] Although the FRSTR required preliminary analysis (GLN 62-1) for the FIs, these data requirements will be fulfilled by data for the technical source product/TGAI.

The Chlorothalonil Guidance Document dated September, 1984, states that levels of hexachlorobenzene (HCB), a recognized impurity in technical chlorothalonil, must be at or below 0.05% (500 ppm) for registration or reregistration of the products, and that analytical methods for determination of HCB must be acceptable to the Agency. Preliminary analysis data presented in the chlorothalonil FRSTR indicated that HCB levels for the ISK Biosciences technicals were below the allowable limit; however, preliminary analysis of the Veterans Ilex 98% T indicated HCB levels above the 0.05% limit. The registrant has since modified the manufacturing process to lower HCB levels. Recent analysis of the Veterans Ilex technical as manufactured by the modified process indicates that HCB levels are now within the allowable limits; however, because the HPLC analytical method used has not yet been validated, additional data are required.

A 6/87 Data Call-In (DCI) required data concerning polyhalogenated dibenzo-p-dioxins and dibenzofurans (PCDDs and PCDFs) in technical chlorothalonil. Although additional data are required concerning the levels of PCDDs/PCDFs in chlorothalonil, initial studies indicate that PCDFs are present in the Veterans Ilex technical, and that no PCDDs/PCDFs are present at levels at or above the Agency-specified LOQs in the ISK Biosciences technical chlorothalonil as produced at the facilities identified as Chlorothalonil Unit I or Chlorothalonil Unit II. The registrant is required to submit a revised CSF in which upper limits are certified for all analytes that were detected. For guidance in proposing these certified limits, the registrant should refer to HED guidance on this issue ("Polyhalogenated Dioxins and Dibenzofurans as Contaminants in Pesticides," Product Chemistry CSF Requirement, S. Funk HED/ CBRS 8/6/96).

A Chlorothalonil reregistration DCI dated 7/31/91 was issued in lieu of the Chlorothalonil FRSTR.

The current status of the product chemistry data requirements for chlorothalonil products is presented in data summary tables attached as Appendix 1. Refer to these tables for a listing of the outstanding product chemistry data requirements.

B. HUMAN HEALTH ASSESSMENT

1a. Hazard/Dose-Response Assessment: Chlorothalonil

The toxicological data base on chlorothalonil is adequate and will support reregistration eligibility.

a) Acute Toxicity

Table 3 summarizes the acute toxicity values and categories for chlorothalonil:

Table 3.
Acute Toxicity of Chlorothalonil

TEST	RESULTS	TOXICITY CATEGORY
Oral LD_{50} - Rat	> 10,000 mg/kg	IV
Dermal LD_{50} - Rabbit	> 10,000 mg/kg	IV
Inhalation LC_{50} - Rat	0.094 mg/L (M); 0.092 mg/L (F)	II
Eye Irritation - Rabbit	Severe irritation	I
Dermal Irritation - Rabbit	Slight erythema at 72 hrs	IV
Dermal Sensitization - Guinea Pig	Non-sensitizing	--

The oral LD_{50} exceeded 10,000 mg/kg (Toxicity Category IV). Clinical signs of toxicity included epistasis, lacrimation, dyspnea, vocalization, ataxia and tremors (MRID 00094941). The dermal LD_{50} also exceeded 10,000 mg/kg (Toxicity Category IV). Signs of toxicity included diarrhea, lacrimation, reduced muscle tone and erythema (MRID 00094940).

The acute inhalation LC_{50} was 0.094 mg/L in males and 0.0925 mg/L in females (Toxicity Category II) (MRID 00094942).

Instillation of chlorothalonil (96%) to rabbit eyes resulted in severe irritation with persistent corneal opacity, iris effects, and conjunctival irritation (MRID 00246769). Another test with rabbits found irritation and corneal opacity (MRID 00030350). Chlorothalonil was considered corrosive (Toxicity Category I).

In a dermal irritation study, slight erythema was seen in some rabbits at 72 hours with the effects clearing by day 4 (Toxicity Category IV)) (MRID 00246843).

Chlorothalonil (96%) was not a dermal sensitizer in guinea pigs (MRID 00144112).

b) Subchronic Toxicity

Chlorothalonil (98%) was administered to CD-1 mice at dietary levels of 0, 7.5, 15, 50, 275 or 750 ppm (0, 1.01, 2.14, 7.14, 39.3 or 107) for 13 weeks. The NOEL was 15 ppm (about 2.5-3.0 mg/kg/day). The LOEL was 50 ppm (about 7.5 mg/kg/day) based upon hyperplasia and hyperkeratosis of the epithelium of the forestomach (MRID 00138148 and 00258769).

Chlorothalonil (100%) was administered in the diet to Sprague Dawley rats at doses of 0, 1.5, 3, 10 or 40 mg/kg/day for 13 weeks. Dilated renal tubules and epithelial hyperplasia plus hyperkeratosis in the non-glandular portion of the stomach were found at 10 and 40 mg/kg/day. Microscopy studies of the rat renal lesions found hyperplasia of the tubules at 40 mg/kg/day. Based on these findings, the NOEL was 3.0 mg/kg/day and the LOEL in rats was 10.0 mg/kg/day (MRID 00127852 and 00258768).

In another 90-day study, CD rats were administered chlorothalonil (98%) in the diet at doses of 0, 40, 80, 175, 375, 750, or 1500 mg/kg/day. There were increases in relative kidney weights, gastritis, decreases in body weight and food consumption for males and females, and changes in enzyme levels, and urinary parameters at all dose levels. The NOEL was less than 40 mg/kg/day (MRID 00127850).

In a subchronic toxicity study, chlorothalonil (97.9-98.2%) was administered orally by gelatin capsules to Marshall beagle dogs at doses of 0, 15, 150 or 500 (reduced from 750 on study day 5) mg/kg/day for 95-98 days. There was an increased incidence of emesis at 500 mg/kg/day (number of episodes for males was 25 versus 18 for controls and, for females, 42 versus 18 for controls). Body weight gains were decreased at 150 and 500 mg/kg/day in males and possibly at 500 mg/kg/day in females, and alanine aminotransferase values were reduced approximately 90% at these doses in all dosed animals compared with controls as well as with pretreatment levels. The NOEL was 15 mg/kg/day, and the LOEL was 150 mg/kg/day based on decreased body weight gain in males (MRID 43653602).

Chlorothalonil (98%) was administered dermally to male Fischer 344 rats at 0, 60, 100, 250 or 600 mg/kg/day, 6 hours/day for 5 days/week during a period of 21 days. Clinical signs at doses $\geq$ 100 mg/kg/day were limited to rough hair coat and colored material around the nose and/or eyes. Dermal irritation, characterized as erythema and desquamation, was observed at all doses. Histopathologically, dermal lesions were described as hyperkeratosis and hyperplasia of the squamous epithelium and were seen in all rats at all dose levels. For systemic toxicity, the NOEL was 600 mg/kg/day. For dermal toxicity, the NOEL was $<$60 mg/kg/day and the LOEL was 60 mg/kg/day (MRID 44119101).

In a 21-day dermal toxicity study, chlorothalonil technical was administered dermally at doses of 0, 0.1, 2.5 or 50 mg/kg/day, 6 hours/day, 5 days/week to New Zealand rabbits for a period of 21-22 days. The only effect was slight erythema in the mid- and high-dose groups. No systemic toxicity was observed at any dose. For systemic toxicity, the NOEL was 50 mg/kg/day and the LOEL was $>$50 mg/kg/day. For dermal toxicity, the NOEL was 50 mg/kg/day and the LOEL was $>$ 50 mg/kg/day (MRID 00158254).

c) Chronic Toxicity/Carcinogenicity

In a carcinogenicity study, chlorothalonil (97.7%) was administered to CD-1 mice at dietary levels of 0, 750, 1500 or 3000 ppm (equivalent to 0, 112.5, 225 or 450 mg/kg/day) for two years. Bone marrow and splenic red pulp hyperplasia, increased kidney weights with surface irregularities,

pelvic dilation, cysts and nodules, and stomach/esophageal hyperplasia as well as hyperkeratosis were found at all dose levels. In males, the incidence of renal tumors was greater than in the control at all treatment levels reaching statistical significance ($p<0.05$) only at 750 ppm (112.5 mg/kg/day); whereas, in females, none were reported in any dose group. The incidence of stomach tumors in all treated males was slightly greater than in the control but was not statistically significant; whereas, in females, the increase was statistically significant ($p<0.01$) in the 1,500 and 3,000 ppm groups compared with the control group. The NOEL was less than 750 ppm (112.5 mg/kg/day) (MRID 00127858).

In another study, male CD-1 mice were given diets containing chlorothalonil (98.0%) at doses of 0, 10/15, 40, 175 or 750 ppm (0, 1.86, 5.35, 23.2 or 99.7 mg/kg/day), for two years. The NOEL was 40 ppm (5.35 mg/kg/day). The LOEL, based on the finding of renal tubular hyperplasia, was 175 ppm (23.2 mg/kg/day). There was no evidence of carcinogenicity in the mice (MRID 40243701).

In a study conducted for the NCI (National Cancer Institute), chlorothalonil (98.0-98.5%) was administered in the diet to B6C3F1 mice at 0, 2688 or 5375 ppm (0, 384 or 768 mg/kg/day) to males and at 0, 3000 or 6000 ppm (0, 429 or 851 mg/kg/day) to females for 91-92 weeks. There was no evidence of carcinogenicity (MRID 00030286).

In a study conducted for NCI, chlorothalonil (98.0-98.5%) was administered in the diet at 0, 5063 or 10126 ppm (0, 253 or 506 mg/kg/day) for 110-111 weeks to male and female Osborne Mendel rats. Renal adenomas and carcinomas were seen in both sexes at both dose levels (MRID 00030286).

In a carcinogenicity study in Fischer 344 rats, chlorothalonil (98.1%) was administered in the diet at 0, 40, 80 or 175 mg/kg/day for 116 weeks to males and 129 weeks to females. There were body weight decreases in both sexes at the high and mid doses. The non-glandular stomach was eroded and ulcerated. Histologically, there were compound related effects on the kidneys, esophagus, stomach and duodenum. Chronic glomerulonephritis, hyperplasia of cortical tubules and pelvic/papillary epithelium, and tubular cysts were found at all dose levels. Renal adenomas and carcinomas as well as stomach papillomas were present at all dose levels. The NOEL was >40 mg/kg/day (MRID 00146945).

In a related study, chlorothalonil (98.3%) was administered in the diet to Fischer 344 rats at levels of 0, 2, 4, 15 or 175 mg/kg/day for 23-29 months. Renal tubular adenomas and carcinomas were seen in males at 15 and 175 mg/kg/day and in females only at 175 mg/kg/day. The incidence of forestomach papillomas and carcinomas was increased only at 175 mg/kg/day in males and at both 15 and 175 mg/kg/day in females. The NOEL was 2 mg/kg/day and the LOEL of 4 mg/kg/day was based on increased kidney weights and hyperplasia of the proximal convoluted tubules in the kidneys as well as ulcers and forestomach hyperplasia (MRID 41250502).

In a chronic toxicity study, beagle dogs received chlorothalonil (97.6%) in the diet at 0, 60 or 120 ppm (0, 1.8 and 3.5 mg/kg/day) for two years. There was an increase in kidney vacuolated epithelium in males at 120 ppm (3.5 mg/kg/day) but only at the 12-month sacrifice. The NOEL was 60 ppm (1.8 mg/kg/day) and the LOEL was 120 ppm (3.5 mg/kg/day) based on the above mentioned kidney findings (MRID 00114034).

In another chronic toxicity study, chlorothalonil (98.3%) was administered orally by gelatin

capsules to Marshall beagle dogs at doses of 0 (empty capsules), 15, 150 or 500 mg/kg/day for 52 weeks. There were decreases in body weight gains in males and females at 500 mg/kg/day. The NOEL was 150 mg/kg/day and the LOEL was 500 mg/kg/day, based on decreased body weight gains in both sexes (MRID 43653603).

d) Mechanistic Data

In a cell proliferation study, 28 male Fischer 344 rats received technical chlorothalonil (97.9% a.i.) in the diet at 175 mg/kg/day for up to 91 days. Scheduled sacrifices occurred on Days 7 (14 rats), 28 (7 rats), and 91 (7 rats) for the purpose of assessing the effect of chlorothalonil administration on cell proliferation in the kidney. Rats were implanted with Alzet minipumps containing bromodeoxyuridine 3.5 and 6.5 days prior to sacrifice (Day 7), or 3.5 days prior to sacrifice (Days 28 and 91). Mean labeling index was statistically increased in the kidneys of male rats treated with 175 mg/kg/day chlorothalonil at all scheduled sacrifice times. From Day 7 to Day 28, the fold increase in labeling index was relatively stable (approximately 10-fold over control), with a decrease to approximately 3.5-fold over control on Day 91. Increased cell proliferation correlated with histopathological lesions of degeneration of the proximal convoluted tubules and epithelial hyperplasia. The results of this study demonstrate a sustained cell proliferative response as a result of dietary administration of technical chlorothalonil at a dose of 175 mg/kg/day. The apparent lack of cytotoxicity compared to the hypertrophic response in this study is not readily explained by the available data (MRID 44223002).

In another study, 96 male SPF rats were divided into test groups of 6 animals per group. Rats received technical chlorothalonil (98.98% a.i.) in the diet at dose levels of 0, 1.5, 15, or 175 mg/kg/day for either 7, 14, 21, or 28 days (total of 24 rats per time point). Histological examination of kidney and stomach tissue was performed for each group after the appropriate exposure. In addition, kidneys were subjected to PCNA staining and stomach to BrdU staining, and the labeling index and labeling count of cell nuclei performed. Duodenum was used as a negative control for PCNA and BrdU staining. Increased absolute and relative weight of the kidneys was observed at 175 mg/kg/day at all time points, and in one animal at 15 mg/kg/day on Day 28. Increased incidence of vacuolization of the epithelium of the proximal convoluted tubules was observed at all time points at 175 mg/kg/day and on Days 7, 14, and 21 at 15 mg/kg/day. PCNA immunostaining of the proximal convoluted tubule epithelial cells showed increased labeling of cells at the 175 mg/kg/day dose level at all time points, and increased labeling at 15 mg/kg/day on Days 7, 14, and 21. BrdU labeling of the rat forestomach showed marked labeling at 175 mg/kg/day at all time points, and increased labeling on Day 28 at 15 mg/kg/day. The results of this study demonstrate a toxic response of the kidney and forestomach to repeated dietary administration of chlorothalonil at doses of 15 and 175 mg/kg/day (MRID 44240901).

e) Developmental Toxicity

In a developmental toxicity study, New Zealand white rabbits were administered 0, 5, 10 or 20 mg/kg/day of chlorothalonil (98.7%) by gavage on gestation days 7-19. For maternal toxicity the NOEL was 10 mg/kg/day and the LOEL was 20 mg/kg/day based upon reductions in body weight gain and food consumption during dosing. No developmental toxicity was seen. For developmental toxicity, the NOEL was 20 mg/kg/day, the highest dose tested (MRID 41250503).

In a developmental toxicity study, Sprague Dawley rats were given chlorothalonil (98%) at 0, 25, 100 or 400 mg/kg/day by gavage on gestation days 6-15. For maternal toxicity, the NOEL

was 100 mg/kg/day and the LOEL was 400 mg/kg/day based on increased mortality and reduced body weight gain. For developmental toxicity, the NOEL was 100 mg/kg/day and LOEL was 400 mg/kg/day based on an increase in total resorptions and resorptions per dam with a related increase in postimplantation loss. No decrease in litter size was reported (MRID 00130733).

f) Reproductive Toxicity

In a two-generation study, Sprague Dawley rats were administered chlorothalonil (98%) in the diet at levels of 0, 500, 1500 or 3000 ppm (0, 38, 115 and 234 mg/kg/day). For parental/systemic toxicity, the NOEL was less than 500 ppm (<38 mg/kg/day). The LOEL was 500 ppm (38 mg/kg/day) based on hyperplasia of renal and forestomach tissues. For reproductive toxicity, the NOEL was 3000 ppm (234 mg/kg/day) and the LOEL was greater than 3000 ppm (>234 mg/kg/day) (MRID 41706201).

g) Mutagenicity

Chlorothalonil was not mutagenic and did not interfere with DNA repair mechanisms in S. typhimurium either in the presence or absence of exogenous metabolic activation derived from Aroclor-induced rat livers and/or kidneys (MRID 00030288, 00030290 and 00147949). There was also no evidence that treatment with nonactivated or S9-activated chlorothalonil induced a mutagenic response in either cultured Chinese hamster V 79 cells or BALB/3T3 mouse fibroblasts (MRID 00030289). Chlorothalonil did not cause phenotypic transformation in two rat embryo cell lines (F1706 and H4536 P+2), and these chlorothalonil-treated cell lines were not tumorigenic in newborn Fischer mice (MRID 00030291).

In an in vitro Chinese hamster (CHO) cell cytogenetic assay, chlorothalonil produced positive results at 0.15 and 0.3 μg/Ml but only in the absence of metabolic activation (MRID 40559103). The compound was also weakly clastogenic in an in vivo bone marrow chromosome aberration assay following 5 consecutive daily oral gavage administrations of 50-250 mg/kg to Chinese hamsters (MRID 00147948). The inclusion of gaps in the incidence of aberrant cells, the lack of a dose response and the absence of an effect in the acute phase of the study with levels up to 5000 mg/kg was, however, noted. Additionally, the result was not reproduced in subsequent studies using a 5-day repeated dosing schedule with Chinese hamsters up to a lethal dose of 750 mg/kg (MRID 43700602) or with rats receiving chlorothalonil levels ≤2000 mg/kg (MRID 43700601). Negative results were also obtained in rats (MRID 00147947) and mice (MRID 00147946) receiving single high doses of 5000 or 2500 mg/kg, respectively. Further testing yielded negative results for chromosomal aberrations and micronuclei induction in either rats or Chinese hamsters administered gavage doses up to 5000 mg/kg once daily for 2 days or mice receiving 2500 mg/kg once daily for 2 consecutive days (MRID 00127853 and 00127854).

Overall, the data from the above studies indicate that chlorothalonil is not mutagenic in bacteria or cultured mammalian cells and does not induce morphological transformation in rat embryo cells. A weak positive response was seen under nonactivated conditions in an in vitro cytogenetic CHO assay and in the subchronic phase of an in vivo bone marrow Chinese hamster cytogenetic assay. However, the relevance of both findings is questionable since genotoxicity was not demonstrated in vitro in the presence of metabolic activation and the in vivo results were not reproducible. In light of the considerable body of evidence from acceptable whole animal testing, it is concluded that chlorothalonil is also not clastogenic or aneugenic in rats, mice or Chinese hamsters.

h) Metabolism

Disposition studies of chlorothalonil were conducted in male and female rats in which either single oral doses (5-200 mg/kg) or multiple oral doses (1.5-160 mg/kg/day for 5 days) of 14C-labelled chlorothalonil were used. Oral absorption of the test material was low (approximately 33% of the administered dose). Peak blood levels were observed between 2-9 hours post dose and were considered low (i.e. less than 1% of the dose present in blood). Apparent saturation of kinetics occurred at doses between 5 and 50 mg/kg, with prolonged elimination and increased blood levels observed at higher dose levels. Chlorothlonil derived radioactivity was eliminated primarily by the gastrointestinal tract, with 80-90% of the administered dose observed in feces. Approximately 15-20% of the dose was observed in bile, with a reduced rate of biliary excretion observed at high doses. Tissue residues of chlorothalonil were highest in the gastrointestinal tract, blood, liver, and kidneys. Available data on metabolism of chlorothalonil in rats and dogs indicates that the parent chemical is conjugated in liver to glutathione or cysteine-S-conjugates. These conjugates are then absorbed from the gastrointestinal tract. Cysteine-S-conjugates, glutathione conjugates, or mercapturic acids reaching the kidney come into contact with proximal tubular cells, where eventual "activation" of pre-mercapturic acids occurs through the action of cysteine conjugate DF-lyase, an enzyme found in the cytosol and mitochondria of the cells of the renal proximal tubules. Nephrotoxicity of cysteine-S-conjugates through activation to thiol metabolites is related to renal cortical mitochondrial dysfunction. Respiratory control has been shown to be distrupted by the di- and tri-thiol analogs of chlorothalonil. Osmotic changes occur within the renal cotrical tubular cells as a result of toxic insult by the thiol metabolites of chlorothalonil, resulting in vacuolar degeneration follwed by cellular regeneration (MRID 44223002 and 44240901). This mechanism has been used to explain the carcinogenicity of chlorothalonil in rats, and formed the basis for the recent re consideration of the carcinogenic potential of chlorothalonil by the Health Effects Division Carcinogenicity Peer Review Committee.

i) Dermal Absorption

In a dermal absorption study, one percent ^{14}C chlorothalonil in latex base paint or in alkyd covering stain (0.1μg/cm^2) was applied to the back of male rats for periods of 8 hours (washed and terminated), 24 hours (washed and terminated) and 24 hours (washed and maintained for an additional 24 hours). For the paint, total recovery was 99-105% with 97-102% being in skin washes, 0.64-1.62% in skin and 0.58-0.99% absorbed (urine, feces, cage wash, blood and carcass). For the stain, total recovery was 89-96%, with 84-95% being in skin washes, 0.56-1.52% in skin and 0.78-2.97% absorbed (MRID 43600103).

An upper limit of 5% of chlorothalonil that contacts the skin during a workday is estimated to be absorbed (MRID 43600103). It is assumed that this rate will over-estimate human dermal absorption because the absorption rate is based on data derived from rat studies.

j) Toxicological Endpoints of Concern Identified for Use in Risk Assessment

(1) Reference Dose (RfD) for Chlorothalonil

An **RfD of 0.02 mg/kg/day** was determined based on the NOEL of 2 mg/kg/day established in a 2-year dietary study in rats and using an uncertainty factor of 100. The LOEL of 4 mg/kg/day was based on increased kidney weights and hyperplasia of the proximal convoluted tubules in the kidneys as well as ulcers and forestomach hyperplasia (MRID 41250502).

For renal tumorigenicity in the rat, the following No Observed Effects Levels were determined by others:
Health Canada.....NOEL = 15 mg/kg/day
World Health Organization.....NOEL = 3.0 mg/kg/day
United Kingdom.....NOEL = 4.0 mg/kg/day

For renal tumorigenicity in the mouse, the following NOELs were determined by others:
Health Canada.....NOEL = 21.3 mg/kg/day
World Health Organization.....NOEL = 21.0 mg/kg/day

(2) Classification of Carcinogenic Potential

On September 4, 1987, the HED Cancer Peer Review Committee (HED/CPRC) classified chlorothalonil as a Group B2 carcinogen; probable human carcinogen. This classification was based on statistically significant increases in the incidence of renal adenomas and carcinomas in male and female Fisher 344 rats, a statistically significant increase in combined renal adenomas/carcinomas in male and female Osborne-Mendel rats, and statistically significant increases in carcinomas of the forestomach in male and female CD-1 mice, as well as a positive dose-related trend for combined renal adenomas/carcinomas in male mice. The Science Advisory Panel on July 20, 1988 concurred with the Agency's classification of chlorothalonil as a Group B2 carcinogen.

On June 11, 1997, the HED/CPRC met to discuss and evaluate the weight-of-the-evidence on chlorothalonil in reference to its carcinogenic potential and to evaluate additional mechanistic data submitted by the registrant in support of the request for re-classification of the carcinogenicity of this chemical. In considering the weight of the evidence for classification of the carcinogenicity of chlorothalonil, the Peer Review Committee utilized the *EPA Proposed Guidelines for Carcinogen Risk Assessment* (April 23, 1996). In accordance with these proposed guidelines, the HED/CPRC unanimously agreed that the weight of the evidence supported a classification of chlorothalonil as "likely" to be a human carcinogen by all routes of exposure. This conclusion was based on the
evidence of increased incidence of renal adenomas, carcinomas, and adenomas/carcinomas combined in rats and mice following chronic administration of chlorothalonil at doses of 15 and 175 mg/kg/day, as well as increased incidence of forestomach carcinomas in CD-1 mice and papillomas and/or carcinomas combined in Fisher 344 rats. The HED/CPRC concurred that the renal tumor type is rare, there is evidence that precursor lesions occur in the kidney at doses just below those producing tumors, and that steps in that mechanism (for production of renal tumors) are present in humans but not to the same degree. For the forestomach tumors, the HED/CPRC concurred that the cell proliferation data supported a non-linear mechanism of action for induction of forestomach tumors and that precursor lesions to these tumors (including cell proliferation, hyperplasia, and hyperkeratosis) occur at doses and/or exposure times just below those producing tumors. Based on the discussion of the mode of action for production of renal and forestomach tumors by chlorothalonil, the HED/CPRC agreed that chlorothalonil met the risk assessment criteria for non-linearity, and that the Margin of Exposure (MOE) approach should be used for the purposes of this risk assessment (MRID 44240901, 44223002).

Since this tumor type is considered rare, for purposes of risk assessment, the MOE should be determined using the 1.5 mg/kg/day dose as the "point of departure," as no tumor response or cell proliferation response was observed at this dose level. Tumor response in the kidney as well as

cell proliferation was observed at the next higher dose level tested (15 mg/kg/day).

(3) Dermal Absorption

An upper limit of 5% of chlorothalonil that contacts the skin during a workday is estimated to be absorbed (MRID 43600103). It is assumed that this rate will over-estimate human dermal absorption because the absorption rate is based on data derived from rat studies. This dermal absorption rate is to be used for all chlorothalonil exposure scenarios except for use in paints and stains containing chlorothalonil. For these scenarios, a 1.22% dermal absorption rate (8 hour period) for latex based paints and a 1.34% dermal absorption rate (8 hour period) for alkyl-based stains are suggested. These values are based on the total dermal absorption rate for washed and unwashed skin (0.58 + 0.64 = 1.22 for latex; 0.78 + 0.56 = 1.34 for alkyd) from a study submitted on these products (MRID 43600103). The 8-hour rate was selected since it is assumed professional painters wash with soap and water after using latex paint and paint thinners after using the alkyl stains (11/13/96).

(4) Acute Dietary

A LOEL of 175 mg/kg/day will be used for acute assessment. This LOEL was based on renal and gastric lesions observed within four days of dosing. Chlorothalonil was administered in the diet to male Fischer 344 rats at 175 mg/kg/day (only dose) for 3 months. Serial sacrifices were conducted on treatment days 4 and 7 as well as at the end of weeks 2, 4, 6, 8, 10, 12, and the 91st day of exposure. The kidneys and stomach were examined histopathologically. The lesions observed in this study appeared to be precursors of kidney and forestomach lesions observed following chronic dietary administration to rats and mice. Since only one dose level was tested and effects were seen at this dose (LOEL), an extra modifying factor of 3 was added for a total Uncertainty Factor of 300) (MRID 40243702). Because a LOEL instead of a NOEL is being used for the chlorothalonil acute dietary risk assessment, the safety margin is 300 instead of 100 (S. Makris and M. VanGemert memo, 8/12/94).

(5) Short Term Occupational and Residential (1-7 days)

The NOEL of equal to or greater than 600 mg/kg/day will be used for this risk assessment. The LOEL was > 600 mg/kg/day and was based on no treatment-related systemic toxicity at the HDT in a 21-day dermal toxicity study in rats (MRID 44119101). An MOE of 100 is required.

(6) Intermediate Term Occupational and Residential (1 week to several months)

The NOEL of equal to or greater than 600 mg/kg/day will be used for this risk assessment. The LOEL was >600 mg/kg/day and was based on no treatment-related systemic toxicity at the HDT in a 21-day dermal toxicity study in rats (MRID 44119101). An MOE of 100 is required.

(7) Chronic (Life Time) Occupational and Residential (several months to lifetime)

The NOEL of 2 mg/kg/day will be used for this risk assessment. The LOEL was based on increased kidney weights and hyperplasia of the proximal convoluted tubule as well as forestomach hyperplasia and ulcers at 4 mg/kg/day in a 2-year dietary admix toxicity study in Fischer 344 rats

(MRID 41250502). The NOEL specified above will be used for risk assessment for the non-cancer effect and the NOEL of 1.5 mg/kg/day will be used in the risk assessment for the carcinogenic endpoint. Since an oral study was used for this exposure scenario, a dermal absorption rate of 5% will be used in this risk assessment (other dermal absorption rates apply for paint uses). Greenhouse use of chlorothalonil is the only use scenario considered potentially chronic.

(8) Inhalation Exposure (Any Time Period)

Except for an acute inhalation toxicity study, no inhalation toxicity studies were available for this assessment. The dose identified for inhalation risk is from an oral study (i.e. oral NOEL). Therefore, the inhalation exposure component (i.e. mg/kg/day) using a 100% (default value) absorption rate should be converted to an oral exposure (mg/kg/day). This exposure should then be compared to the oral NOEL of 2 mg/kg/day to calculate the inhalation Margin of Exposure (MOE_i). Separate risk calculations should be made for inhalation and dermal exposures since doses and endpoints have been identified for separate (i.e. dermal and inhalation) risk assessments.

1b. Hazard Assessment: 4-Hydroxy metabolite of chlorothalonil (4-Hydroxy-2,5,6-Trichloroisophthalonitrile,"SDS-3701")

The SDS-3701 metabolite has not been evaluated by the HED Peer Review Committees; therefore, no Dose-Response Assessment is available. Therefore, the metabolite was not included in the carcinogenic assessment, but was included in the acute and chronic (non-cancer) assessments.
Residues of chlorothalonil per se are not expected to transfer from feed items to meat and milk, but residues of SDS-3701 have been shown to occur in these commodities.

a) Acute Toxicity

The acute oral LD50 for male rats was 422 mg/kg and for female rats was 242 mg/kg, with the combined sexes value being 332 mg/kg with a toxicity category of II (MRID 00047938, 00047939 and 00095783).

b) Subchronic Toxicity

In a 4-month feeding study in Sprague-Dawley rats, SDS-3701 was administered at 0, 10, 50, 100 or 200 ppm (approximately 0, 0.5, 2.5, 5 or 10 mg/kg/day). The NOEL was 5 mg/kg/day. The LOEL was 10 mg/kg/day based on depression of body weight and an increase in liver weight in males (MRID 00047936).

Sprague-Dawley rats of both sexes were administered SDS-3701 in the diet for 61-69 days at doses of 0, 10, 20, 40, 75, 125, 250, 500 or 750 mg/kg/day. Mortality occurred $\geq$75 mg/kg/day. The NOEL was 20 mg/kg/day. The LOEL was 40 mg/kg/day based on decreased body weights compared with controls, anemia and renal cortical atrophy (MRID 00127847).

In a 3-month feeding study in beagle dogs, the SDS-3701 was administered at 0, 50, 100 or 200 ppm (approximately 0, 1.25, 2.5 or 5.0 mg/kg/day). The NOEL was 2.5 mg/kg/day. The LOEL was 5.0 mg/kg/day based on renal tubular degeneration and vacuolation in males (MRID 00047940).

c) Chronic Toxicity and Carcinogenicity

In a 2-year feeding study in Sprague-Dawley rats, the SDS-3701 was administered at doses of 0, 0.5, 3.0 or 15 (reduced to 10 at week 30) or 30 (reduced to 20 at week 30) mg/kg/day. The NOEL was 3.0 mg/kg/day. The LOEL was 10 mg/kg/day based on reduced body weight, microcytic anemia, hemosiderin and decreased serum potassium. There was no evidence of carcinogenicity in either sex (MRID 00127848 and 00137124).

In a 2-year feeding study in CD-1 mice, the SDS-3701 was administered at nominal doses of 0, 375, 750 or 1500 ppm (approximately 0, 54, 107 or 214 mg/kg/day). A NOEL was not established; the LOEL was <54 mg/kg/day based on increased liver-to-body weight ratios in males. There was no evidence of carcinogenicity in either sex (MRID 00127849).

d) Developmental Toxicity

In a developmental toxicity study, SDS-3701 was administered to pregnant female Dutch Belted rabbits at dose levels of 1, 2.5 or 5 mg/kg/day on gestation days six through fifteen. For maternal toxicity the NOEL was 1 mg/kg/day and the LOEL was 2.5 mg/kg/day based on a dose dependent increase in maternal death and abortion. For developmental toxicity the NOEL was 5 mg/kg/day; a LOEL was not established (MRID 00047944).

e) Reproductive Toxicity

In a 1-generation reproduction study in Sprague-Dawley CD rats, SDS-3701 was administered at 0, 10, 20, 30, 60, or 120 ppm (approximately 0, 0.5, 1.0, 1.5, 3.0 or 6.0 mg/kg/day). For parental systemic toxicity, the NOEL was 1.5 mg/kg/day and the LOEL was 3.0 mg/kg/day. For reproductive toxicity, the NOEL was 6.0 mg/kg/day based on reduced weanling body weights (MRID 00127845).

In a 3-generation reproduction study in Sprague-Dawley CD rats, SDS-3701 was administered at 0, 10, 60 or 125 ppm (approximately 0, 0.5, 3.0 or 6.25 mg/kg/day). The parental systemic NOEL was 0.5 mg/kg/day and the LOEL was 3.0 mg/kg/day based on a modest reduction in pup body weight. For reproductive toxicity the NOEL was 6.25 mg/kg/day (MRID 00127844).

f) Mutagenicity

The SDS-3701 metabolite of chlorothalonil did not cause DNA damage in S. typhimurium or induce a mutagenic response in this microbial species or in cultured Chinese hamster V 79 cells or BALB/3T3 mouse fibroblasts. No evidence of mutagenesis was found in a host mediated assay using S. typhimurium tester strains and mice exposed daily for 5 days to 6.5 mg/kg/day of the compound (MRID 00030288, 00030289, 00030290 and 00030291). Phenotypic transformation was not observed in rat embryo cells treated with concentrations of the metabolite up to 10 μg/ml; however, F1706 cells treated with 10 μg/ml did induce late tumors in newborn Fischer rats. The latter finding was considered inconclusive since the more sensitive cell line (H4536 P+2) was not tumorigenic under similar conditions (MRID 00127846).

The S9-activated SDS-3701 metabolite at 260-520 μg/ml induced reproducible, significant and dose-related increases in the yield of cells with abnormal chromosome morphology (MRID

44022201). Clastogenic activity was, however, not uncovered in bone marrow cytogenetic assays conducted in Chinese hamsters receiving a single oral administration of 500 mg/kg (MRID 44022202) or in mice receiving a single oral dose of 6.5 mg/kg (MRID 00044728). Mouse and rat dominant lethal assays were also negative using either a subchronic 5-day exposure to 6.5 mg/kg (mice) or an acute and subchronic experimental design with treatment levels up to 8 mg/kg/day in rats (MRID 00047941 and 00047942).

Based on this evaluation, it was concluded that the SDS-3701 metabolite of chlorothalonil was positive for clastogenic activity in cultured mammalian cells; however, damage to chromosomes was not expressed in either the somatic or germinal cells of whole animals. Hence, the concern for genotoxic potential is lessened.

1c. Hazard/Dose-Response Assessment: Hexachlorobenzene (HCB)

HED classified HCB, an impurity in chlorothalonil products, as a B2, probable human carcinogen, based on data sets which showed significant increases in tumor incidences in two species: hamsters and rats. In a June 21, 1995 memo from W. Burnam/SAB, the Q_1* for HCB was revised using a 3/4 scaling factor to be 1.02 $(mg/kg/day)^{-1}$.

The RfD for HCB is 0.0008 mg/kg/day based on a NOEL of 0.08 mg/kg/day in a 130-week feeding study in rats. (Effects observed were hepatic centrilobular basophilic chromogenesis.) An uncertainty factor of 100 was used to account for the inter-species extrapolation and intra-species variability.

The dermal penetration factor is estimated to be 26%. This is based on a previous assessment for DCPA which also is contaminated with HCB.

2. Exposure Assessment

a) Registered Uses

Chlorothalonil is a broad spectrum fungicide applied to turfgrass, vegetables, stone fruits, peanuts, soybeans, ornamentals (including greenhouse grown), minor crops (cranberry) and conifers (forestry) to control plant diseases such as powdery mildew, *Botrytis*, *Rhizoctonia*, and *Phytophthora*. Formulations of chlorothalonil include wettable powders, aqueous flowable concentrates, and solid flowables (water dispersable granules). Chlorothalonil is also formulated into paints for interior and exterior applications.

(1) Agricultural Products

There are 12 chlorothalonil end-use products (EPs) with food/feed uses registered to ISK Biosciences Corporation, the basic producer. These EPs are listed below.

Table 4.
Chlorothalonil Food/Feed Use Products Registered by ISK Biosciences Corp.

HED Reg. No.	Acceptance Date	Formulation Class	Product Name
50534-8 [1]	3/17/94	4.17 lb/gal FIC	Bravo 500
50534-23 [2]	1/6/94	75% WP	Bravo W-75
50534-157 [3]	1/6/94	90% DF	Bravo 90DG
50534-159	3/18/94	2.08 lb/gal FIC	Bravo S
50534-161	1/15/90	4.16 lb/gal FIC	Bravo Flowable Fungicide
50534-188 [4]	3/17/94	6 lb/gal FIC	Bravo 720
50534-189	3/7/94	75% WP	Chlorothalonil 75 WP
50534-191	10/21/94	27% DF	Bravo C/M
50534-201	1/6/94	82.5% DF	Bravo 825
50534-203	1/21/94	4.16 lb/gal FIC	Reach Agricultural Fungicide
50534-204	3/18/94	4.17 lb/gal FIC	Bravo ZN
50534-205	6/21/94	75% WP	Bravo W-75 WSB

1. Includes SLN Nos. CA850066, OR810032, OR860005, PR830002, and TN840003.
2. Includes SLN No. CA850067.
3. Includes SLN No. CO880022.
4. Includes SLN Nos. AL900003, AR900001, CO880021, DE900003, FL900006, FL910018, KS910001, KS940003, LA900008, MA900001, MS900001, NE940002, NJ910003, NC920012, SC890007, TX880005, TX920022, VA900003, VA930007, and WI940002.

(2) Non-Agricultural Products

The non-agricultural uses of chlorothalonil include turf use on golf courses and sod farms, inside greenhouses, nurseries, in homeowner "push type" spreaders and hose end sprayers, and paint uses (brush-on and sprayed-on) and as a gel paint additive. The nonagricultural uses of chlorothalonil also include uses on fresh cut lumber to control sapstain and molds (dip vats and sprayed-on), uses in caulks, sealants, grout and in pressure treatment of wood.

b) Dietary Exposure

OPPTS GLN 860.1300: Plant Metabolism

The qualitative nature of the residues in plants is adequately understood based on metabolism studies with carrots, celery, lettuce, snap beans, and tomatoes. The residues of concern are chlorothalonil and its 4-hydroxy metabolite (SDS-3701). Chlorothalonil comprised ca. 90% of the total radioactive residues (TRR) in lettuce harvested 1-21 days following four foliar applications of [^{14}C]chlorothalonil. Chlorothalonil, at 70-95% of TRR, and its 4-hydroxy metabolite, at 2-8% of TRR, were the major residues identified in carrots harvested 1-21 days and tomatoes harvested 1-14 days following three foliar applications of [^{14}C]chlorothalonil. Chlorothalonil, at 20-31% of TRR, was the only residue identified in snap beans harvested 7 days following the last of four foliar applications of [^{14}C]chlorothalonil at ca. 1x the maximum registered single application rate. Chlorothalonil, at 24.1-76.9% of TRR, was also the only residue identified in celery foliage

and stalks harvested 7 and 21 days following the last of 12 foliar applications of [^{14}C]chlorothalonil at 1x the maximum registered single application rate. Although no polar metabolites were conclusively identified in the celery study, the data suggested that these residues were glutathione conjugates of chlorothalonil and related compounds in which the glutathione moiety had undergone further transformation.

On December 5, 1995, the HED Metabolism Committee met to consider whether the Agency should continue to regulate chlorothalonil residues as the combined residues of parent and the 4-hydroxy metabolite (SDS-3701) or should SDS-3701 be removed from the tolerance expression. On December 19, 1995, the Committee concluded that since available toxicological data indicate that SDS-3701 can contribute to the non-cancer dietary risk from uses of chlorothalonil on food and feed commodities, it should remain in the tolerance expression.

OPPTS GLN 860.1300: Animal Metabolism

The qualitative nature of the residue in animals is adequately understood. The residue of concern in meat and milk is the 4-hydroxy metabolite of chlorothalonil (SDS-3701). Chlorothalonil, per se, has been shown to be so unstable in ruminant tissues that it is impractical to establish tolerances that include the parent. Tolerances are needed on meat and milk for SDS-3701. Tolerances are not required for residues of either chlorothalonil or SDS-3701 in poultry. Little metabolism of SDS-3701 occurs in ruminants and the unchanged test substance accounted for 88-99% of the TRR in milk and edible tissues.

The metabolic fate of chlorothalonil and SDS-3701 in ruminants is adequately understood based on goat metabolism studies. The proposed pathway for chlorothalonil metabolism in ruminants involves substitution of one or more of the chlorine atoms with glutathione; these complexes may undergo further modification of the glutathione side chains to yield a variety of products.

Based on poultry metabolism studies using [^{14}C]chlorothalonil and 4-hydroxy-[^{14}C]chlorothalonil, HED concluded that there is no significant transfer of chlorothalonil to poultry tissues or eggs, and that the levels of transfer of SDS-3701 are too low to require feeding studies or tolerances for poultry commodities.

OPPTS GLN 860.1340: Residue Analytical Methods-Plants and Animals

Adequate residue analytical methods are available for purposes of reregistration. The Pesticide Analytical Manual (PAM) Vol. II lists Method I, a GC method with electron capture detection (ECD), for the enforcement of tolerances for plant commodities. Residue data for plant commodities were collected using methods based on the enforcement method. HED has recommended for establishment of tolerances for residues of SDS-3701 on meat and milk contingent upon receipt of an acceptable enforcement method for these commodities. The registrant (ISK) has submitted a method to the agency which has undergone successful independent laboratory validation. This method is currently being validated by the Agency. The registrant has proposed a GC/ECD method for enforcement of tolerances for peanuts, potatoes, and tomatoes which is a modification of the current enforcement method. Pending a successful Agency method trial, HED will consider this method for publication in PAM, Vol. II.

The FDA PESTDATA database dated 1/94 (PAM Vol. I, Appendix I) indicates that

chlorothalonil is completely recovered (>80%) using multiresidue methods PAM Vol. I Sections 303 (Mills, Onley, Gaither method) and 304 (Mills fatty food method) and has a low recovery (<50%) using Section 302 (Luke method).

OPPTS GLN 860.1380: Storage Stability

All data pertaining to storage stability have been evaluated and deemed adequate. The existing evidence indicates that residues of chlorothalonil, SDS-3701 and HCB are generally stable during frozen storage for up to 6 years. The data support the trial data used in establishing tolerances.

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

A 28-day ruminant feeding study has been reviewed and accepted by HED. HED recommends the establishment of tolerances for the 4-hydroxy metabolite (SDS-3701) in meat and milk contingent upon a satisfactory validation of an enforcement analytical method for SDS-3701 residues in these commodities which has been submitted by ISK Biosciences. The requirement for a poultry feeding study was waived based on the results of the poultry metabolism study.

The requirements for additional HCB poultry and ruminant feeding studies (7/31/91 DCI) have been waived. HCB feeding studies are available to the Agency. These feeding studies indicate that residues of HCB accumulate only in fatty matrices.

OPPTS GLN 860.1300: Magnitude of the Residue in Plants

The reregistration requirements for magnitude of the residue in plants are fulfilled for the following commodities: apricots; asparagus; beans, dry and succulent; blueberries; carrots; celery; cherries; field corn; field corn fodder; sweet corn (K+CWHR); sweet corn fodder; sweet corn forage; cranberries; cucumbers; filberts; garlic; grass seed screenings; melons; mint; mushrooms; nectarines; onions, dry bulb; papayas; parsnips; passion fruit; peaches; peanuts; plums; fresh prunes; potatoes; pumpkins; soybeans; squash, summer and winter; and tomatoes. An increased tolerance must be proposed for green onions.

The product labels for all chlorothalonil end-use products with use directions on food/feed crops must be amended to specify a maximum number of applications per season or a maximum seasonal rate for each crop, which must be supported by appropriate field residue data.

The 7/31/91 DCI required residue data for HCB from field trials on eight representative crops for the purposes of risk assessment. HED has since recommended that these data requirements be waived. Based on additional information provided by ISK Biosciences, HED has concluded that for the purposes of estimating the dietary risk of HCB resulting from its presence as a contaminant in formulations of chlorothalonil, and in those cases where residues on crops are below the limit of detection of the analytical method, residues of HCB should be estimated to be present in the same ratio relative to chlorothalonil as was present in the formulation applied to the crop.

HED recommends that labels be amended to reflect that chlorothalonil-treated plant parts remaining after harvest of seed are allowed to be fed to livestock.

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

All data for magnitude of the residue in processed food/feed have been evaluated and deemed adequate. No tolerances for processed commodities are required for chlorothalonil.

OPPTS GLN 860.1560: Reduction in Residues

All data pertaining to reduction in residues have been evaluated and deemed adequate. No additional data are required (see "Anticipated Residues" section below).

OPPTS GLN 860.1850: Confined/Field Rotational Crops

All data pertaining to rotational crops have been evaluated and deemed adequate. In response to Agency evaluations of confined rotational crop data, the registrant established a 12-month rotational crop restriction on all pertinent product labels and submitted several rotational crop studies. These data indicated that the only residue that was detected in rotated crops was the soil metabolite (SDS-46851). Because of the low toxicity of this metabolite, an exemption for the requirement of a tolerance for residues of the soil metabolite 3-carbamyl-2,4,5-trichlorobenzoic acid (SDS-46851) as inadvertent residues in rotated crops has been established (40 CFR §180.1110). In addition, the registrant's request to delete rotational crop restrictions from chlorothalonil labels was approved.

Anticipated Residues

The following assumptions were used in determining the anticipated residue estimates in Table 5 and should be noted in any dietary risk assessment based on these values.

- Although chlorothalonil and SDS-3701 are both regulated, only chlorothalonil is considered to be a probable human carcinogen by the Agency. Therefore, these anticipated residues do not include SDS-3701.

- Hexachlorobenzene, which is a B2 probable human carcinogen, is present as an impurity in chlorothalonil formulations and is considered to be a residue of concern on chlorothalonil treated crops. Anticipated residues of HCB on plant food commodities will be estimated by assuming that residues will be present at a level proportional to the maximum level certified to be present in chlorothalonil formulations, i.e., if the maximum certified limit of HCB is 0.05%, then HCB anticipated residues on a plant commodity will be estimated as 0.0005 x the anticipated residues of chlorothalonil on that commodity.

- The maximum level of HCB in chlorothalonil allowed by the Agency is 0.05%. The basic producer has committed to reducing the level of HCB in their technical formulations to less than 0.004% and requests that the Agency take this into consideration in dietary risk assessments. Since there are other producers of chlorothalonil that have not committed to this reduction, we will assume a level of 0.05% in this assessment. For purposes of evaluating risk mitigation due to this reduction in level of HCB, the anticipated residues in Table 5 can be multiplied by a factor of 0.08 if all formulations achieve the 0.004% HCB level.

- The Agency has concluded that residues of chlorothalonil per se will not transfer to meat, milk, poultry and eggs; therefore, only anticipated residues for HCB on these commodities will be provided (W.Smith memo, 6/13/95).

Table 5.
Anticipated Residues of Chlorothalonil and HCB From the Use of Chlorothalonil on Food or Feed Crops [1,2].

Commodity	Anticipated Residues (ppm)	
	Chlorothalonil	HCB
apricots	0.0078	3.9×10^{-6}
banana pulp	0.0005	0.3×10^{-6}
beans, dry	0.0087	4.4×10^{-6}
beans, snap	0.0133	6.7×10^{-6}
broccoli	0.0015	0.8×10^{-6}
Brussels sprouts	0.0135	6.8×10^{-6}
cabbage	0.0137	6.9×10^{-6}
cabbage, Chinese	0.0116	5.8×10^{-6}
cocoa	0.05	2.5×10^{-6}
cantaloupe	0.0191	9.6×10^{-6}
carrots	0.0036	1.8×10^{-6}
cauliflower	0.0115	5.8×10^{-6}
celery	0.0874	43.7×10^{-6}
cherries	0.002	1×10^{-6}
cranberries	0.4125	206×10^{-6}
coffee	0.20	1×10^{-4}
corn, sweet	0.0002	0.1×10^{-6}
cucumbers	0.0062	3.1×10^{-6}
garlic	0.0005	0.3×10^{-6}
honeydew	0.0033	1.7×10^{-6}
nectarines	0.00175	0.9×10^{-6}
onions, bulb	0.0033	1.7×10^{-6}
onions, green & leeks	0.0262	13.1×10^{-6}
papayas	0.005	2.5×10^{-6}
parsnips	0.0052	2.6×10^{-6}

Commodity	Anticipated Residues (ppm)	
	Chlorothalonil	HCB
passion fruit	3	1.5×10^{-3}
peaches	0.0018	0.9×10^{-6}
peanuts	0.0045	2.3×10^{-6}
plums	0.0005	0.3×10^{-6}
potatoes	0.0030	1.5×10^{-6}
pumpkins	0.0065	3.3×10^{-6}
soybeans	0.00005	2.5×10^{-8}
squash	0.0058	2.9×10^{-6}
tomatoes	0.0716	35.8×10^{-6}
watermelon	0.0228	11.4×10^{-6}
Residues in Animal Commodities		
Cattle fat	0	1.65×10^{-4}
meat	0	1.24×10^{-5}
liver	0	8×10^{-6}
kidney	0	8×10^{-6}
Poultry fat	0	2.2×10^{-6}
meat	0	3.7×10^{-8}
liver	0	7.3×10^{-7}
Milk	0	1.7×10^{-6}
Egg-white only	0	1.5×10^{-9}
Egg-yolk only	0	7.3×10^{-7}
Eggs-whole (36.55% yolk)	0	2.7×10^{-7}

The dietary exposure analysis for chlorothalonil also includes the pending uses on pistachios, asparagus, mangoes, almonds, and non-bell peppers.

c) Occupational and Residential Exposure

(1) Handler Exposures & Assumptions

The daily exposure for handlers is calculated using the following formula:

Daily exposure (mg ai/kg bw/day)

$$\frac{\text{unit exp.(mg ai/lb ai used) X lb ai/A X A/day X dermal absorption}}{\text{body weight (75.9 kg)}}$$

Since the Agency is participating in a project through NAFTA to harmonize risk assessments for chlorothalonil, the following body weights are used in the occupational and residential exposure risk assessments: handler or worker: 75.9 kilograms; female worker: 61.5 kilograms.

EPA has determined that there is an exposure potential for mixers, loaders, applicators, or other handlers during usual use-patterns associated with chlorothalonil.

Handler exposure scenarios for chlorothalonil :

Large scale mixing/loading and applying chlorothalonil for airblast, ground-boom, and aerial application equipment;

Mixing/loading chlorothalonil for applications through irrigation equipment;

Mixer/loader and applicator exposure while using hand-held equipment such as backpack sprayers, hose-end sprayers and granular spreaders;

Flaggers supporting aerial applications;

Painting with airless sprayers and paint brushes while using paints and stains containing chlorothalonil;

Mixing liquid chlorothalonil into paints.

Additionally, the registrant has asserted that "the non-agricultural uses of chlorothalonil also include uses on fresh cut lumber to control sapstain and molds (dip vats and sprayed-on), uses in caulks, sealants, grout and in pressure treatment of wood."

Until recently, HED was unaware of the wood treatment uses for chlorothalonil (described above). Exposure data for those uses should be considered a data gap. The registrant has conducted a study addressing exposure during the application of paints and stains containing chlorothalonil. The painter study is assumed to represent a higher exposure than the use of chlorothalonil treated caulks.

Mixer/loader/applicator (M/L/A) exposure data were required during Phase IV of the reregistration process. Additional M/L/A data were required in 1991 for painters and greenhouse applicators. The registrant has submitted the following handler exposure monitoring studies to support the reregistration of chlorothalonil:

- A Mixer, Applicator, and Mower Exposure Study with Chlorothalonil for Golf Course Maintenance [MRID 42433810];
- Potential Exposure of Workers to Chlorothalonil when Handling and Applying Paint containing Chlorothalonil [MRID 43600102];

- Chlorothalonil Worker Exposure During application of Daconil 2787 Flowable Fungicide in Greenhouses [MRID 43623201].

Surrogate data (unit exposures) provided in the Pesticide Handlers Exposure Database (PHED) are also available for estimating other handler exposure scenarios. These scenarios include handling tasks associated with the use of aerial, chemigation, airblast, ground-boom, and hand-held equipment. Where appropriate, the data from handler exposure monitoring studies submitted by the registrant (backpack, paint sprayer, and golf course applications) have been merged with data contained in PHED. These scenarios are shown in Tables 8-11. The clothing and PPE scenarios for each type of exposure reflect the clothing and PPE worn in the study from which the unit exposure values were derived. The crops listed with each exposure scenario are the crops with the higher application ranges representing reasonable and high end exposure scenarios.

There are very limited data regarding professional lawn care applications to residential turf. An "Assessment of Lawn Care Worker Exposure to Dithiopyr" is available in the open literature (Cowell, J.E., Lottman, C.M., and Manning, M.J. 1991. Arch. Environ. Contam. Toxicol. 21:195-201). In this study, applicator exposure was measured using biological monitoring techniques. Since the dermal absorption rate of dithiopyr is known as is chlorothalonil, an estimation of exposure to handlers using chlorothalonil can be made using these surrogate data.

(2) Post-Application Exposures and Assumptions

As a non-systemic fungicide, when applied to plant tissues, chlorothalonil is strongly bound to leaf and stem cuticular waxes. According to the registrant, dissipation is influenced primarily by rainfall and irrigation. In the absence of rain or irrigation, dissipation is influenced primarily by leaf expansion. Repeated applications are made to many crops because chlorothalonil is used as a preventative treatment rather than curative treatment.

Chlorothalonil is applied to several crops requiring hand-labor resulting in a significant potential for workers to be exposed to treated foliage. For many crops, frequent applications are made up-to, and throughout the harvest period.

An extensive risk assessment was not made for HCB as a contaminant in chlorothalonil. Based on high end exposure; a mixer/loader using a wettable powder to support aerial applications to celery, a risk of 2.8×10^{-5} was estimated. Risk for the other scenarios are assumed to be lower than this. This is a worst case estimate based on 0.05% HCB, newer formulations contain lower concentrations such as 0.02%.

Post-application exposure may be mitigated by the establishment of restricted entry intervals (REI) for occupational uses. REI's allow sufficient time to pass for field residues to dissipate to levels that result in acceptable MOEs for reentry workers (100 or greater). Restricted Entry Intervals (REI) and post-application exposure for chlorothalonil was calculated by using the following data submitted by ISK Biosciences:

- Determination of Dislodgeable Foliar Residues of Chlorothalonil and HCB from Bravo 720 Treated Cherry Leaves [MRID 42875902];

- Determination of Dislodgeable Foliar Residues of Chlorothalonil and HCB from Bravo 720 Treated Broccoli Plants [MRID 42875903];

- Determination of Dislodgeable Foliar Residues of Chlorothalonil and HCB from Bravo 720 Treated Cucumber Plants [MRID 42875904];
- A Tomato Harvester Exposure Study with Chlorothalonil [MRID 470025045];
- A Golfer Exposure Study with Chlorothalonil Used for Golf Course Maintenance [MRID 42433811];
- A Mixer, Applicator, and Mower Exposure Study with Chlorothalonil for Golf Course Maintenance [MRID 42433810].

Except for tomatoes, the above referenced dislodgeable foliar residue studies were conducted without concurrently monitoring worker exposure. Therefore, worker exposure (μg/hr) to those dislodgeable foliar residues (μg/cm^2) was estimated using estimated transfer factors (cm^2/hr). Transfer factors bridge worker exposure tasks to field-measured dislodgeable foliar residues. The estimated transfer factors used in this chapter are based on professional judgment and discussions with personnel at the California Department of Pesticide Regulation. Generic transfer factors corresponding to agricultural reentry exposure are presently being developed by the Agricultural Reentry Task Force (ARTF). The registrant, ISK Bioscineces, is a member of this task force.

The above referenced data do not address post-application exposure to treated turfgrass in residential situations. Although two of the studies address post-application exposure of golfers and mowers following chlorothalonil treatments to golf courses, no measurements of foliar dislodgeable residues were made. By measuring both human exposure and available dislodgeable foliar residues concurrently, transfer factors can be calculated. The registrant asserts that chlorothalonil use on turfgrass is primarily limited to golf courses; however, uses on residential lawns are not prohibited on the label. The data gap addressing residential exposure to treated turfgrass is to be fulfilled by the Outdoor Residential Exposure Task Force (ORETF) of which the registrant is a member. Data for reentry to turfgrass treated with chlorothalonil was required in a recently issued DCI for products registered on turfgrass (3/31/95).

Post-application/reentry daily exposure (mg/kg/day) is calculated as follows:

$$\frac{\text{DFR } (\mu\text{g/cm}^2) \times \text{transfer factor } (\text{cm}^2/\text{hr}) \times 8 \text{ hours/day} \times \text{dermal absorption}}{\text{body weight (75.9 kg)}}$$

For post-application risk to workers in greenhouses, a body weight of 61.5 kg was used to account for the lower body weight of women.

3. Risk Assessment

a) Dietary Risk Assessment

Food uses evaluated in the DRES analysis were the published uses of chlorothalonil listed in 40 CFR §180.275 and the Tolerance Index System (TIS). The chronic non-cancer analysis for chlorothalonil (parent only) and HCB used anticipated residues and the results were compared to

the RfD for chlorothalonil and HCB, respectively. Residues of chlorothalonil per se are not expected to transfer from feed items to meat and milk, but residues of SDS-3701 could occur in these commodities. Thus, there is no carcinogenic risk attributable to chlorothalonil from its use on livestock feed items. SDS-3701 was not measured in monitoring studies used to determine anticipated residues. The upper bound carcinogenic risk from chlorothalonil and HCB was calculated using the Margin of Exposure (MOE) and Q * approach, respectively.

Reassessed Tolerances: In the Product and Residue Chemistry Chapter of the Reregistration Eligibility Document, HED concluded that tolerances for chlorothalonil are adequate for reregistration (W. Smith memo, 3/16/95).

Currently there are no tolerances for chlorothalonil on cattle, goat, hogs, horse and sheep meat, fat and meat byproducts, milk, poultry or eggs. HED does not recommend for tolerances for poultry and eggs for reregistration of chlorothalonil. A 28-day ruminant feeding study has been reviewed and accepted by HED. We recommend the establishment of tolerances for the 4-hydroxy metabolite (SDS-3701) in meat and milk.

At this time HED recommends that all of the above animal commodities be considered in the risk assessment for HCB since secondary residues of HCB are found in meat, milk and eggs at low levels.

Pending Tolerances: Tolerances on pecans (0.02 ppm), pistachios (0.2 ppm), asparagus (0.1 ppm), mangoes (1 ppm), almonds (0.05 ppm), almond hulls (1 ppm), and non-bell peppers (5 ppm) have been included in the risk analysis as pending tolerances. Anticipated residues were used for pistachios (0.068 ppm) and mangoes (0.3 ppm) and asparagus (0.03 ppm). Anticipated residues for blueberries (1 ppm), and filberts (0.1 ppm) are set at tolerance levels. Residues for mushrooms were set at 7 ppm, the proposed tolerance at the time of the analysis. A tolerance of 1 ppm has since been established for mushrooms based on an altered use pattern. Imported snow peas from Guatemala have not been included in the analysis but have been assessed by DRES in the past. Chronic and carcinogenic risk estimates from the pending uses are included for risk management information only.

Anticipated Residues and Percent Crop Treated Information: Anticipated residues have been provided for the purpose of dietary risk analysis. One set of residues is for chlorothalonil and another is for residues of the contaminant, HCB (W. Smith memo, 6/13/95). U.S. FDA monitoring data (1988-1993), USDA PDP survey data (1992-1994 partial), and field trial data are types of anticipated residue data provided for HCB and chlorothalonil. Percent Crop Treated information for some of the food crops was provided from BEAD (G.Ali, 6/94) and other sources cited in the Anticipated Residues memo (W. Smith memo, D208333, 6/13/95).

Residues of HCB in plant commodities were estimated to be present at a level not exceeding 0.05% of the residues of chlorothalonil. This is equivalent to the maximum level of HCB that is allowed in formulations of chlorothalonil. In meat products, ARs were estimated based on HCB feeding studies (W.Smith memo, 6/13/95). ARs were used to calculate both chronic and carcinogenic dietary exposure.

Table 6
Residue Sources and Toxicity values used for Dietary Risk Calculations

Risk Assessment	Residue Source	For **Chlorothalonil** Risk, Compare to:	For **HCB** Risk, Compare to:
Acute Dietary	TMRC or AR's - All commodities[1]	LOEL for chlorothalonil: 175 mg/kg/day (for MOE>300)	N/A: no acute dietary endpoint for HCB
Chronic Non-Cancer Dietary	For Chlorothalonil: TMRC with PCT; include MMPE[2]	RfD for chlorothalonil:0.02 mg/kg/day (for %RfD)	N/A
	For HCB: AR's for HCB in 6/13/95 (tolerances multiplied times 0.0005 except MMPE[2])	N/A	RfD for HCB:0.0008 mg/kg/day
Dietary Cancer	For Chlorothalonil: AR's excluding MMPE[2]	NOEL for chlorothalonil cancer: 1.5 mg/kg/day (for MOE>100)	N/A
	For HCB: AR's including MMPE	N/A	Q_1* for HCB: 1.02 $(mg/kg/day)^{-1}$

1. 'All Commodities' means to include meat and milk, eggs and poultry.
2. 'MMPE' means meat, milk, poultry and eggs.

(1) Acute Dietary Risk

The DRES detailed acute exposure analysis estimates the distribution of single-day exposures for the overall U.S. population and certain subgroups. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-1978 Nationwide Food Consumption Survey (NFCS) and accumulates exposure to chlorothalonil and HCB for each commodity. Each analysis assumes uniform distribution of chlorothalonil in the commodity supply.

Since the toxicological effects to which high-end exposure is being compared in this analysis are renal and gastric lesions (found in the kidneys and stomach), all standard DRES subgroups are of concern. The analysis includes the U.S. population - 48 states and four subgroups: Infants (<1 year), children (1-6 years), females (13+years) and males (13+years).

The Margin of Exposure (MOE) is a measure of how closely the high end exposure comes to the NOEL (the highest dose at which no effects were observed in the laboratory test), and is calculated as the ratio of the NOEL to the exposure (NOEL/exposure = MOE). When the endpoint is taken from an animal study, as in this case, the Agency is not generally concerned unless the MOE is below 100. However, because a LOEL instead of a NOEL is being used for the chlorothalonil acute dietary risk assessment, the safety margin is 300 instead of 100 (S. Makris and M. VanGemert memo, 8/12/94).

The analysis included tolerances being recommended through reregistration for chlorothalonil. Pending tolerances and tolerances for meat and milk were included in the acute risk

assessment.

The analyses calculated the exposure of the highest exposed individual for the U.S. population in the distribution and compared the exposure to the LOEL of 175 mg/kg bwt/day from the subchronic study in rats (S. Makris and M. VanGemert memo, 8/12/94). The table below provides the calculated MOEs for the general population and the five highest subgroups. The percent of the population which consumes at least one of the commodities for which chlorothalonil is registered is 92-99% of all persons in the food survey.

Table 7
Acute Dietary Exposure Analysis Results using Supported and Pending Tolerances for Chlorothalonil

DRES Subgroup	MOE NOEL/Exposure
U.S. population (48 states)	1166
Infants (<1 year)	875
Children (1-6 years)	875
Females (13+ years)	1750
Males (13+ years)	1750

(2) Chronic Non-Cancer Dietary Risk

Chronic Non-Cancer Exposure from combined residues of chlorothalonil and its metabolite SDS-3701

Tolerance level residues were used in the analysis to calculate a Theoretical Maximum Residue Contribution (TMRC). The analysis was futher refined by considering percent of crop treated information (anticipated residue contribution: ARC). These exposure estimates were then compared to the RfD for chlorothalonil for chronic dietary risk.

Using Tolerance level Residues:
The Theoretical Maximum Residue Contribution (TMRC) for the over all U.S. population and the subgroup with the highest estimated risk from all currently published and pending chlorothalonil tolerances, *and proposed meat and milk tolerances* are listed below.

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.013868	77
Children (1-6)	0.025800	143

Using Tolerance level Residues Corrected for Percent Crop Treated Information:
The Anticipated Residue Contribution (ARC) for the overall U.S. population and the subgroup with

the highest estimated risk from all published, pending and new uses *and new meat and milk residues* are listed below.

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.006474	32
Non-nursing Infants (< 1year old)	0.012059	60

Chronic Non-Cancer Exposure from HCB

Tolerance level residues corrected for 0.05% HCB in the formulation were used in the analysis to calculate a Theoretical Maximum Residue Contribution (TMRC). The analysis was futher refined by considering percent of crop treated information (anticipated residue contribution:ARC). These exposure estimates were then compared to the RfD for HCB for chronic dietary risk.

Using Anticipated Residues:

The Anticipated Residue Concentration (ARC) for HCB for the over all U.S. population and the subgroup with the highest estimated risk related to all currently published chlorothalonil tolerances *and new meat and milk residues* are listed below.

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.0000002	0.029
Children (1-6 years)	0.0000004	0.050

(3) Carcinogenic Risk

Carcinogenic Exposure from Chlorothalonil, per se

The carcinogenic risk from food uses of chlorothalonil for the general U.S. population was calculated by comparing the dietary exposure from chlorothalonil to the NOEL identified for use with the cancer risk assessment. The NOEL of 1.5 mg/kg/day comes form a somatic cell proliferation study in mice (MRID 44223002). The following equation was used to determine dietary cancer risk:

Cancer Risk = NOEL (1.5 mg/kg/day) / Dietary Exposure (ARC) mg/kg/day

Chronic dietary exposure was about 0.000471 mg/kg/day, based on the ARC minus concentrations in meat and milk. Meat and milk are not reflected since only SDS-3701, which is not carcinogenic, is found in these food forms. Based on the cancer NOEL of 1.5 mg/kg/day, the cancer risk was estimated to result in an MOE of 3185, contributed through all the published, pending and new uses for chlorothalonil. This figure is at the level which the Agency does not consider raising a concern for excess life time cancer risk.

Carcinogenic Exposure from HCB

The upper bound carcinogenic risk from food uses of HCB for the general U.S. population was calculated using the following equation:

$$\text{HCB Upper Bound Cancer Risk} = \text{Dietary Exposure (ARC)} \times Q_1^*$$

Based on a Q^* of 1.02 $(mg/kg/day)^{-1}$, the upper bound cancer risk was calculated to be

2.4 x 10 $^{-7}$, contributed through all the published, pending and new uses for chlorothalonil.

The upper bound risk for HCB is below the range the Agency generally considers negligible for excess life time cancer risk and is no cause for concern. A summary of the commodity contribution by raw agricultural commodity (RAC) for the overall U.S. population for HCB is attached (Attachment 3).

(4) Dietary Risk Summary/Risk Characterization

Estimated dietary exposure based on the published, pending and new uses of chlorothalonil and HCB for acute, chronic or carcinogenic risk are not of concern.

b) Drinking Water Risk Assessment

HED has concluded that only the parent compound, chlorothalonil, has carcinogenic potential. Therefore, water monitoring data in which only detections of the metabolites of chlorothalonil were found were considered for the chronic non-cancer risk assessment, and only detections of chlorothalonil, per se, were considered for the cancer risk assessment.

The carcinogenic risk from drinking water sources of chlorothalonil for the general U.S. population was calculated by comparing the drinking water exposure from chlorothalonil to the NOEL (1.5 mg/kg/day) from the somatic cell proliferation study (MRID44240901), using the following equation:

Chlorothalonil Cancer Risk = MOE = NOEL (1.5 mg/kg/day) / Drinking Water Exposure (mg/kg/day)

Where:
The NOEL for chlorothalonil (1.5 mg/kg/day) is used for the parent compound, chlorothalonil, for which a complete data base exists. A complete data base does not exist for the metabolites of chlorothalonil. Carcinogenicity studies in rats and mice indicate that the primary metabolite, SDS-3701 or 4-hydroxy-Chlorothalonil, is not carcinogenic to either species.

Chronic Non-Cancer Risk for drinking water was calculated by comparing exposure through drinking water sources to the appropriate Reference Dose, and acute drinking water risk was calculated by dividing the LOEL identified for acute dietary risk assessment by the exposure from drinking water sources (an MOE of at least 300 is considered adequate for acute risk).

Chlorothalonil is not currently regulated under the Safe Drinking Water Act (SDWA). Therefore no MCL has been established for it and water supply systems are not required to sample and analyze for it. No lifetime HAL has been established for it. The intermediate soil/water partitioning of chlorothalonil should make the primary treatment processes employed by most surface water source supply systems at least partially effective in removing it.

The following surface water label advisory is required for Chlorothalonil:

> "Chlorothalonil can contaminate surface water through spray drift. Under some conditions, Chlorothalonil may also have a high potential for runoff into surface water (via both dissolution in runoff water and adsorption to eroding soil), for several weeks to months post-application. These include poorly draining or wet soils with readily visible slopes

toward adjacent surface waters, frequently flooded areas, areas over-laying extremely shallow ground water, areas with in-field canals or ditches that drain to surface water, areas not separated from adjacent surface waters with vegetated filter strips, and highly erodible soils."

Sufficient information is available on local detections of chlorothalonil which can be used to extrapolate the following conclusions/generalizations.

(1) Ground Water

Available Ground Water Data

Degradates (metabolites) of chlorothalonil, not chlorothalonil itself, have been found in groundwater in the states of New York, Massachusetts, Florida, Maine, and California (U.S. HED, 1993). The reported groundwater metabolites are SDS-46851, SDS-47525, SDS-3701, and SDS-19221, and were measured at the highest combined concentration of approximately 16 ppb in New York's Suffolk County (Long Island) in 1981. Chlorothalonil and the two isomeric metabolites SDS-47523/SDS-4752 were not detected. These observations were predictable based on laboratory mobility studies and evidence of metabolite persistence. The groundwater database is not necessarily complete or up-to-date. EPA has assigned a Health Advisory (HA) Drinking Water Equivalent Level (DWEL) of 500 ppb (U.S. EPA, 1994).

Although it is not clear how the use of chlorothalonil in New York compares to use other areas, it is expected that the levels of chlorothalonil metabolites detected in the ground water in New York are unrepresentatively high compared to the country as a whole.

A prospective small-scale groundwater monitoring study which was precipitated by the presence of chlorothalonil degradates (metabolites) in groundwater is underway, and will give the Agency a more quantitative measure of groundwater contamination potential. As these data are received, resultant drinking water risk will be reviewed and evaluated based on the new data. Conclusions concerning the potential of chlorothalonil and its degredates to contaminate ground water cannot be made until the study is completed. However, if the conservative assumption is made that the metabolites of chlorothalonil have the same toxicity as the parent chlorothalonil, and this assessment is considered an unlikely worst-case scenario, the following conclusions can be drawn with respect to exposure and risk from ground water-based drinking water.

Ground Water Exposure

HED used the 16 ppb metabolite concentration to calculate an acute (one day) and chronic non-cancer exposure estimate for chlorothalonil. Since the metabolites of chlorothalonil are not of carcinogenic concern, cancer risk assessment was not calculated.

HED assumes that adults weighing 70 kg consume two liters of drinking water per day while children weighing 10 kg drink one liter. Based on the highest measured concentration (16 ppb), estimated exposure to children is 0.0016 mg/kg/day. For adults, exposure is 0.00046 mg/kg/day. With most groundwater sources, there are no known predictable seasonal or longer-term trends in concentrations of pesticide contaminants. Therefore, these exposure values were used to calculate both acute and chronic risk.

Ground Water Risk

In order to calculate acute drinking water risk, the highest concentration in ground water was compared to the acute dietary exposure LOEL of 175 mg/kg/day. For chronic non-cancer risk, the same concentration was compared to the RfD for chlorothalonil (0.02 mg/kg/day). Using the highest concentrations for the corresponding time period, drinking water risk* can be estimated as follows:

Acute Drinking Water Risk

MOE for Children = 110,000; MOE for Adults = 380,000

*Note: for acute drinking water risk, MOE's should exceed 300 because a LOEL was used.

Chronic Non-Cancer Drinking Water Risk

Exposure to Children occupies 8% RfD for Chlorothalonil;
Exposure to Adults occupies 2% RfD.

(2) Surface Water

Chlorothalonil can contaminate surface water at application via spray drift. The intermediate soil/water partitioning of chlorothalonil indicates that its concentration in suspended and bottom sediment will be substantially greater than its concentration in water. The major degradate of chlorothalonil in the soil under aerobic conditions is SDS-3701. SDS-3701 appears to be more persistent and mobile than chlorothalonil because unlike chlorothalonil, SDS-3701 has been detected in some ground water. Consequently, substantial amounts of SDS-3701 may be available for runoff for longer periods than chlorothalonil and SDS-3701 may be more persistent in water/sediment systems than chlorothalonil. The apparent greater mobility of SDS-3701 suggests that it exhibits lower soil/water partitioning than chlorothalonil. Therefore, the ratio of SDS-3701 runoff loss via dissolution in runoff to runoff loss via adsorption to eroding soil for SDS-3701 may be substantially greater than for chlorothalonil. In addition, the ratios of concentrations dissolved in the water column to concentrations adsorbed to suspended and bottom sediment may be substantially higher for SDS-3701 than for chlorothalonil.

Available Surface Water Data

The South Florida Water Management District (SFWMD; Miles and Pfeuffer 1994) summarized chlorothalonil detections in samples collected every two to three months from 27 surface water sites within the SFWMD from November 1988 through November 1993. Approximately 810 samples (30 sampling intervals X 27 sites sampled/interval) were collected from the 27 sites from November 1988 through November 1993. Chlorothalonil was detected (above detection limits generally ranging from 0.001 to 0.006 μg/L (0.001 ppb to 0.006 ppb); quantification limit of approximately 0.2 μg/L or 0.2 ppb) in 25 samples at concentrations ranging from 0.003 to 0.035 μg/L (0.003 ppb to 0.035 ppb). Six of the samples had concentrations $\geq$ 0.010 μg/L (0.01 ppb). The maximum concentration detected was 0.035 μg/L.

Surface Water Exposure

The available surface water monitoring information was used to perform an exposure assessment of surface water as a drinking water source. In order to produce a conservative estimate of drinking water risk, the sample with the highest concentration of chlorothalonil detected was used to perform the exposure assessment.

HED assumes that adults weighing 70 kg consume two liters of drinking water per day while children weighing 10 kg drink one liter. Based on the highest measured concentration (0.035 μg/L), exposure to children is 0.000035 mg/kg/day and exposure to adults is 0.00001 mg/kg/day. These exposure values were used to calculate both acute and chronic risk.

Surface Water Risk to Chlorothalonil

In order to calculate acute drinking water risk, the peak concentration (0.035 ug/L) was compared to the acute dietary exposure LOEL of 175 mg/kg/day. For chronic non-cancer risk, the same value was compared to the RfD for chlorothalonil (0.02 mg/kg/day). Using the highest concentrations for the corresponding time period, drinking water risk* can be estimated as follows:

Acute Drinking Water Risk

MOE for Children = 5,000,000; MOE for Adults = 17,500,000

*Note: for acute drinking water risk, MOE's should exceed 300 because a LOEL was used.

Chronic Non-Cancer Drinking Water Risk

Exposure to Children occupies < 1 % of the RfD for Chlorothalonil;
Exposure to Adults occupies < 1 % of the RfD

Drinking Water Cancer Risk

Cancer Risk for Adults = MOE = > 1.5 million

The assumption that water comes from the same source containing the same contaminant level, consumed throughout a 36-year period, is extremely conservative, since it is likely that frequency and amounts of chlorothalonil used vary widely over this time, and most of the U.S. population moves at some time and does not live in the same area, drinking the from the same water source for a 36 year period.

Surface Water Risk to HCB

Acute drinking water risk to HCB was not calculated since no acute dietary endpoint has been identified for HCB. Chlorothalonil concentrations were assumed to be contaminated with 0.05% HCB. The resulting concentration was compared to the RfD for HCB (0.0008 mg/kg/day) for the non-cancer chronic risk, and the cancer potency factor for HCB [1.02 $(mg/kg/day)^{-1}$] for the cancer risk. Using the highest concentrations for the corresponding time period, drinking water risk can be estimated as follows:

Chronic Non-Cancer Drinking Water Risk for HCB

Exposure to Children occupies < 1 % of the RfD for HCB;
Exposure to Adults occupies < 1 % of the RfD for HCB

Drinking Water Cancer Risk to HCB

Cancer Risk for Adults = 5×10^{-9}

c) Occupational and Residential Risk Assessment for Handlers

(1) Risk From Short-Term (1-7 days) and Intermediate-Term (1 week to several months) for Occupational and Residential Handlers

Short-Term and Intermediate-Term Dermal Margins of Exposure (MOE_D) are calculated as follows:

$$\frac{\text{NOEL}}{\text{Dose}} = \frac{\text{600 mg/kg/day}}{\text{Daily Dermal Exposure (mg/kg/day)}}$$

Risk From Inhalation Exposure

Although there are limited data to address inhalation exposure to chlorothalonil, it does not appear that this is a significant route of exposure for most reentry workers. However, in a study in which tomato harvesters were monitored while hand-harvesting tomatoes (MRID 47002545), inhalation exposure was 0.82 μg/kg/day. This scenario represents significant dermal exposure. Worker exposure to dusts contaminated with chlorothalonil during the mechanical harvesting of bush tomatoes was measured by California Department of Pesticide Regulation personnel (Spencer et al., 1992, no MRID). In that study, inhalation exposure was 0.02 mg/person per 8 hour day.

Except for an acute inhalation toxicity study, no inhalation toxicity studies were available for this assessment. The dose identified for determining inhalation risk is from an oral toxicity study (i.e. oral NOEL). Therefore, the inhalation exposure component (using a 100% default value absorption rate) was converted to an equivalent oral exposure (mg/kg/day) using the defalt respiratory volume of 29 L/minute, the value used for estimation of dose from PHED, Version 1.1. This exposure should then be compared to the oral NOEL of 2 mg/kg/day to calculate the inhalation Margin of Exposure (MOE_I). Separate risk calculations should be made for inhalation and dermal exposures since doses and endpoints have been identified for separate (i.e. dermal and inhalation) risk assessments.

The Inhalation Margin of Exposure (MOE_I) was calculated as follows:

$$MOE_I = \frac{NOEL_{oral} = \text{2.0 mg/kg/day}}{\text{inhalation exposure (mg/kg/day)}}$$

(2) Risk From Chronic Handler Exposure

Exposure from residential uses and all occupational uses of chlorothalonil are not considered chronic (daily exposure occurring continuously for several months) scenarios. Therefore, neither chronic nor cancer risk assessments were conducted for these use scenarios.

It is possible that chronic exposure, representing several months or more per year of exposure, may apply to greenhouse workers because successive greenhouse crops can be continuously grown throughout the year. It is not clear to what extent greenhouse crops are treated continuously with chlorothalonil. It would seem prudent from a pest management standpoint to treat greenhouse crops with a variety of fungicides to prevent disease resistance. If alternate fungicides are used, then it is likely that greenhouse worker exposure is of a short-term or intermediate-term nature.

(3) Cancer Risk from Occupational Exposure

Based on re-evaluation of mechanistic data for chlorothalonil, HED has concluded that the 'Margin of Exposure Approach' is the most appropriate method of cancer risk assessment for chlorothalonil. The MOE approach is only applicable to exposure scenarios in which workers may be exposed continuously for more than several months. Greenhouse uses are the only exposure scenarios that may result in chronic occupational exposure. Therefore, HED calculated cancer risk MOE's only for post-application occupational use scenarios in greenhouses.

However, carcinogenic risk from lifetime exposure to HCB was calculated using the following equation:

$$\text{Daily exposure} \times \frac{\text{days exposure/yr}}{365 \text{ days}} \times \frac{40 \text{ years exposure}}{75 \text{ years}} \times Q_1^*$$

Since HCB has been assigned a Q_1^*, cancer risk may be calculated for all exposure scenarios.

(4) Exposure and Risk for Other Handlers

Caulks, Sealants, Polymer Lattices, Grouts, Joint Compounds, and Paper Coatings Containing Chlorothalonil

In a memorandum dated January 28, 1997, the Agency's Antimicrobial Division (AD) completed an exposure assessment for proposed new uses of chlorothalonil (40.4 % a.i.) in caulks, sealants, polyer lattices, grouts, joint compounds, and paper coatings. AD considered all occupational and residential exposure scenarios based on application rates proposed by the registrant. Based on exposure data submitted by the Chemical Manufacturer's Association (MRIDs 41412201, 41742601, 41761201 & 42587501), and relevant toxicological endpoints, primary occupational risk estimates appear to be within the range that the Agency generally considers negligible for workers. However, data were not available to estimate exposure and risk for post-application exposure to primary occupational handlers, secondary occupational handlers, and primary or secondary homeowner exposure (for both application exposure and post-application exposure). For these use scenarios, no risk assessment was conducted.

Professional Lawn Care Operators

There are limited surrogate data available to address application of chlorothalonil by

professional lawn care operators (LCO). These exposures are being addressed by the Outdoor Residential Exposure Task Force (ORETF). There is a study available in the literature that measured LCO exposure using biomonitoring techniques. Biomonitoring studies can be used as surrogates to estimate exposure for other chemicals if the dermal absorption rates for both chemicals are known. This coupled with establishing a ratio between the two chemical application rates can roughly estimate exposure for LCOs using chlorothalonil. The dermal absorption rate of dithiopyr is reportedly 0.08% and the dermal absorption rate of chlorothalonil is 5%. **The absorbed dose from the published dithiopyr study is 4.6 x 10^{-5} mg/kg/pound active ingredient handled. Therefore, the absorbed dose of chlorothalonil from a similar application using dithiopyr can be estimated as follows:**

$$\frac{0.000046 \text{ mg/kg/lb ai} \times 12.5 \text{ lb ai/A Chlorothalonil} \times 2\text{A/da} \times 5\%}{1 \text{ lb ai/A dithiopyr} \times 0.08\% \text{ dermal absorption (da)}} =$$

= 1.44 mg/kg/day

= 0.072 mg/kg/day when corrected for 5% dermal absorption

(5) Occupational and Residential Exposure and Risk from HCB

An extensive risk assessment was not made for HCB as a contaminant in chlorothalonil. Based on high-end exposure, a mixer/loader using a wettable powder to support aerial applications to celery, a risk of 2.8 x 10^{-5} was estimated. Risk for the other scenarios are assumed to be lower. This is a worst case estimate based on 0.05% HCB.

(6) Daily Exposure/Risk Tables for Occupational and Residential Handlers

Table 8
Estimated Exposure and Risk for Mixer/loaders Using Chlorothalonil (Occupational)

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Area Treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Mixer/Loader Exposure									
Wettable Powder-Open Bag (Aerial and Chemigation Applications to Tomatoes)	Long-sleeved shirt, long pants, gloves	0.1737	0.0434	1.04 - 2.08	350 acres	0.83 - 1.67	0.208 - 0.416	359-723	5-10
Wettable Powders-Open Bag (Aerial and Chemigation Applications to Celery)	Long-sleeved shirt, long pants, gloves	0.1737	0.0434	0.78 - 2.21	350 acres	0.62 - 1.78	0.156 - 0.442	337-968	5-13
Wettable Powders-Open Bag (Ground Applications to Tomatoes)	Long-sleeved shirt, long pants, gloves	0.1737	0.0434	1.04 - 2.08	50 acres	0.12 - 0.24	0.03 - 0.06	2500-5000	33-67
Wettable Powders-Open Bag (Ground Applications to Celery)	Long-sleeved shirt, long pants, gloves	0.1737	0.0434	0.78 - 2.21	50 acres	0.09 - 0.25	0.022 - 0.06	2400-6667	33-91
Wettable Powders-Open Bag (Ground Applications to Stone Fruits)	Long-sleeved shirt, long pants, gloves	0.1737	0.0434	2.34 - 4.16	20 acres	0.11 - 0.19	0.027 - 0.048	3158-5455	42-74
Liquid Flowable-Open Pour (Aerial and Chemigation Applications to Tomatoes)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	1.04 - 2.08	350 acres	0.23 - 0.45	0.006 - 0.012	1333-2609	167-333
Liquid Flowable-Open Pour (Aerial and Chemigation Applications to Celery)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	0.78 - 2.21	350 acres	0.17 - 0.48	0.004 - 0.012	1250-3529	167-500
Liquid Flowable-Open Pour (Aerial and Chemigation Applications to Christmas Trees)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	1.04 - 4.16	100 acres	0.064 - 0.26	0.002 - 0.003	2308-9375	667-1000

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Area Treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Liquid Flowable-Open Pour (Ground Applications to Stone Fruits and Christmas Trees)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	1.04 - 4.16	20 acres	0.013 - 0.052	0.0003 - 0.0013	11,500-46,000	1538-6667
Liquid Flowable-Open Pour (Ground Applications to Tomatoes)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	1.04 - 2.08	50 acres	0.032 - 0.064	0.0008 -0.0016	9375-18,000	1250-2500
Liquid Flowable-Open Pour (Ground Applications to Celery)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	0.78 - 2.21	50 acres	0.024 - 0.068	0.0006 -0.0012	8824-25,000	1667-3000
Liquid Flowable-Open Pour (Ground Applications to Golf Courses)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	2.08 - 12.51	40 acres	0.052 - 0.31	0.0013-0.0079	1935-11,000	253-1538
Liquid Flowable-Open Pour (Ground Applications to Sod Farms)	Long-sleeved shirt, long pants, gloves	0.047	0.0012	2.08 - 12.51	100 acres	0.13 - 0.775	0.003 - 0.02	774-4615	100-667
Dry Flowable-Open Pour (Aerial and Chemigation Applications to Tomatoes)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	1.04 - 2.08	350 acres	0.384 - 0.767	0.004 - 0.008	782-1563	250-500
Dry Flowable-Open Pour (Aerial and Chemigation Applications to Celery)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	0.78 - 2.21	350 acres	0.29 - 0.82	0.003 - 0.006	732-2069	333-667
Dry Flowable-Open Pour (Aerial and Chemigation Applications to Christmas Trees)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	1.04 - 4.16	100 acres	0.11 - 0.44	0.001 - 0.004	1364-5455	500-2000
Dry Flowable-Open Pour (Ground Applications to Stone Fruits and Christmas Trees)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	1.04 - 4.16	20 acres	0.022 - 0.088	0.0002 - 0.0009	6818-27,000	2222-10,000
Dry Flowable-Open Pour (Ground Applications to Tomatoes)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	1.04 - 2.08	50 acres	0.055 - 0.11	0.0006 - 0.0011	5455-10,000	1818-3333
Dry Flowable-Open Pour (Ground Applications to Celery)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	0.78 - 2.21	50 acres	0.04 - 0.12	0.0004 - 0.0012	5000-15,000	1667-5000
Dry Flowable-Open Pour (Ground Applications to Golf Courses)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	2.08 - 12.51	40 acres	0.088 - 0.53	0.0009 - 0.005	1132-6818	400-2222

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Area Treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Dry flowable-Open Pour (Ground Applications to Sod Farms)	Long-sleeved shirt, long pants, gloves	0.08	0.0008	2.08 - 12.51	100 acres	0.22 - 1.325	0.002 - 0.013	453-2727	154-1000

Table 9
Estimated Exposure and Risk for Applicators Using Chlorothalonil (Occupational)

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Area Treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Applicator Exposure									
Aerial Applications to Tomatoes	Long-sleeved shirt, long pants, no gloves	0.009	not a significant route of exposure	1.04 - 2.08	350 acres	0.043 - 0.086	--	6977-13,000	
Aerial Applications to Celery	Long-sleeved shirt, long pants, no gloves	0.009	not a significant route of exposure	0.78 - 2.21	350 acres	0.032 - 0.092	--	6522-18,000	
Aerial Applications to Christmas Trees	Long-sleeved shirt, long pants, no gloves	0.009	not a significant route of exposure	1.04 - 4.16	100 acres	0.012 - 0.049	--	12,000-50,000	
Ground-Boom Applications to Tomatoes (Open Cab)	Long-sleeved shirt, long pants, no gloves	0.017	0.0007	1.04 - 2.08	50 acres	0.012 - 0.023	0.0005 - 0.001	26,000-50,000	2000-4000
Ground-Boom Applications to Celery (Open Cab)	Long-sleeved shirt, long pants, no gloves	0.017	0.0007	0.78 - 2.21	50 acres	0.0087 - 0.025	0.0004 - 0.001	24,000-69,000	2000-5000
Airblast Applications to Stone Fruits and Christmas Trees (Open Cab)	Long-sleeved shirt, long pants, no gloves	0.4	0.0045	1.04 - 4.16	20 acres	0.11 - 0.44	0.001 - 0.005	1364-5455	400-2000
Specialty Airblast Applications to Golf Courses (Open Cab)	Long-sleeved shirt, long pants, no gloves	1.71	0.001	2.08 - 12.51	40 acres	1.87 - 11.27	0.001 - 0.007	53-321	286-2000

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Area Treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Ground-Boom Applications to Golf Courses (Open Cab)	Long-sleeved shirt, long pants, no gloves	0.075	0.002	2.08 - 12.51	40 acres	0.082 - 0.49	0.002 - 0.01	1224-7317	200-1000
Ground-Boom Applications to Sod Farms (Open Cab)	Long-sleeved shirt, long pants, no gloves	0.017	0.0007	2.08 - 12.51	100 acres	0.046 - 0.28	0.002 - 0.01	2143-13,000	200-1000

Table 10

Estimated Exposure and Risk for Mixer/Loader/Applicators Using Chlorothalonil (Occupational and Residential)

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Area treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Mixer/Loader/Applicator Exposure									
Backpack Sprayer (Greenhouse Application)	Long-sleeved shirt, long pants, gloves, respirator	2.19	0.006	1.04 - 4.16	2 acres	0.06 - 0.24	0.0002-0.0007	2500-10,000	2857-10,000
Backpack Sprayer (Outdoor Applications) - Forestry and Nursery Uses	Long-sleeved shirt, long pants, gloves	2.19	0.06	1.04 - 4.16	2 acres	0.06 - 0.24	0.002 - 0.007	2500-10,000	286-1000
Handgun Sprayer using Water Dispersable Granules - Forestry and Nursery Uses	Long-sleeved shirt, long pants, no gloves	0.35	0.001	1.04 - 4.16	2 acres	0.01 - 0.038	0.00003 - 0.0001	15,000-60,000	20,000-66,000
Homeowner Push-Type Granular Spreader	Long-sleeves shirt, long pants, no gloves	4.7	0.006	1 - 1.8 lb ai/5,000 sq.ft	5,000 sq.ft	0.06 - 0.11	0.00008 - 0.0001	5455-10,000	20,000-25,000
Homeowner Hose-End Sprayer	Total deposition	39.1	0.002	1 - 1.8 lb ai/5,000 sq.ft	5,000 sq.ft	0.52 - 0.93	0.00002 - 0.00005	645-1154	40,000-100,000

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Area treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Paint Brush Application Using Chlorothalonil Treated Paint - Interior Latex	Long-sleeved shirt, long pants, no gloves	290	0.507	0.048 lb ai/gallon	2 gallons	0.367	0.0006	1635	3333
Paint Brush Application Using Chlorothalonil Treated Paint - Exterior Latex	Long-sleeved shirt, long pants, no gloves	290	0.507	0.096 lb ai/gallon	2 gallons	0.734	0.001	817	2000
Paint Brush Application Using Chlorothalonil Treated Paint - Exterior Alkyd	Long-sleeved shirt, long pants, no gloves	290	0.507	0.11 lb ai/gallon	2 gallons	0.84	0.001	714	2000
Indoor Painting Using an Airless Sprayer - Interior Latex	Long-sleeved shirt, long pants, no gloves	36.22	2.35	0.048 lb ai/gallon	40 gallons	0.916	0.06	655	33
Indoor Painting Using an Airless Sprayer - Interior Latex	Long-sleeved shirt, long pants, gloves	12	2.35	0.048 lb ai/gallon	40 gallons	0.3	0.06	2000	33
Outdoor Painting Using an Airless Sprayer - Exterior Alkyd	Long-sleeved shirt, long pants, no gloves	33.33	0.433	0.11 lb ai/gallon	40 gallons	1.9	0.025	316	80
Outdoor Painting Using an Airless Sprayer - Exterior Latex	Long-sleeved shirt, long pants, no gloves	33.33	0.433	0.096 lb ai/gallon	40 gallons	1.69	0.02	355	100
Outdoor Painting Using an Airless Sprayer - Exterior Alkyd	Long-sleeved shirt, long pants, gloves	8.87	0.433	0.11 lb ai/gallon	40 gallons	0.514	0.025	1167	80

Table 11

Estimated Exposure and Risk for Flaggers Exposed to Chlorothalonil Sprays (Occupational)

Exposure Scenario	Clothing and PPE Parameters	Unit Dermal Exposure (mg/lb ai)	Unit Inhalation Exposure (mg/lb ai)	Application Rate (lb ai/cycle)	Acres Treated per Day	Daily Dermal Exposure (mg/kg/day)	Daily Inhalation Exposure (mg/kg/day)	Dermal Margin of Exposure	Inhalation Margin of Exposure
Flagger Exposure									
Flaggers	Long-sleeved shirt, long pants	0.011	0.0003	0.78 - 2.21	350 acres	0.04 - 0.11	0.001 - 0.003	5455-15,000	667-2000

(7) Handler Risk Summary

The following scenarios result in **handler inhalation risk concerns:**

Mixer/Loaders:

Wettable Powder-open bag, for aerial application to tomatoes ($MOE_I = 5$) and celery ($MOE_I = 5$); and for ground application to tomatoes ($MOE_I = 33$), celery ($MOE_I = 33$) and stone fruits ($MOE_I = 42$).

Mixer/Loader/Applicators (Occupational Uses):

Indoor Painting Using an Airless Sprayer, Interior Latex ($MOE_I = 33$);
Outdoor Painting Using an Airless Sprayer-Exterior Alkyd ($MOE_I = 80$)

The inhalation risk resulting from these uses can be mitigated by wettable powder products require mixer/loaders to wear a respirator. For the painting uses, the label should also require painters to use a fitted respirator (see WPS Section).

With the exception of specialty airblast application to golf courses ($MOE_D = 53$), all use scenarios, including home uses, result in dermal margins of exposure that exceed 100 and are not of concern. The low MOE for specialty airblast applicators can be mitigated by EITHER a reduction in the maximum application rate from 12.51 lb ai/acre to 6 lb ai/acre (MOE = 111) OR by requiring these handlers to wear gloves (MOE = 263). HED recommends one of these mitigation measured be implemented so that the resultant risk is not a concern.

(8) Incidence Information for Chlorothalonil

California is the only state that requires physicians to report the treatment of illnesses related to pesticide exposure. Between 1982 and 1992, 133 incident case reports involving chlorothalonil were received by the California Pesticide Illness Surveillance Program. In these reports, adverse health effects were attributed to exposure to chlorothalonil or chlorothalonil used in combination with other pesticides. In most cases, the incidents involved mixer/loaders and applicators and were the result of accidents such as splashes or carelessness such as not wearing protective eyewear. The reported symptoms attributed to chlorothalonil were primarily eye irritations and skin rashes.

For reentry workers, 13 incidents were reported as "possible" or "probable" consisting of skin sensitization and eye irritation. Dermatitis has been reported resulting from contact with treated wood (Johnson *et al.*, 1983; and Bach and Pedersen, 1983). Symptoms of facial erythema and tightness in the chest was reported involving a female nursery worker (Maibach, 1990). The incident was reportedly investigated by Dannaker *et al.* (1995) in which a test confirmed that a dilute concentration of 0.01 percent caused an anaphylactoid reaction in the worker. It has been suggested (Maibach *et al.* (1993)) that chlorothalonil be listed as a cause of contact urticaria syndrome. It should be noted however, that a dermal sensitization study conducted using guinea pigs (MRID 40546001) was negative.

According to EPA's Recognition and Management of Pesticide Poisonings (March 1989), chlorothalonil has caused skin irritation and irritation of mucous membranes of the eye and respiratory tract. Dermal sensitization is reportedly rare and no cases of human systemic poisoning have been reported.

d) Post Application Exposure and Risk to Chlorothalonil

The current restricted-entry interval (REI) for chlorothalonil is 48-hours, the default (interim) REI set by the Worker Protection Standard (WPS). WPS interim REIs are determined based on the acute toxicity of the technical grade active ingredient (TGAI). For chlorothalonil, the interim REI of

48 hours is based on chlorothalonil's potential for primary eye irritation (Acute Toxicity Category 1). REI's do not apply to post application exposure from treatment of residential lawns or golf courses.

(1) Post-Application Risk From Short-Term and Intermediate-Term Exposure

HED has assumed that the post-application exposures to chlorothalonil for outdoor grown agricultural crops are seasonal and should be compared to the endpoints selected for short-term and intermediate-term periods; 1 to 7 days and 1 week to several months exposure, respectively.

(2) Post-Application Inhalation Risk

There are limited data to address inhalation exposure to chlorothalonil, although in most cases, it does not appear that this is a significant route of exposure for reentry workers. However, in a study in which tomato harvesters were monitored while hand-harvesting tomatoes (MRID 470025045), inhalation exposure was 0.82 μg/kg/day. This scenario, which represents significant worker exposure, results in an MOE of greater than 10,000, and is not a concern. California Department of Pesticide Regulation personnel measured worker exposure to dusts contaminated with chlorothalonil during the mechanical harvesting of bush tomatoes (Spencer et al., 1992). In that study, inhalation exposure was 0.02 mg/person per 8 hour day resulting in an MOE greater than 40,000. Therefore, HED does not have a concern with post-application inhalation risk.

(3) Restricted-Entry Intervals (REIs)

The risk assessment presented in this document was generated using data available in the published literature (Brouwer et al.) and data collected by the California Department of Pesticide Regulation.

REIs are proposed for crops based on the toxicological considerations discussed above for the intermediate and short-term endpoint. Tables 12 to 21 show risks for postapplication/reentry workers for most agricultural and horticultural scenarios. Exposure calculations for greenhouse workers are presented in Tables 19 and 21. Based on the exposure assessment, **it appears that a 12-hour REI is adequate to protect workers from the systemic effects of chlorothalonil** for most scenarios. However, the reentry data do not address the potential adverse eye effects of chlorothalonil. Available incident data indicate that irritation to worker's eyes can occur beyond the 48 hour REI. It should also be noted that data show that residues do not often dissipate significantly within 48 hours of application. In the absence of a model in which to assess reentry exposure to compounds that have adverse eye effects, the following label language/product stewardship is recommended **in lieu** of the interim 48 hour REI imposed by the WPS:

"**Special Eye Irritation Provisions:** This product is a severe eye irritant. Do not enter or allow workers to enter a treated area within 7 days of application, unless the following safety measures have been taken:
(1) At least one container designed specifically for flushing eyes must be available in operating condition at the WPS-required decontamination site intended for workers entering the treated area.
(2) Workers must be informed, in a manner they can understand:
-- that residues in the treated area may be highly irritating to their eyes,
--that they should take precautions, such as refraining from rubbing their eyes, to keep the residues out of their eyes,
-- that if they do get residues in their eyes, they should immediately flush their eyes using the eyeflush container that is located at the decontamination site or using other readily available clean water, and
-- how to operate the eyeflush container."

There are no data to address post-application exposure from residential lawns treated with chlorothalonil. However, there are limited exposure monitoring data for golfers and persons mowing fairways and greens on golf courses. This monitoring data are not applicable to other turfgrass scenarios because dislodgeable foliar residue (DFR) data were not collected. Thus, exposures to individuals other than mowers and golfers (such as residential exposure) cannot be calculated using this data.

(4) Post Application Exposure and Risk Tables

Please Note: Tables 12 through 21 show exposures ranging from 5 to 14 days post-application.

Table 12 presents the daily exposures for workers reentering treated papaya and stone fruit orchards, conifer nurseries (not seedlings), and Christmas tree plantations.

Tasks: For stone fruits, most applications are made early in the growing season (early bloom and shuck-split), except cherries which is treated after harvest. Hand labor tasks include pruning and topping cherry trees, pruning conifers and Christmas trees, balling and burlapping conifers.

Assumptions: Eight hour work days (30 work days per year), dislodgeable foliar residue data from a cherry study, application rates of 2.34 - 4.16 lb ai/acre, a transfer factor of 3,800 cm^2/hr, and a body weight of 75.9 kg.

Incidence: 1990, one possible case involving a worker thinning nectarines for three days - eye irritation. The field was treated with chlorothalonil and triforine.

Table 12
Estimated Daily Exposure for Workers Re-entering Treated Papaya and Stone Fruit Orchards, Conifer Nurseries (not seedlings), and Christmas Tree Plantations

Day after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption (mg/kg/day)
0	1.81	0.72	0.036
1	1.48	0.6	0.03
2	1.20	0.48	0.024
3	0.98	0.4	0.02
4	0.80	0.32	0.016
5	0.65	0.26	0.013

MOE's for short-term and intermediate term exposure are greater than 17,000.

Table 13 presents the daily exposures for workers reentering treated tomato fields.

Tasks: Hand harvesting tomatoes (not mechanical) and staking.

Assumptions: Eight hour work days (120 work days per year), dislodgeable foliar residue data from a tomato study, application rates of 1.04 - 2.08 lb ai/acre, a transfer factor of 1,300 cm^2/hr from a tomato harvester study, and a body weight of 75.9 kg. There is no preharvest interval for tomatoes.

Incidence: 1989, one possible case involving a worker hoeing weeds - conjunctivitis. The field treated with chlorothalonil, sulfur, and metalaxyl.

1990, one possible case where a worker got rash while harvesting tomatoes treated 12 days prior with an adjuvant, chlorothalonil, esfenvalerate, methomyl, and sulfur.

1990, one worker developed a rash on forearm while moving tomato vines in a field treated with an adjuvant, chlorothalonil, esfenvalerate, methomyl, and sulfur.

Table 13
Estimated Daily Exposure for Workers Re-entering Treated Tomato Fields

Day after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption
0	4.19	0.58	0.029
1	4.01	0.56	0.028
2	3.83	0.52	0.026
3	3.66	0.5	0.025
4	3.50	0.48	0.024
5	3.34	0.46	0.023
6	3.19	0.44	0.022
7	3.05	0.42	0.021
14	2.22	0.3	0.015

MOE's for short-term and intermediate-term exposure are greater than 20,000.

Table 14 presents the daily exposures for workers reentering treated cucurbits, snap beans fields.

Tasks: Hand harvesting, vine turning, covering watermelons with vines to prevent sunburn. Hand harvesting snap beans.

Assumptions: Eight hour work days (120 days worked per year), dislodgeable foliar residue data from a cucumber study, application rates of 1.17 - 2.2 lb ai/acre, a transfer factor of 1,000 cm^2/hr, and a 75.9 kg body weight. There is no preharvest interval for cucumbers and a 7 day preharvest interval for snap beans.

Incidence: 1989, one possible case involving a worker developing a rash while picking cucumbers. The rash occurred when the worker removed their plastic picking gloves. These gloves are worn by some workers because the fuzz on cucumbers can cause skin irritation. The field was treated with chlorothalonil and oxydemeton-methyl.

Table 14
Estimated Daily Exposure for Workers Re-entering Curcurbits and Snap Beans Fields

Day after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption (mg/kg/day)
0	7.74	0.82	0.041
1	5.95	0.64	0.032
2	4.58	0.48	0.024
3	3.52	0.38	0.019
4	2.71	0.3	0.015
5	2.09	0.22	0.011
7	1.23	0.14	0.007

MOE's for short-term and intermediate-term exposure are greater than 14, 000.

Table 15 presents the daily exposures for workers reentering treated cole crop fields.

Tasks: Hand harvesting (cutters and packers), terminal point removal (Brussels sprouts), leaf removal (Brussels sprouts), head wrapping (cauliflower).

Assumptions: Eight hour work day (120 work days per year) dislodgeable foliar residue data from a broccoli study, application rates of 1.17 - 1.43 lb ai/acre, a transfer factor of 700 cm^2/hr, and a body weight of 75.9 kg. Chinese cabbage and Chinese broccoli have a 7 day preharvest interval. Packer exposure is expected to be lower.

Incidence: 1985, one possible case involving a worker developing a rash while harvesting cauliflower. The field was treated with chlorothalonil, oxydemeton-methyl, and mevinphos.

1988, one possible case involving a worker developing hives. The field was treated with chlorothalonil and metalaxyl.

Table 15
Estimated Daily Exposure for Workers Re-entering Treated Cole Crop Fields

Day after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption
0	1.84	0.14	0.007
1	1.51	0.12	0.006
2	1.25	0.01	0.005
3	1.03	0.08	0.004
4	0.84	0.06	0.003
5	0.69	0.06	0.003
7	0.47	0.04	0.002

The study from which these data were taken is considered supplemental because it rained on the day following the last application. This represents a best case scenario. MOE's for short-term and intermediate-term exposure are greater than 85,000.

Table 16 presents the daily exposures for workers reentering treated corn fields (sweet and grown for seed).

Tasks: Hand harvesting sweet corn. Removing tassels and performing other tasks associated with seed corn production.

Assumptions: Eight hour work day (60 work days per year), dislodgeable foliar residue data from the cucumber study, adjusted for an application rate of 0.59 - 1.43 lb ai/acre, a transfer factor of 1,000 cm^2/hr, and a body weight of 75.9 kg. Sweet corn has a 14 day preharvest interval.

Incidence: None.

Table 16
Estimated Daily Exposure for Workers Re-entering Treated Corn Fields

Day after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption (mg/kg/day)
0	5.16	0.54	0.027
1	3.97	0.42	0.021
2	3.05	0.32	0.016
3	2.35	0.26	0.013
4	1.81	0.2	0.01
5	1.39	0.16	0.008
14	0.13	0.02	0.001

MOE's for short-term and intermediate-term exposure are greater than 22,000.

Table 17 presents the daily exposures for workers reentering treated celery fields:

Tasks: Celery cutting and field packing; moving irrigation pipe.

Assumptions: Eight hour work days (120 work days per year), dislodgeable foliar residue data from a cucumber study, application rates of 1.17 - 2.2 lb ai/acre, a transfer factor of 700 cm^2/hr, and a 75.9 kg body weight. Celery has a seven day preharvest interval. Packer exposure is expected to be lower than cutter exposure.

Incidence: 1987, one possible case involving an irrigation worker getting dizzy and feeling itchy around the neck. The worker was wearing rubber pants, jacket, and gloves and had entered the field 2 hours after it was treated with bacillus thuringiensis, chlorothalonil, mevinphos, and permethrin.

Table 17
Estimated Daily Exposure for Workers Re-entering Treated Celery Fields

Day after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption (mg/kg/day)
0	7.75	0.58	0.029
1	5.96	0.44	0.022
2	4.58	0.34	0.017
3	3.52	0.26	0.013
4	2.71	0.2	0.01
5	2.08	0.16	0.008
6	1.60	0.12	0.006
7	1.23	0.1	0.005

MOE's for short-term and intermediate-term exposure are greater than 20,000.

Table 18 presents the daily exposures for workers reentering treated conifer nurseries (seedlings).

Tasks: Packing, and moving irrigation equipment. Other non-hand labor tasks.

Assumptions: Eight hour work days (120 work days per year), dislodgeable foliar residue data from a cherry study, application rates of 2.34 - 4.16 lb ai/acre, a transfer factor of 700 cm^2/hr, and a body weight of 61.5 kg. This reduced body weight was chosen to reflect female exposure since many nursery workers are women.

Incidence: 1989, one probable case involving a nursery worker handling treated conifer seedlings damp form a recent irrigation. The worker was wearing gloves. However, during unloading, some seedlings brushed against the workers face. The seedlings had been treated with chlorothalonil. (300 ppm of chlorothalonil were detected on the seedlings)

Table 18
Estimated Daily Exposure for Workers Re-entering Treated Conifer Nurseries (seedlings)

Day after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption (mg/kg/day)
0	1.81	0.16	0.008
1	1.48	0.14	0.007
2	1.20	0.12	0.006
3	0.98	0.1	0.005
4	0.80	0.08	0.004
5	0.65	0.06	0.003

MOE's for short-term and intermediate-term risk are greater than 75,000.

Table 19 presents daily exposures showing daily exposure for greenhouse workers following the use of a high application rate (2.4 lb a.i./acre).

In the Brouwer study, an application rate of 0.6 lb ai/@ 80 - 100 gallons of water/0.25 acre (@ 2.4 lb ai/A) was applied to carnation sprays and carnations grown for cut flowers. Because greenhouse application rates are expressed in terms of pounds per 100 gallons, the amount of ai applied per acre depends on the density of the crop. Exposure for reentry workers cutting and bundling flowers was 14.4 mg/hour and a transfer factor of 2,900 cm^2/hour was calculated. Based on the worker exposure (μg/hr) and the transfer factor (cm^2/hr) reported by Brouwer, dislodgeable residues in that study are estimated to be @4.97 $\mu g/cm^2$, single sided (2.5 $\mu g/cm^2$ double sided). These measurements were taken from sampling conducted 35 hours after treatment. **It should be noted that Brouwer et al. reported that the chlorothalonil residues did not dissipate.**

Tasks: Cutting and bundling field and greenhouse grown flowers.

Assumptions: For estimating worker exposure while cutting and bundling flowers, an eight hour work day is assumed. For chronic exposure, workers are assumed to work 5 days per week. A body weight of 61.5 kg was assumed since large numbers of women work in greenhouses.

Incidence: 1982, a probable incident occurred when a worker was cutting lilies still wet with spray. Liquid from a stem splashed into the workers eye. The lilies were treated with chlorothalonil.

1991, a possible incident occurred when a worker developed symptoms (not specified) while handling plants treated with chlorothalonil and vinclozolin.

1991, a possible incident involving a flower cutter developing a rash after working with irises. The field was treated either 6 - 14 days prior with an adjuvant, chlorothalonil, and iprodione.

Table 19
Daily Exposure for Workers Re-entering Greenhouses Treated With Chlorothalonil (@ 2.4 lb ai/A)

Hours after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal exposure (mg/kg/day)
35	2.5	1.89	0.095

The MOE's for short-term and intermediate term risk are greater than 6000. The MOE for cancer risk is 11.

Table 20 presents daily exposures for greenhouse workers following the application of a lower application rate (1.83 lb ai/acre).

Tasks: Cutting and bundling.

Assumptions: In California, 1.83 lb ai/100 gallons of water per acre were applied to poinsettias . The dislodgeable foliar residues measured ranged from 0.54 to 0.74 $\mu g/cm^2$ at 3 to 36 hours after treatment. Because greenhouse application rates are expressed in terms of pounds per 100 gallons, the amount of ai applied per acre depends on the density of the crop. HED used the transfer factor 5,800 cm^2/hr (double sided) which is based on the transfer factor generated by the Brouwer study. **It should be noted that Brouwer et al. reported that the chlorothalonil residues did not dissipate.** For estimating worker exposure while cutting and bundling flowers, an eight hour work day is assumed. For chronic exposure, workers are assumed to work 5 days per week. A body weight of 61.5 kg was assumed since large numbers of women work in greenhouses.

Table 20
Daily Exposure for Workers Re-entering Greenhouses Treated With Chlorothalonil (@ 1.83 lb ai/A)

Hours after application	Field residue ($\mu g/cm^2$)	Daily exposure (mg/kg/day)	Daily exposure corrected for dermal absorption (mg/kg/day)	Cancer Risk (MOE)
3	0.54	0.4	0.02	54
4	0.74	0.58	0.029	37
6	0.7	0.52	0.026	41
12	0.62	0.46	0.023	47
24	0.55	0.42	0.021	51
36	0.6	0.46	0.023	47

MOE's for short-term and intermediate-term exposure are greater than 20,000. The MOEs for cancer risks range from 54 to 37.

Table 21 presents lifetime risks from applications to golf courses.

Assumptions: For golfers HED assumed 30 days of golf per year and 50 years of golfing.

For mowers, HED assumed 60 days of mowing per year and 40 years of mowing.

Table 21
Estimated Daily Exposure for Workers Re-entering Treated Golf Courses

Activity	Daily Exposure (mg/kg/day)	Daily Exposure Corrected for Dermal Absorption (mg/kg/day)
Golfer - walking	0.001	0.00005
Greens mower (2 acres/day)	0.006	0.0003
Fairways mower (20 acres/day)	0.002	0.0001

Risks for other golfing scenarios such as using a golf cart are much lower and not included in this table. Short-term and intermediate-term MOE's for mowers and golfers are greater than 6 million.

(10) Post Application Risk Summary

Occupational Risk

Short-term and Intermediate-term post-application MOE's for all chlorothalonil use scenarios exceed 14,000 and are not a concern. Cancer risk to chlorothalonil was only calculated for the greenhouse chronic use scenario, cutting and bundling cut flowers, since it is unlikely that other uses scenarios would involve continuous exposure over several months. Cancer risk based on the MOE - approach and the cancer NOEL (1.5 mg/kg/day) range from MOE's of 54-47 over 36 hours following application. **HED has concerns with post-application cancer risk to greenhouse workers in the cut flower industry.** Cancer risk to HCB was not calculated; risk from chlorothalonil-derived HCB is not expected to be a concern based on the low post-application levels of HCB.

Residential Risk

An extensive risk assessment was not made for HCB as a contaminant in chlorothalonil. Based on high-end exposure, a mixer/loader using a wettable powder to support aerial applications to celery, a risk of 2.8×10^{-5} was estimated. Risk for the other scenarios are assumed to be lower. This is a worst case estimate based on 0.05% HCB, Newer formulations contain lower concentrations 0.02%.

HED does not have post-application data with which to estimate exposure to children or adults from the residential uses of chlorothalonil. Residential uses include the use of chlorothalonil-containing paints, the gel paint additive, lawn and garden use of chlorothalonil products, and caulk uses. Post-application exposure from the use of chlorothalonil-containing paints and caulks is not expected to be a risk of concern compared to the quantitaive risk of occupational handlers and considering the low percentage of chlorothalonil in home use products.

e) Food Quality Protection Act (FQPA) Considerations

(1) Potential Risk to Infants and Children

In determining whether an FQPA uncertainty factor is or is not appropriate for assessing risks to infants and children, EPA uses a weight of evidence approach taking into account the completeness and adequacy of the toxicity and exposure data bases, the nature and severity of the effects observed in pre- and post-natal studies, and other information such as epidemiological data.

For purposes of assessing the pre- and post-natal toxicity of chlorothalonil, EPA has evaluated two developmental studies and one reproduction study. Based on current toxicological data requirements, the data base for chlorothalonil relative to pre- and post-natal toxicity is complete. However, as EPA fully implements the requirements of FQPA, additional data related to the special sensitivity of infants and children may be required.

Developmental and Reproductive Effects

The developmental and reproductive data for chlorothalonil indicate that there is no evidence of an increased sensitivity to chlorothalonil from pre- or post-natal exposures. In the rat developmental toxicity study, the developmental NOEL and LOEL were based on an increase in total resorptions and resorptions per dam with a related increase in postimplantation loss. These observations occurred at a dose (400 mg/kg/day) which produced increased mortality and reduced body weight gain in the maternal animals. No developmental toxicity was observed (at any dose level) in the rabbit developmental toxicity study, while no maternal toxicity was observed at the highest dose tested (20 mg/kg/day).

(2) Uncertainty Factor

Based on the considerations outlined above, the Agency concludes the uncertainty factor applied according to FQPA to account for special sensitivity to infants and children is not warranted for the chlorothalonil risk assessment, and therefore should be removed. No reproductive effects were observed in any study. Developmental effects occurred only in the presence of significant maternal toxicity.

(3) Aggregate Exposure

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from pesticide residues in food and other exposures for which there is reliable information. These other exposures include drinking water and non-occupational exposures, e.g., to pesticides used in and around the home. Risk assessments for aggregate exposure consider both short-term and long-term (chronic) exposure scenarios considering the toxic effects which would likely be seen for each exposure duration.

Short-term aggregate exposure considers high-end spikes in exposure that could occur during a short time period (typically 1-7 days) for a variety of reasons; e.g., a lawn/indoor pesticide application is made on a particular day on which a person would also consume residues of this same pesticide in the diet (food and water). To estimate risk, this short-term exposure spike is compared to pesticide levels at which toxic effects were seen in short-term toxicity studies.

Similarly, long-term aggregate exposure considers average exposure to a population over a lifetime. This average exposure is then compared to pesticide levels at which toxic effects were seen in long-term (usually chronic) toxicity studies to estimate risk.

Chlorothalonil has food uses as a broad spectrum fungicide applied to vegetables, stone fruits, peanuts, soybeans, minor crops (cranberry) to control plant diseases such as powdery mildew, botrytis, rhizoctonia, and phytophthora. Chlorothalonil is available for use by homeowners, groundskeepers, and golf course employees for application to turfgrass, ornamentals and in paint (interior and exterior). Formulations of chlorothalonil include dusts, wettable powders, aqueous flowable concentrates, and solid flowables (water dispersable granules) and gels. Homeowner-use

products are applied using "push type" spreaders, hose-end sprayers, paint brushes and paint sprayers.

$$\text{Aggregate Acute Risk} = \frac{\text{Acute Dietary NOEL (175 mg/kg/day)}}{\text{(Acute Water Exposure + Acute Dietary Exposure)}}$$

$$\text{Aggregate Chronic Risk} = \frac{\text{(Chronic Water Exposure + Chronic Dietary Exposure)}}{\text{Reference Dose for Chlorothalonil (0.02 mg/kg/day)}}$$

Table 7
Food Quality Protection Act Considerations/Risk

Risk Type	Population Group	Estimated Risk	
		Chlorothalonil	HCB
DIETARY RISK			
Acute Dietary Risk	Non-nursing Infants	MOE = 875	N/A
	Children (1-6)	MOE = 875	N/A
	U.S. Population	MOE = 1166	N/A
Chronic Dietary Risk	Non-nursing Infants	60% RfD	0.01% RfD
	Children (Ages 1-6)	60% RfD	0.03% RfD
	U.S. Population	32% RfD	0.05% RfD
Dietary Cancer Risk		MOE = 3185	2.4×10^{-7}
DRINKING WATER RISK: Ground Water[1]			
Acute Risk	Children	MOE = 109,375	N/A
	Adults	MOE = 380,435	N/A
Chronic Risk	Children	8 % RfD	< 1 % RfD
	Adults	2 % RfD	< 1 % RfD
DRINKING WATER RISK: Surface Water			
Acute Risk	Children	MOE = 5,000,000	N/A
	Adults	MOE = 17,500,000	N/A
Chronic Risk	Children	< 1 % RfD	< 1 % RfD
	Adults	< 1 % RfD	< 1 % RfD
Cancer Risk	Adults	MOE = > 1.5 million	5×10^{-9}
RESIDENTIAL RISK			
Inter/Shrt-Term Risk - Handlers	Children	N/A	N/A
	Adults (paint uses)	$MOE_D = 316$; $MOE_I = 33$	Not a concern[3]

Inter/Shrt-Term Risk - Post-Application	Children	No Data	Not a Concern[3]
	Adults	No Data	Not a Concern[3]
Chronic Risk - Handlers and Post-Application	Children	N/A[4]	N/A[4]
	Adults	N/A[4]	N/A[4]
AGGREGATE RISK-All Sources-not including potential risk to children and adults from lawn uses[2]	Acute Risk (diet + water)	MOE> or = to 875	N/A
	Chronic Non-Cancer Risk (diet + water)	68 % RfD	< 1% RfD
	Cancer Risk (diet + water)	MOE = 3185	2.4×10^{-7}

1. Cancer risk was not calculated for drinking water risk from ground water sources. Ground water monitoring results were for the metabolites of chlorothalonil, not chlorothalonil itself. Only the parent, chlorothalonil, is considered carcinogenic.
2. Aggregate Risk is the combined risk from drinking water and food sources, risk from residential uses was not included because current policy states that if a dermal NOEL was used, aggregate short-term or intermediate-term risk is not required.
3. Residential risk to HCB was not assessed due to the expected extremely low level of potential HCB exposure.
4. Residential uses are not expected to be chronic exposure scenarios.

Chronic Dietary Exposure - Food Source:

Tolerances listed in 40 CFR §180.275(a) are for the combined residues of chlorothalonil and SDS-3701 in/on various raw agricultural commodities and animal feeds. Tolerances range from 0.05 ppm in/on edible banana pulp, cocoa beans, and field corn-grain to 50 ppm in/on field corn-fodder. Because both chlorothalonil and HCB are classified as B2 carcinogens, for the cancer risk assessment, residues of each were compared to their respective cancer potency values.

Chronic Dietary Exposure - Drinking Water Source:

Drinking Water Risk

Calculations for both ground water and surface water sources indicate risk from chlorothalonil and HCB is not of concern for short, intermediate-term, and cancer exposure.

Non-occupational Exposure:

The registrant asserts that turf applications to golf courses are primarily the only non-occupational use of chlorothalonil. However, chlorothalonil products are available to homeowners, groundskeepers, and golf course maintenance employees. Risks from some uses of chlorothalonil-containing paint products results in an **inhalation concern (MOE=33)**. The risk from lawn and garden uses of chlorothalonil products was not determined because post-application exposure for these uses is a data gap.

Chronic Dietary Risk, food source:

The chronic DRES analysis for chlorothalonil and HCB used anticipated residues and percent of crop treated information to calculate dietary risks calculated to be 32% of the chlorothalonil RfD for the U.S. general population, 60% for non-nursing infants (<1 year old), and 60% for children 1-6 years old. Chronic dietary risk from HCB was <1% for all population subgroups. Therefore, HED does not have a concern with regard to chronic dietary risk from chlorothalonil or HCB.

Cancer Risk, food source:

The total dietary cancer risk for residues of chlorothalonil for the published, pending and new tolerances for the overall U.S. population results in an MOE of approximately 3185. Based on the same uses, the cancer risk from HCB is approximately 2.4×10^{-7} . The U.S. population and all the DRES subgroups result in chronic dietary risk within the levels generally considered safe when anticipated residues are considered.

Acute Dietary Risk, food source:

The acute dietary risk estimate for chlorothalonil for the overall U.S. population and all subgroups are minimal with all margins of exposure (MOE) well above 300.

(4) Conclusions on Aggregate Exposure/Risk to Chlorothalonil

The estimated acute, chronic and carcinogenic risk to chlorothalonil from drinking water sources and from dietary/food sources for children and adults is within the range the Agency generally considers negligible. Combined, excluding the risk to children from residential uses, the total risk from these sources is also negligible. Therefore, HED does not have a concern regarding the combined risk to chlorothalonil from drinking water and food sources. However, risks from the use of airless sprayers to apply chlorothalonil-containing paint products results in an **inhalation concern.** If possible, fitted, OSHA-approved respirators should be required for painters using airless sprayers to help mitigate the inhalation risk. It may not be realistic to require OSHA-approved PPE on homeowner products. In order to help mitigate the risk from lawn and garden uses of chlorothalonil products in residential settings, HED has determined that restricting entry into treated areas until the sprays have dried is an applicable prudent safety practice. However, HED does have concerns regarding the potential exposure to children from residential uses of chlorothalonil. Risk to children from these uses is a data gap and was not included in this risk assessment due to a lack of data (post-application exposure to painted surfaces, treated lawns). These data are required for reregistration of uses on turfgrass at residential sites, and are expected to be submitted in response to the DCI issued 3/31/95. When submitted, these data will be used to re-evaluate chlorothalonil post-application exposure and re-examine potential residential exposure. Until these data are recieved, HED considers risk to chlorothalonil from residential uses a concern.

Cumulative Effects

Chlorothalonil is a member of the polychlorinated fungicides class of pesticides. Other members of this class include hexachlorobenzene, pentachlorophenol, pentachloronitrobenzene

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity". The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical-specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

HED does not have, at this time, available data to determine whether chlorothalonil has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, therefore, HED has not assumed that chlorothalonil has a common mechanism of toxicity with other substances.

4. HED Recommendations for Risk Mitigation/Reduction

a) Tolerance Reassessment Summary

Tolerances Listed Under 40 CFR §180.275(a):

The tolerances listed in 40 CFR §180.275(a) are for the combined residues of chlorothalonil and SDS-3701. Sufficient data are available to ascertain the adequacy of the established tolerances for: apricots; asparagus; bananas; beans, dry; beans, succulent; blueberries; broccoli; Brussels sprouts; cabbage; carrots; cauliflower; celery; cherries; cocoa beans; coffee beans; corn, sweet (K + CWHR); cranberries; cucumbers; melons; mushrooms; nectarines; onions, dry bulb; papaya; parsnips, roots; passion fruit; peaches; peanuts; plums; potatoes; prunes; pumpkins; soybeans; squash, summer; squash, winter; and tomatoes.

The available field trial data indicate that the established tolerance for green onions is too low. The registrant must either propose a higher tolerance or a longer PHI

Tolerances must be proposed for the combined residues of chlorothalonil and its 4-hydroxy metabolite in/on sweet corn forage. Available field trial residue data indicate that a level of 65 ppm would be appropriate.

New tolerances for the combined residues of chlorothalonil and SDS-3701 have recently been established for asparagus (0.1 ppm, PP#2E04042; proposed rule, PR Notice dated 6/19/96, pp 31073-31075), blueberries (1 ppm, PP#0E3899; FR dated 3/13/96, pp.10280-10282), filberts (0.1 ppm, PP#2E04113; FR dated 3/13/96, pp. 10280-10282), and mushrooms (1 ppm, PP#6E03410;FR dated 3/13/96, pp. 10280-10282). Tolerances for the combined residues of chlorothalonil and SDS-3701 have been proposed for almonds (0.05 ppm, PP#3F02875), almond hulls (0.2 ppm, PP#3F02875), mangoes (1 ppm, PP#2E04018), and pecans (0.02 ppm, PP#7F03471). In addition, the registrant has proposed a new tolerance for peaches (3 ppm, PP#3F2815), and new tolerances for cherries (PP#5F03183) at 0.5 ppm for sweet cherries (the current tolerance) and 3 ppm for sour cherries to support a proposed amended use which would allow applications after shuck split.

Efforts are being made to obtain a tolerance for residues of chlorothalonil in/on snowpeas since chlorothalonil is used on snowpeas grown in Guatemala. FDA monitoring data from 93 samples of snowpeas imported from Guatemala during 1992 showed detectable residues in/on 48 samples with an average residue of 0.036 ppm and a high residue of 0.9 ppm (CBTS No. 11929, DP Barcode D191687, 8/16/93, M. Flood).

Tolerances have been proposed (PP#6f4611) for residues of SDS-3701 in milk (0.1 ppm), fat (0.1 ppm), kidney (0.5 ppm), meat byproducts except kidney (0.05 ppm) and meat (0.03 ppm).

Tolerances Listed Under 40 CFR §180.275(b):

The tolerances with regional registrations listed in 40 CFR §180.275(b) are for the combined residues of chlorothalonil and its metabolite. Sufficient data are available to ascertain the adequacy of the established tolerances for mint hay and filberts.

Feed Additive Tolerances (40 CFR § 186.275):

No food/feed additive tolerances are required for the combined residues of chlorothalonil and SDS-3701.

Table 22.
Tolerance Reassessment Summary

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances listed under 40 CFR 180.275(a):			
Apricots	0.5	0.5	
Asparagus	0.1	0.1	
Bananas (NMT 0.05 ppm in edible pulp)	0.5	0.5 0.05	*Bananas* *Bananas, pulp*
Beans (dry)	0.1	0.1	*Beans, dry*
Beans, snap	5	5	*Beans, succulent*
Blueberries	1	1	
Broccoli	5	5	
Brussels sprouts	5	5	
Cabbage	5	5	
Carrots	1	1	
Cauliflower	5	5	
Celery	15	15	
Cherries (sweet and sour)	0.5	0.5	
Cocoa beans	0.05	0.05	
Coffee beans	0.20	0.20	*Coffee beans, green*
Corn, sweet (K - CWHR)	1	1	*Corn, sweet (K + CWHR)*
Cranberries	5	5	
Cucumbers	5	5	
Melons	5	5	
Mushrooms	1	1	
Nectarines	0.5	0.5	
Onions, dry bulb	0.5	0.5	
Onions, green	5	TBD [1]	The registrant must either propose a higher tolerance or increase the PHI.
Papayas	15	15	
Parsnips (root)	1	1	*Parsnips, roots*
Passion fruit	3	3	
Peaches	0.5	0.5	
Peanuts	0.3	0.3	
Plums	0.2	0.2	

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Potatoes	0.1	0.1	
Prunes	0.2	0.2	*Prunes, fresh*
Pumpkins	5	5	
Soybeans	0.2	0.2	
Squash, summer	5	5	
Squash, winter	5	5	
Tomatoes	5	5	
Tolerances listed under 40 CFR 180.275(b):			
Filberts	0.1	0.1	
Mint hay	2	2	
Tolerances to be established under 40 CFR 180.275(a):			
Corn, field, grain		0.05	
Corn, field, fodder		50	
Corn, sweet, forage		65	
Corn, sweet, fodder		50	
Peanut hay		20	
Tolerances to be established under 40 CFR 180.275(c):			
Milk		0.1	Tolerances for residues of SDS-3701 only
Fat		0.1	
Kidney		0.5	
Meat Byproducts except kidney		0.05	
Meat		0.03	

1. TBD = To be determined.

b) CODEX Harmonization

Numerous maximum residue limits (MRLs) for chlorothalonil residues in plant commodities have been established by Codex. Codex currently sets MRLs based on residues of chlorothalonil *per se* in plant commodities; however, the U.S. tolerance expression is for combined residues of chlorothalonil and SDS-3701. The Codex MRLs and the applicable U.S. tolerances are presented below in Table 23.

Table 23.

Codex MRLs and Applicable U.S. Tolerances

Commodity	MRL (mg/kg) [1]	U.S. Tolerance (ppm) [2]
Banana	0.2 (Step 8)	0.5
Blackberries	10	--
Broccoli	5	5
Brussels sprouts	5	5
Cabbages, head	5	5
Carrot	1	1
Cauliflower	5	5
Celery	15	15
Cereal grains	0.2 (Step 8)	(0.05; field corn grain) [4]
Cherries	10	0.5
Citrus fruits	5	--
Common bean (pods and/or immature seeds)	5	5
Cranberry	5	5
Cucumber	5	5
Currants, black, red, white	25	--
Endive	10	--
Grapes	10 (Step 7B)	--
Kale	10	--
Lettuce, head	10	--
Lima bean (dry)	0.5	0.1
Melons, except watermelon	5	5
Onion, bulb	5	0.5
Peach	25	0.5
Peanut	0.1	0.3
Peanut, whole	0.5	0.3
Peppers	10	--
Potato	0.1	0.1
Pumpkins	5	5

Commodity	MRL (mg/kg) [1]	U.S. Tolerance (ppm) [2]
Raspberries, red, black	10	--
Squash, summer	5	5
Sugar beet	1	--
Sweet corn (corn-on-the-cob)	1	1
Tomato	5	5
Winter squash	5	5
Witloof chicory (sprouts)	10	--

1. All chlorothalonil MRLs are based on residues of chlorothalonil *per se* and are final (CXL) unless otherwise indicated in parentheses.
2. Based on the combined residues of chlorothalonil and SDS-3701.
3. As the tolerance definitions for Codex MRLs and U.S. tolerances are different, harmonization of Codex MRLs and U.S. tolerances is not currently possible.
4. A tolerance of 0.05 ppm has been proposed on corn grain.

c) Occupational/Residential Labeling Rationale

Worker Protection Standard (WPS)

Occupational and Residential Labeling Rationale/Risk Mitigation

At this time, some products containing chlorothalonil are intended primarily for occupational use and some are intended primarily for homeowner use.

The Worker Protection Standard (WPS)

The Agency has issued the Worker Protection Standard for Agricultural Pesticides (WPS) affecting all pesticide products whose labeling reasonably permits use in the commercial or research production of agricultural plants on any farm, forest, nursery, or greenhouse. In general, WPS products had to bear WPS-complying labeling when sold or distributed after April 21, 1994. The WPS labeling requirements pertaining to personal protective equipment (PPE), restricted entry intervals (REI), and notification are interim. These requirements are to be reviewed and revised, as appropriate, during reregistration and other Agency review processes.

At this time some of the registered uses of chlorothalonil are within the scope of the WPS and some uses are outside the WPS scope.

Requirements for Handlers

For each end-use product, personal protective equipment and engineering control requirements for pesticide handlers are set during reregistration as follows:

- *Based on risks posed to handlers by the active ingredient, EPA may establish active-ingredient-specific ("a-i specific") handler requirements for end-use products containing that active ingredient. If the risks to handlers posed by the active ingredient are minimal, EPA*

may establish no a-i-specific handler requirements.

- *Based on the acute toxicity characteristics of the end-use product, EPA usually establishes handler PPE requirements for each end-use product.*

- *If a-i-specific requirements have been established, they must be compared to the end-use-product-specific PPE and the more stringent choice for each type of PPE (i.e., bodywear, hand protection, footwear, eyewear, etc.) must be placed on the label of the end-use product. Engineering controls are more stringent than PPE requirements.*

Occupational-Use Products

EPA is establishing a-i-specific requirements for some occupational handlers for chlorothalonil. Chlorothalonil is classified as a probable human carcinogen (Group B2) based on evidence of carcinogenicity in rats and mice (kidney). In addition, for short- and intermediate-term dermal exposure, a no observed effect level (NOEL) of 600 mg/kg/day was identified, for chronic (non-carcinogenic) exposure, a NOEL (2 mg/kg/day) was identified, and for short- and intermediate-term inhalation exposure, a NOEL of 12.2 mg/kg/day was identified. The MOE's for inhalation exposure were a concern for occupational mixers, loaders, and applicators using airless sprayers for indoor painting with latex paint unless respirators are used. The MOE's for inhalation exposure were a concern for mixers and loaders handling wettable powder formulations to support aerial and chemigation applications unless a dust/mist filtering respirator is used. EPA is requiring active-ingredient-based PPE for handlers of chlorothalonil in these exposure situations.

In addition, the handlers participating in the exposure studies upon which the risks were calculated wore chemical-resistant gloves in some scenarios and respirators in some scenarios. Since the risks to handlers were calculated as acceptable based on the use of the PPE worn in the studies, the Agency will require such PPE in those scenarios.

The Pesticide Handlers Exposure Database (version 1.1) does not contain sufficient data to estimate exposure to applicators using aircraft with open cockpits. Therefore, the exposure and risk assessment for aerial applicators was estimated using enclosed cockpits. Although the vast majority of aerial applicators use aircraft with enclosed cockpits, EPA does not have concerns for handlers who may apply chlorothalonil using aircraft with open cockpits, since the MOEs for enclosed cockpits are in the thousands.

WPS and NonWPS Uses:

Since potential handler exposure is similar for WPS and nonWPS uses, the a-i-specific handler requirements (specified in Section V) are the same for WPS and nonWPS occupational uses of chlorothalonil end-use products.

Homeowner-Use Products

EPA is not establishing a-i-specific requirements for homeowner handlers for chlorothalonil. Requiring PPE for homeowner uses is not a feasible option.

Post-Application/Entry Restrictions

Occupational-Use Products (WPS Uses)

NOTE: This section has been completed based upon the assumption that post-application

cancer risks are not of concern ON THE DAY OF APPLICATION (risk estimates show MOEs commonly below 100). Entry restrictions are based solely on the short-term dermal exposures and risks. The entry restrictions for greenhouse uses are deferred pending the outcome of additional Monte Carlo post-application risk assessments for possible chronic exposure.

Restricted-Entry Intervals, Early-Entry PPE, and "Double" Notification:

The interim Worker Protection Standard (WPS) restricted-entry intervals (REIs) for agricultural workers are based solely on the acute dermal toxicity and skin and eye irritation potential of the active ingredient. In addition, the WPS retains two types of REI's established by the Agency prior to the promulgation of the WPS: (1) product-specific REI's established on the basis of adequate data, and (2) interim REI's that are longer than those that would be established under the WPS. The WPS prohibits routine entry to perform hand labor tasks during the REI and requires PPE to be worn for other early-entry tasks that require contact with treated surfaces. "Double" notification is the statement on the labels of some WPS pesticide products requiring employers to notify workers about pesticide-treated areas orally as well as by posting of the treated areas. The interim WPS "double" notification requirement was imposed if the active ingredient is classified as toxicity category I for acute dermal toxicity or skin irritation potential.

During the reregistration process, EPA establishes REIs, early-entry PPE, and double notification requirements based on consideration of all available relevant information about the active ingredient, including acute toxicity, other adverse effects, epidemiological information, and post-application data.

EPA is establishing a 12-hour REI and the following early-entry PPE for all in-scope WPS uses of products containing chlorothalonil: coveralls, chemical-resistant gloves, shoes plus socks, and protective eyewear. EPA has determined that double notification is not required. The basis for these decisions is that the reregistration evaluation of the short- and intermediate-term and carcinogenic effects of chlorothalonil has resulted in the EPA's determination that the risks from post-application exposures to chlorothalonil by workers are adequately mitigated by a 12-hour REI and minimum early-entry PPE and that no double notification requirement is warranted.

Under the Worker Protection Standard, a 48-hour restricted-entry interval was established for chlorothalonil, since the active ingredient is classified as toxicity category I for eye irritation potential. During the reregistration evaluation, the Agency considered whether to retain the 48-hour REI due to eye irritation concerns. However, by the end of the 48-hour interval, the residues from chlorothalonil would not necessarily have dissipated to a level where eye irritation is no longer a concern. Depending on plant growth, rainfall, and the timing and type of irrigation, residues of eye irritation concern might exist for seven days or more following application. In one indoor study (Brouwer), it was noted that the residues of chlorothalonil did not dissipate over the time of the study. Due to the uncertainties in determining a set time interval when eye irritation from residues are no longer a concern and the economic urgency for the use chlorothalonil at a time that coincides with necessary hand-labor tasks, such as harvesting, the Agency sought an alternative to a 48-hour (or other length) REI as a means of adequately mitigating eye irritation concerns. To mitigate eye irritation concerns from post-application exposures, the Agency is requiring that, for at least seven days following the application of chlorothalonil:

- at least one container designed specifically for flushing eyes is available in operating condition at the WPS-required decontamination site for workers entering the area treated with chlorothalonil, and

- workers are informed orally, in a manner they can understand:
  -- that residues in the treated area may be highly irritating to their eyes,
  --that they should take precautions, such as refraining from rubbing their eyes, to keep the residues out of their eyes,

-- that if they do get residues in their eyes, they should immediately flush their eyes with the eyeflush container that is located at the decontamination site, and
-- how to operate the eyeflush container.

At this time, chlorothalonil is not a candidate for a 4-hour REI, since it is classified as a probable human carcinogen (group B2), and there are short-term, intermediate-term and chronic dermal endpoints of concern.

Occupational-Use Products (NonWPS Uses)

EPA is not establishing entry restrictions at this time for nonWPS occupational uses of chlorothalonil in paint products, since the anticipated frequency, duration, and degree of dermal exposure following paint applications do not warrant special risk mitigation measures and it is not anticipated that offgassing of vapors will be significant.

However, EPA is establishing entry restrictions at this time for nonWPS chlorothalonil applications to plants (e.g., uses on golf courses, on turfgrass in residential and commercial settings). The Agency has determined that restricting entry into treated areas until sprays have dried is a prudent safety practice applicable in such settings.

Homeowner-Use Products

EPA is establishing entry restrictions at this time for chlorothalonil end-use products that are intended primarily for homeowner use. The Agency has determined that restricting entry into treated areas until sprays have dried is a prudent safety practice applicable in residential settings at the use-sites where chlorothalonil will be applied.

Other Labeling Requirements

The Agency is also requiring other use and safety information to be placed on the labeling of all end-use products containing chlorothalonil. For the specific labeling statements, refer to Section V of this document.

LABELING REQUIREMENTS FOR END-USE PRODUCTS

The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR 156.10 and other applicable notices. All end-use product labels [e.g. multiple active ingredient (MAI) labels, SLN's, and products subject to generic data exemption] must be amended such that they are consistent with the basic producer labels. See Appendix A for appropriate rates and restrictions for those supported uses.

OCCUPATIONAL/HOMEOWNER PROTECTION

PPE/Engineering Control Requirements for Pesticide Handlers

For **sole-active-ingredient** end-use products that contain chlorothalonil, the product labeling must be revised to adopt the handler personal protective equipment and/or engineering control requirements set forth in this section. Any conflicting PPE requirements on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain chlorothalonil, the handler personal protective equipment and/or engineering control requirements set forth in

this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use

Active-Ingredient-Specific PPE or Engineering Control Requirements

EPA is not establishing active-ingredient-specific engineering controls for chlorothalonil end-use products.

EPA is establishing the following active-ingredient-specific PPE for some occupational uses of chlorothalonil end-use products.

For all end-use products intended primarily for occupational use, except chlorothalonil-containing paint products:

"Applicators and other handlers must wear:
--long-sleeved shirt and long pants, and
--shoes plus socks.
In addition, applicators using handheld equipment or specialty turfgrass airblast equipment and all mixers and loaders must wear:
--chemical-resistant gloves*."

* For the glove statement, use the statement established for chlorothalonil through the instructions in Supplement Three of PR Notice 93-7.

For wettable powder formulations (except wettable powder formulations contained in water-soluble packaging) that permit aerial or chemigation applications, add:
"In addition, mixers and loaders supporting aerial or chemigation applications must wear a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)."

For end-use products that contain directions for use on plants and do not prohibit use in a greenhouse, add:
"In addition, persons handling (mixing, loading, applying, etc) in a greenhouse or other enclosed area must wear a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)."

Determining PPE Requirements for End-use Product Labels

The PPE that would be established on the basis of the acute toxicity category of the end-use product must be compared to the active-ingredient-specific personal protective equipment specified above. The more protective PPE must be placed on the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Risks from the use of airless sprayers to apply chlorothalonil-containing paint products results in an **inhalation concern**. If possible, fitted, OSHA-approved respirators should be required for painters using airless sprayers to help mitigate the inhalation risk. However, it may not be realistic to require OSHA-approved PPE on homeowner products.

Placement in Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7, and the format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

Products Intended Primarily for Homeowner Use

Active-Ingredient-Specific PPE Requirements

Concentrated chlorothalonil end-use products that are intended primarily for homeowner use must state:

> "Uses should wear protective eyewear, such as shielded safety glasses, because this product is a severe eye irritant."

Determining PPE Requirements for End-Use Product Labels

The PPE, if any, that would be established on the basis of the acute toxicity category of each end-use product must be compared to the active-ingredient-specific personal protective equipment specified above. The more protective PPE must be placed on the product labeling. A requirement is considered more protective than a recommendation (e.g., "must wear" is more protective than "should wear"). For guidance on which PPE is considered more protective, see PR Notice 93-7.

Placement in Labeling

The personal protective equipment requirements and recommendations must be placed on the end-use product labeling immediately following the precautionary statements in the labeling section "Hazards to Humans (and domestic animals)."

Entry Restrictions

For **sole-active-ingredient** end-use products that contain chlorothalonil, the product labeling must be revised to adopt the entry restrictions set forth in this section. Any conflicting entry restrictions on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain chlorothalonil the entry restrictions set forth in this section must be compared to the entry restrictions on the current labeling and the more protective must be retained. A specific time period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

Products Intended Primarily for Occupational Use

WPS Uses NOTE! THIS SECTION DOES NOT REFLECT ENTRY RESTRICTIONS FOR GREENHOUSE USES. THOSE RESTRICTIONS ARE PENDING.

Restricted-entry interval:

A 12-hour restricted-entry interval (REI) is required for all uses within the scope of the WPS.

Early-entry personal protective equipment (PPE):

The PPE required for early entry is:
-- coveralls,
-- chemical-resistant gloves,
-- shoes plus socks, and
-- protective eyewear.

Eye Irritation Warnings:

The following statements must be placed on the labeling of every chlorothalonil end-use product that contains directions for WPS uses.

"**Special Eye Irritation Provisions:** This product is a severe eye irritant. Do not enter or allow workers to enter a treated area within 7 days of application, unless the following safety measures have been taken:
(1) At least one container designed specifically for flushing eyes must be available in operating condition at the WPS-required decontamination site intended for workers entering the treated area.
(2) Workers must be informed, in a manner they can understand:
-- that residues in the treated area may be highly irritating to their eyes,
--that they should take precautions, such as refraining from rubbing their eyes, to keep the residues out of their eyes,
-- that if they do get residues in their eyes, they should immediately flush their eyes using the eyeflush container that is located at the decontamination site or using other readily available clean water, and
-- how to operate the eyeflush container.

Placement in labeling:

The REI must be inserted into the standardized REI statement required by Supplement Three of PR Notice 93-7. The PPE required for early entry must be inserted into the standardized early-entry PPE statement required by Supplement Three of PR Notice 93-7. The eye irritation statements must be placed into the Agricultural Use Requirements box immediately following the early-entry personal protective equipment requirements.

<u>NonWPS uses</u>

Entry restrictions:

There are no entry restrictions for uses of chlorothalonil in paint products.

The Agency is establishing the following entry restrictions for nonWPS occupational uses on plants, such as golf course turfgrass or residential/commercial turfgrass):

"Do not enter or allow others to enter the treated area until sprays have dried."

Placement in labeling:

If WPS uses are also on label -- Follow the instructions in PR Notice 93-7 for establishing a

Non-Agricultural Use Requirements box, and place the appropriate nonWPS entry restrictions in that box.

If no WPS uses are on the label -- Place the appropriate nonWPS entry restrictions in the Directions for Use, under the heading "Entry Restrictions."

Products Intended Primarily for Homeowner Use

Entry restrictions:

"Do not allow people or pets to touch treated plants until the sprays have dried."

Placement in labeling: Place the appropriate entry restrictions in the Directions for Use, under the heading "Entry Restrictions."

Other Labeling Requirements

Products Intended Primarily for Occupational Use

HED recommends that the maximum application rate for specialty airblast applicators be reduced to no more than 6 pounds chlorothalonil per acre OR workers be required to wear gloves so that the resultant risk is not a concern.

The Agency is requiring the following labeling statements to be located on all end-use products containing chlorothalonil that are intended primarily for occupational use.

Application Restrictions

"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."

Engineering Controls

"When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS."

User Safety Requirements

1. {Select this if coveralls are required for pesticide handlers on the end-use product label:}

Discard clothing or other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them.

2.{Select this always:}

Follow manufacturer's instructions for cleaning/maintaining PPE. If no such

instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."
- "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Products Intended Primarily for Home Use

Application Restrictions

"Do not apply this product in a way that will contact any person or pet, either directly or through drift. Keep people and pets out of the area during application."

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

d) Required Studies

(1) Residue Chemistry Data and Recommendations

Residue data have been submitted in support of establishing a tolerance on sweet corn forage and are currently under review. These data are required as a result of changes to the livestock feeds table (Table II) in Subdivision O of the Pesticide Assessment Guidelines, and therefore should not delay a reregistration eligibility decision for chlorothalonil. Additional storage stability information to support residue studies is required; however, this information is expected to be confirmatory to our conclusion that chlorothalonil residues of concern are stable under frozen storage.

There are presently no tolerances on animal commodities. Data reviewed in poultry metabolism studies indicate that tolerances are not needed at this time for poultry and eggs. Tolerances have been proposed for meat and milk commodities based on an acceptable ruminant feeding study. These tolerances will be established contingent upon a successful Agency validation of an enforcement analytical method.

Although all the data requirements of the Registration Standard have not been met at this time, the outstanding data are considered to be confirmatory to our reregistration eligibility decision in these documents. Sufficient data are available to conduct reasonable anticipated residue

assessments both for plant and animal commodities. Two sets of anticipated residues have been provided to DRES in a separate memorandum; one for residues of chlorothalonil and the other for residues of the chlorothalonil contaminant, hexachlorobenzene (HCB).

(2) Additional Occupational/Residential Exposure Studies

Handler Studies

There are few data addressing handler exposure when treating residential turf. The registrant is a member of the Outdoor Residential Exposure Task Force (ORETF). Data for mixer/loader/applicator treating turfgrass with chlorothalonil were required in a recently issued DCI for products registered on turfgrass (3/31/95). These data will be used to re-evaluate chlorothalonil handler exposure when they are submitted by the Task Force. HED recommends that these data be submitted immediately if the residential uses of chlorothalonil are supported.

Also, until recently, HED was unaware of the wood treatment uses for chlorothalonil (described earlier). Exposure data for those uses are considered a data gap. The registrant has conducted a study addressing exposure during the application of paints and stains containing chlorothalonil. The painter study is assumed to represent a higher exposure than the use of chlorothalonil treated caulks.

Post-Application Studies

The registrant must submit post-application exposure studies as confirmatory data.

Postapplication/reentry exposure studies are required as confirmatory data to determine definitive REIs for all cole crops and floral crops. The interim REIs established in this document for these crops will be adjusted accordingly upon submission of the additional data. In addition, post-application/reentry exposure studies are required for reregistration of uses on turfgrass at residential sites.

Requirements for such post-application exposure studies are addressed by Subdivision K of the Pesticide Assessment Guidelines. The required data include:

Guidelines:	132-1(a)	Foliar Residue Dissipation
	*133-3	Postapplication Dermal Passive Dosimetry Exposure
	*133-4	Postapplication Inhalation Passive Dosimetry Exposure

*Guidelines 133-3 and 133-4 may be reserved at this time pending completion of the databases on agricultural and residential postapplication/reentry exposure currently being developed by the Agricultural Reentry Task Force and Outdoor Residential Exposure Task Force, since the registrant is a member of both Task Forces.

Recommendations

Use Information

Due to the uncertainty of the assessment, it is recommended that the registrant submit a probability analysis of the greenhouse use of chlorothalonil addressing frequency of chlorothalonil applications and the variety of post-application work tasks associated with the cut flower industry.

Application Rate Reduction

With the exception of specialty airblast application to golf courses (MOE = 53), all use scenarios result in margins of exposure that exceed 100 and are not of concern. For specialty airblast applicators to golf courses, HED recommends EITHER a reduction in the maximum application rate from 12.51 lb ai/acre to 6 lb ai/acre (MOE=111) OR by requiring these handlers to wear gloves (MOE=263) be implemented so that the resultant risk is not a concern.

Attachments
1. Hazard Assessment/Dose Response Assessment
2. Product and Residue Chemistry Assessments
3. Dietary Exposure Analysis
4. Occupational and Residential Exposure Assessment

Appendices
1. Product Chemistry Data Summary
2. Residue Chemistry Science Assessments Summary