159

CASWELL FILE

10-15-84

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

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Revised Captan, PD 2/3, Quantitative Risk Assessment

FROM: Herbert Lacayo and Bertram Litt 10/15/84
Toxicology Branch
Hazard Evaluation Division (TS-769)

TO: Carol Langley
Special Review Branch
Registration Division (TS-767

THRU: Reto Engler, Chief
Mission Support Staff
Toxicology Branch/HED (TS-769)

Summary

The analysis of three captan chronic feeding studies show a dose-tumor relationship yielding an average (Geometric Mean) potency of $Q_1^* = 2.3X10^{-3}$ (for dose in mg/kg/day) with a weight of evidence classification B2 (probable human carcinogen under the draft EPA guidelines). This conclusion is based on adeno-carcinomas of the digestive tract in both sexes of three mouse studies and on kidney tumors in male rats. This is further supported by evidence from short term studies(1) that show captan to be an alkylator.

Specific potency estimates, Q_1^*, by sex for each registrant study are given for animals with adenomas and/or adenocarcinomas of the digestive tract (stomach, duodenun, jejunum-ileum). The studies and the estimated Q_1^* are:

High Dose Mouse Study (HDS):

Chevron Chemical report entitled "Socal 1150, Lifetime Oncogenic Feeding Study of Captan Technical, (SX-944), in CD-1 Mice (ICR derived)", January 9, 1981, EPA Accession No. 244220-244226. Estimated potencies - $Q_1^* = 3.4x10^{-3}$ (Females), and $3.9x10^{-3}$ (Males). Note: This study was designed to demonstrate that the National Institutes of Health NCI Bioassay NCI-CG-TR-15 findings of duodenal tumors in mice was an artifact resulting from the conditions of the experiment.

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(1) Reference - Schneider's internal memo

1

Rat Study (RS):

Stauffer Chemical Company report entitled "Two Year Oral Toxicity/Carcinogenicity Study of Captan in Rats", June 23, 1982, EPA Accession No. 249335-249338. Estimated potency for males only - $Q_1^* = 2.4 \times 10^{-3}$.

Low Dose Study (LDS):

Chevron Chemical Company report entitled "Project No. 80-2491, A Lifetime Oral Oncogenicity Study of Captan in Mice", April 13, 1983, EPA Accession No. 249942-249948. Estimated potencies - $Q_1^* = 2.0 \times 10^{-3}$ for Females, and 1.0×10^{-3} for Males.

I. Hazard Evaluation - Qualitative Analysis

A. High Dose Mouse Study (HDS):

This study was prompted by the 1977 NCI-CG-TR-15 report (entitled "Bioassay of Captan for Possible Carcinogenicity") in B6C3F1 mice and Osborne-Mendel rats which reported a statistically significant dose-related increase in the 96 week incidence rate of duodenal tumors in mice (adenocarcinomas and adenomatous polyp). Chevron undertook the task of demonstrating that this was a false positive finding; specifically Chevron in the HDS tested the assumption that captan fed to Charles River CD-1 mice (ICR derived) for two years at doses of 6,000, 10,000, and 16,000 ppm would not result in tumors of the digestive tract. The study started August 14, 1977 and terminated October 20, 1979.

During the HDS no unusual diseases or complicating factors were observed.

Survival appears dose-related as can be seen from the "at risk" mortality data given below.

Table 1 - HDS Mortality Rates

(Number of Deaths/Number of Animals at Risk)

MALES	Dose (ppm)			
Time Interval (weeks)	0	6,000	10,000	16,000
0-52	5/80	3/80	4/79	8/80
53-75	9/75	12/77	16/75	16/72
76-90	14/61	8/65	12/59	28/56
Survivors	52	57	47	27
FEMALES				
0-52	4/80	3/80	4/80	4/80
53-75	8/76	6/77	5/76	17/76
76-95	17/68	11/71	10/71	30/59
Survivors	49	60	61	29

In males there is a statistically significant dose related trend in mortality which is exacerabated if one examines dosed animals only. The survival pattern of females is less clear but still statistically significant due to the higher mortality of the high dose (16,000 ppm) group. Using Peto's trend test (Reference 1) on the above interval mortality data gives:

Time Interval (Weeks)	Significance Level (one-tailed P value) Males	Females
0-52	.15	.46
53-75	.04	.02
76-95	.0001	.002
Overall	< .0001	.0003

This is reasonably compelling evidence that captan effects the survival distribution of CD-1 mice.

We concur with the company's evaluation of body weight: (Vol. I of HDS)

> "In all treatment groups, average body weights were significantly lower than the controls throughout the study."

These data indicate that there is a dose-weight related trend for captan in CD-1 mice.

B. Low Dose Mouse Study (LDS):

This study was done by Bio/dynamics Inc. for the Chevron Chemical Company starting October 8, 1980 and terminating on August 2, 1982. Test animals were Charles River CD-1 mice (ICR derived). The experimental design utilized five dose levels (0, 100, 400, 800, 6000 ppm) of captan with 100 mice of each sex being randomly assigned to each dose level. No unusual diseases or complications were observed.

Although there was an unusually high mortality among control animals, there is evidence of a mortality-dose related trend (but not as strong as in the HDS) as can be seen from the "at risk" mortality data given below.

Table 2 - LDS Mortality Rates

(Number of Deaths/Number of Animals at Risk)

MALES	Dose (ppm)				
Time Interval (weeks)	0	100	400	800	6,000
0-52	7/100	4/99	4/100	5/100	13/100
53-72	38/93	32/95	24/96	31/95	54/87
73-88	23/55	32/63	43/72	32/64	24/33
Survivors	22	30	29	32	9
FEMALES					
0-52	12/100	6/100	4/100	8/100	3/100
53-72	22/88	22/94	17/96	16/92	28/97
73-88	24/66	26/72	32/79	26/76	29/69
Survivors	42	46	47	50	40

4

Using Peto's trend test (Reference 1) on the above data yields:

Time (Weeks)	Significance Level (one-tailed P value) Males	Females
0-52	.0025	.95
53-72	.00001	.07
73-88	.0078	.22
Overall	.00001	.21

This provides fairly convincing evidence that captan effects the survival distribution of male CD-1 mice and some evidence that female mice are similarly effected (during weeks 53-72).

The dose-weight trend observed in the HDS is present also in the LDS. The Company states that mean body weights for high dose males were lower than controls and that this difference was "for the most part statistically significant" during the first year. The weight of high dose females was also lower than their study controls and statistically significant "for the most part" for the first 18 months of the study. We interpret these data as indicating a captan related effect which is evident for a significant portion of the mouse lifetime; the normal aging process results in control animals 'catching-up' during months 19-24.

C. Rat Study (RS):

This study was carried out by the International Research and Development Corporation for Stauffer Chemical Company starting October 4, 1978 and terminating two years later on October 3, 1980. Test animals were Charles River CD rats.

The experimental design specified four dose levels (0, 20, 100, 250 mg/kg/day) of captan fed to 70 mice of each sex per level for a duration of two years. No unusual diseases or complications were observed. The survival rates are of interest. While the reported survival rates at one and two years appear similar for male rats, there is weak but consistent evidence of a dose related mortality trend which

5

is statistically significant at $p \leq .02$ computed by Peto's trend test (Reference 1). The situation is less clear for female rats. However, there is some evidence of a mortality-dose trend for the initial one and half years (i.e. 78 weeks). The adjusted mortality data and time specific results of Peto's trend tests are given below for completeness. Time intervals were chosen so as to avoid crossing over zones of planned kills.

Table 3 - Rat Study Mortality

MALES	Dose (mg/kg/day)			
Time (weeks)	0	25	100	250
0-52	2/70	3/70	3/70	3/70
54-78	5/58	3/57	3/57	9/57
80-88	3/43	4/44	6/44	5/38
90-96	4/40	7/40	7/38	7/37
Survivors	36	33	31	30
FEMALES				
0-52	2/70	1/70	1/70	3/70
54-78	1/58	7/59	3/59	7/57
80-88	4/47	7/42	4/46	2/46
90-96	4/43	6/35	5/42	3/38
Survivors	39	29	37	35

Time Interval (Weeks)	Significance Level Males	Females
0-52	.38	.20
54-78	.04	.08
80-88	.18	.88
90-96	.14	.75

With respect to body weights, the Company states in volume 1 (pg 14) of the rat study that "throughout the study, group mean body weights for rats at the 100 and 250 mg/kg/day dose levels were considerably lower when compared with the control means. These changes were considered statistically significant i.e., $p \leq .05$ at all intervals analyzed and considered compound related."

II. Hazard Evaluation - Qualitative Analysis

Our analysis of the rat data focuses on kidney adenomas and carcinomas while the corresponding work for mice also counts adenomas and carcinomas of the stomach, duodenum, and jejunum-ileum. The rationale for combining these organ sites and tumor types in the mouse studies is outlined in the National Toxicology Program - Board of Scientific Councillors Meeting, September 23 and 24, 1982. Its appropriateness in this case was approved by Dr. Louis Kasza, the resident pathologist in HED.

The raw data and analysis of findings for the mouse studies are summarized in Table 4A for the females and 4B for the male mice. There are statistically significant increases in digestive tract adeno-carcinomas associated with increased doses of captan in both sexes for both High and Low Dose studies. The survival at final kill (Tables 4A and 4B) when compared to the earlier analysis is clearly inadequate as an adjustment. Therefore, the data have been analyzed using unadjusted rates and adjusting for mortality with equal weight on all outcomes (Cox's procedure, Reference 2) and placing more weight on earlier deaths with tumors (Gehan and Breslow, Reference 3, 4). A high level of statistical significance is observed for all dose-response trends. This indicates that the response (adeno-carcinomas of the digestive tract) increases with the dose in both sexes for both high and low dose mouse feeding studies.

Table 4-A Adenoma, and Carcinoma in the Stomach,
Duodenum, and Jejunum-Ileum of Female Mice
In Two Year Feeding Studies
Chevron Project No. 80-2491 (LDS), Socal 1150 Jan. 81 (HDS)

DOSE (ppm)	0	100	400	800	6000	10000	16000	Total
LDS TBA/Total	0/100	1/100	3/100	3/100	7/100			14/500
'No. Survivors)	(26)	(31)	(35)	(38)	(27)			
HDS TBA/Total	3/80				26/80	21/80	29/80	79/320
(No. Survivors)	(28)				(40)	(45)	(19)	

COMPARSIONS of 0 ppm vs. Other Groups for P $\leq$ .25 (One Tail Chi - Square Test)

DOSE (ppm)	100	400	800	6000	10000	16000
LDS		.2458 NS	.2458 NS	.0213*		
HDS				$\leq$ .0001**	.0002**	$\leq$ .0001**
Combined				$\leq$ .0001**	.0001**	$\leq$ .0001**

REND ANALYSIS	UNADJUSTED		ADJUSTED (EQUA. Wt.) Cox		ADJUSTED (EARLY DEATHS) Gehan - Breslow	
	Trend	Departure	Trend	Departure	Trend	Departure
LDS	.0028**	.6562 NS	.0120*	.0006**	.0003**	.9619 NS
HDS	$\leq$ .0001**	.089*	$\leq$ .0001**	.0940 NS	$\leq$ .0001**	.0435*
Combined	$\leq$ .0001**	.8465	$\leq$ .0001**	$\leq$ .0001**	$\leq$ .0001**	.0032

TBA = Tumor Bearing Animals

* = Significant at approximately 5% or less

** = Significant at approximately 1% or less

Table 4-B Adenoma, and Carcinoma in the Stomach,
Duodenum, and Jejunum-Ileum of Male Mice
In Two Year Feeding Studies
Chevron Project No. 80-2491 (LDS), Socal 1150 Jan. 81 (HDS)

DOSE (ppm)	0	100	400	800	6000	10000	16000	Total
LDS TBA/Total	0/100	6/100	1/100	1/100	5/100			13/500
(No. Survivors)	(12)	(19)	(20)	(24)	(7)			
HDS TBA/Total	3/80				19/80	22/79	39/80	83/319
(No. Survivors)	(33)				(42)	(25)	(10)	

COMPARSIONS of 0 ppm vs. Other Groups for $p \leq .10$ (One Tail Chi - Square Test)

DOSE (ppm)	100	400	800	6000	10000	16000
LDS	.0375*			.0707 NS		
HDS				.0006**	.0001**	$\leq$ .0001**
Combined	.1030 NS			.0001*	$\leq$ .0001**	$\leq$ .0001**

TREND ANALYSIS	UNADJUSTED		ADJUSTED (EQUAL Wt.) Cox		ADJUSTED (EARLY DEATHS) Gehan - Breslow	
	Trend	Departure	Trend	Departure	Trend	Departure
LDS	.1168 NS	.0275*	.0145**	.0284*	.0713 NS	.0174*
HDS	$\leq$ .0001**	.6028 NS	$\leq$ .0001**	.0066**	$\leq$ .0001**	.0003**
Combined	$\leq$ .0001**	.2285 NS	$\leq$ .0001**	.0031**	$\leq$ .0001**	$\leq$ .0001**

TBA = Tumor Bearing Animals

* = Significant at approximately 5% or less

** = Significant at approximately 1% or less

A variety of standard risk assessment models (see Table 5A and B) were fit to the LDS and HDS data. None of the these provided an ideal fit to the observed data; however the multistage model does show a smaller gap between the point estimate and the lower 95% bound on the dose associated with the cancer risks of 10^{-4} and 10^{-6}. The one-hit and multi-stage models indicate that higher exposures (i.e. doses) were related to specific risk levels than predicted by other models. For example, using either of these models a dose of approximately 10^{-2} mg/kg/day is needed (i.e. 10^{-2} mg/kg/day is a lower 95% Bound on Exposure) to generate a risk level of 10^{-4}. However, under this same risk (i.e.10^{-4}), the associated lower bounds on the doses generated by the other models examined (see tables 5A and 5B) are $2x10^{-53}$ for the Probit, zero for the Weibull, and $4x10^{-21}$ for the Multi-stage model.

In the male rats the data demonstrate a statistically significant trend for kidney tumors, 1/70 controls, 1/70 fed 25 mg/kg/day, 3/70 fed 100 mg/kg/day and 4/70 fed 250 mg/kg/day; as shown by the Armitage trend test $P<.05$. The 95% lower confidence bounds for dose are 4.25×10^{-2} and 4.25×10^{-4} mg/kg/day respectively for risks of 10^{-4} and 10^{-6} when fitting the Multi-stage model to these data. These estimates are consistent with the mouse data discussed above.

The multistage model has been used to estimate the potency Q_1^* because it provides a consistently adequate fit to both male and female tumor data and because it appears to be the most stable estimator. (2) Consider the following potencies:

male mice HDS	3.9×10^{-3}
male mice LDS	1.0×10^{-3}
female mice HDS	3.4×10^{-3}
female mice LDS	2.0×10^{-3}
male rats	2.4×10^{-3}

All of the Q_1^* values are tightly grouped. If we assume that the distribution of the Q_1^* is a positive random variable but is otherwise unknown, and if the tight grouping of the Q_1^*'s is indicative of the true value, then a reasonable way to pool the values is to estimate an overall Q_1^* by the geometric mean. This gives the value of

$$Q_1^* = 2.3 \times 10^{-3}$$

shown in the first paragraph of this memo.

(2) The multi-stage model is stable with respect to the data in that minor changes in the input data cause little or no change in model parameters such as Q_1^*.

Table 5-A Comparison of Risk Models For Female Mice

	One Hit Model		Multi Stage Model		Probit Model		Weibull Model		Multi-Hit Model	
Risk = 10^{-4} for	MLE Dose	.95 Conf bound	MLE Dose	.95 Conf bound	MLE Dose	.95 Conf bound	MLE Dose	.95 Conf bound	MLE Dose	.95 Conf bound
LD Study	9.48×10^{-2}	4.56×10^{-2}	9.59×10^{-2}	4.99×10^{-2}	4.23×10^{-4}	2.0×10^{-7}	8.34×10^{-6}	1.67×10^{-10}	8.99×10^{-6}	1.12×10^{-6}
HD "	3.71×10^{-2}	2.0×10^{-2}	3.9×10^{-2}	3.0×10^{-2}	3.026×10^{-11}	1.86×10^{-53}	7.15×10^{-26}	0	9.38×10^{-20}	3.94×10^{-21}
Combined	3.86×10^{-2}	3.14×10^{-2}	3.91×10^{-2}	3.23×10^{-2}	.496	6.86×10^{02}	2.89×10^{-2}	1.56×10^{-3}	2.93×10^{-2}	9.92×10^{-4}
Risk = 10^{-6} for										
LD Study	9.48×10^{-2}	4.56×10^{-4}	9.59×10^{-4}	4.99×10^{-4}	1.73×10^{-6}	1.53×10^{-11}	1.28×10^{-10}	7.4×10^{-14}	1.36×10^{-10}	1.69×10^{-11}
HD "	3.71×10^{-2}	2.05×10^{-4}	3.92×10^{-4}	3.0×10^{-4}	2.27×10^{-14}	9.31×10^{-73}	1.73×10^{-33}	0	8.27×10^{-32}	3.47×10^{-33}
Combined	3.86×10^{-4}	3.14×10^{-4}	3.91×10^{-4}	3.23×10^{-4}	7.91×10^{-2}	5.566×10^{-3}	2.43×10^{-4}	2.46×10^{-6}	2.48×10^{-4}	1.07×10^{-6}

MLE = Maximum Likelihood Estimated

Table 5-B Comparison of Risk Models for Male Mice

	One Hit Model		Multi Stage Model		Probit Model		Weilbull Model		Multi-Hit Model	
	MLE Dose	.95 Conf. bound	MLE Dose	.95 Conf. bound	MLE Dose	.95 Conf. bound	MLE. Dose	.95 conf. Bound	MLE. Dose	.95 conf. Bound
Risk 10^{-4}										
LD Study	2.41×10^{-1}	5.46×10^{-2}	1.609 x 10	9.81×10^{-2}	7.24×10^{-77}	0	7.24×10^{-77}	0	3.61×10^{-7}	2.45×10^{-8}
HD "	7.58×10^{-2}	5.08×10^{-4}	3.7×10^{-2}	2.64×10^{-2}	1.78	2.05×10^{-1}	7.10×10^{-2}	1.49×10^{-3}	7.58×10^{-2}	5.08×10^{-4}
Combined	2.16×10^{-2}	4.72×10^{-1}	2.7×10^{-1}	4.82×10^{-2}	8.04	3.78	1.24	3.29×10^{-1}	2.16×10^{-2}	4.72×10^{-1}
Risk = 10^{-6} for										
LD Study	2.41×10^{-3}	5.45×10^{-4}	5.09	9.81×10^{-4}	7.24×10^{-77}	0	7.24×10^{-77}	0	3.4×10^{-13}	2.3×10^{-14}
HD "	1.27×10^{-3}	4.54×10^{-7}	3.71×10^{-4}	2.64×10^{-4}	4.66×10^{-1}	2.71×10^{-2}	1.1×10^{-3}	2.72×10^{-6}	1.27×10^{-3}	4.54×10^{-7}
Combined	2.56×10^{-1}	2.19×10^{-2}	2.75×10^{-3}	4.82×10^{-4}	3.33	1.22	9.13×10^{-2}	1.16×10^{-2}	2.56×10^{-1}	2.19×10^{-2}

LE = Maximum Likelihood Estimate

III Estimates of Risk Associated with Diet:

Accurate data are not yet available on daily intake of Captan. We therefore use the best available data of 7.013 mg/1.5 kg diet/day for a TMRC (Theoretical maximum residue concentration) value and .011 mg/1.5 kg diet/day for are intake based or residues, March 18, 1980 memo from Janice K. Jensen to Carol Langley (Subject: Captan Dietary Analysis for the PD 2/3).

The best available dietary estimates of intake divided by 60 kg approximates the daily intake of Captan as .1169 mg/kg (body weight)/day and .00018 mg/kg/day based respectively on tolerances and actual residues. When multiplied by Q_1* these exposure estimates give an upper 95% bound on cancer risk of

2.70×10^{-4} for Tolerances and
4.16×10^{-7} for actual residues.

IV Estimation of Risk Increment Associated with Application Captan:

For dermal absorption, we used the rat skin penetration estimate of 1.3%/hour from the company study (3) and the method outlined in Robert P. Zendzian's memo to William Butler dated 11/18/82 (Subject: Captan, Dermal Penetration Study). The formula used was derived by H. Lacayo from basic mathematical principals and is given in the appendix. The interspecies conversion factor is also given in the appendix.

(3) Captan 50-WP: A Dermal Absorption Study in Rats, T-11008 Stauffer Chemical Company, July 26, 1982.

The risk to workers is given in tables 6-a,b,c,d under the following senarios.

I On a Single Exposure: A No Protective Clothing (4) - Table 6-A
B Protective Clothing (4) - Table 6-B

II Lifetime Average, Daily Dose (LADD)
A No Protective Clothin (4) - Table 6-C
B Protective Clothing (4) - Table 6-D

Exposure on a single day is a worst case assumption that assumes that exposure on one day is equivalent to exposure on every day of a lifetime.

The basic exposure data for the tables was obtained from Janice K. Jensen memo to Carol Langley dated May 21, 1982 - Subject: Captan PD 2/3 Application Exposure Analysis - Final Report. The dermal absorption figures of the Jensen memo were modified in accordance with the procedures outlined in Robert P. Zendzian's memo to Homer K. Hall dated Nov 18, 1982 (Subject: Captan, Dermal Penetration study). The total mg/day absorbed were then divided by 70 kg to express the worker exposure in mg/kg/day.

Tables 6C and 6D, for LADD were derived from Table 6A and 6B by the formula:

$$\text{LADD Risk} = \text{Daily Exposure} \times \frac{\text{No. Exposed days/year}}{365} \times \frac{\text{40 Work Years}}{\text{70 Year Lifetime}}$$

Consequently the LADD risks for Tables 6C and 6D are less than the Daily Exposure (Tables 6A, 6B).

There does not appear to be any thing of special note in the worker-exposure-risk tables 6, A, B, C, D with the possible exception of certain Crops in Table 6A (Daily Exposure - Worse Case; and for workers in apple post-harvest operations (PH) where there is a high risk (6.9×10^{-5}) even with protective clothing. This is due to the long, 224 days, post season processing time.

(4) The Jensen memo also assumes that protective clothing reduces by 80% the amount of agent reaching a worker.

Table 6A Daily Exposure And Assoc Risk For Worst Case Without Protective Clothing
(Q_1*, = 2.31 x 10^{-3} when dose is in mg/kg/day)

Crop	Typical Case[a] Exp	Risk[b]	Low Exp	Risk	High Exp	Risk
Apple Loader	.125	2.9 x 10^{-4}	.04785	1.1 x 10^{-4}	.19343	4.5 x 10^{-4}
Sprayer	.0054	1.2 x 10^{-5}	.00154	3.6 x 10^{-6}	.00607	1.4 x 10^{-5}
Strawberries	.00063	1.5 x 10^{-6}	2.2 x 10^{-4}	5.1 x 10^{-7}	.00271	6.3 x 10^{-6}
Home Garden	.00011	2.5 x 10^{-7}	2.3 x 10^{-5}	5.2 x 10^{-8}	.00016	3.7 x 10^{-7}
Almonds: Pilot	.00084	1.9 x 10^{-6}	8.4 x 10^{-4}	1.9 x 10^{-6}	.00084	1.9 x 10^{-6}
Mixer/loader	.11986	2.8 x 10^{-4}	.11985	2.8 x 10^{-4}	.11986	2.8 x 10^{-4}
Apples Post-harvest	.02228	5.1 x 10^{-5}	.00739	1.7 x 10^{-5}	.02983	6.9 x 10^{-5}
Potatoes:	.011	2.5 x 10^{-5}	.01096	2.5 x 10^{-5}	.01096	2.5 x 10^{-5}
Filler/cutters	.00314	7.3 x 10^{-6}	.00308	7.1 x 10^{-6}	.00309	7.1 x 10^{-6}
Planters						
Soybeans	.01433	3.3 x 10^{-5}	.01433	3.3 x 10^{-5}	.01433	3.3 x 10^{-5}

Table B Daily Exposure And Associated Risk for Worst Case with Protective Clothing
(Q_1*, = 2.31 x 10^{-3} when dose is in mg/kg/day)

Crop	Typical Case[a] Exp	Risk[b]	Low Exp	Risk	High Exp	Risk
Apple: Loader	.02043	4.7 x 10^{-5}	.00714	1.7 x 10^{-5}	.03254	7.5 x 10^{-5}
Sprayer	.00536	1.2 x 10^{-5}	.00155	3.6 x 10^{-6}	.00607	1.4 x 10^{-5}
Strawberries	9.7 x 10^{-5}	2.2 x 10^{-7}	3 x 10^{-5}	6.9 x 10^{-8}	.00046	1.1 x 10^{-6}
Home Garden	3.1 x 10^{-5}	7.3 x 10^{-8}	7.1 x 10^{-6}	1.7 x 10^{-8}	4.6 x 10^{-5}	1.1 x 10^{-7}
Almonds: Pilot	8.4 x 10^{-4}	1.9 x 10^{-6}	8.4 x 10^{-4}	1.9 x 10^{-6}	8.4 x 10^{-4}	1.9 x 10^{-6}
Mixer/loader	.0194	4.5 x 10^{-5}	.0194	4.5 x 10^{-5}	.0194	4.5 x 10^{-5}
Apple Post/harvest	.00232	5.4 x 10^{-6}	.00766	1.8 x 10^{-5}	.00311	7.2 x 10^{-6}
Potatoes:	.00148	3.4 x 10^{-6}	.00148	3.4 x 10^{-6}	.00148	3.4 x 10^{-6}
Filler/cutters	.00308	7.1 x 10^{-6}	.00309	7.1 x 10^{-6}	.00309	7.1 x 10^{-6}
Planters						
Soybeans	.0001437	3.3 x 10^{-6}	1.5 x 10^{-4}	3.5 x 10^{-7}	1.5 x 10^{-4}	3.5 x 10^{-7}

[a] Exp = exposure, all exposures are in mg/kg/day

[b] Upper 95% bound on risk

15

Table 6-C LADD Exposure and Associated Risk Without Protective Clothing
($Q_1^* = 2.3 \times 10^{-3}$ when dose is in mg/kg/day)

Crop	Typical LADD No. of Days	Typical LADD Upper 95% Bound on Risk	Low LADD No. of Days	Low LADD Upper 95% Bound on Risk	High LADD No. of Days	High LADD Upper 95% Bound on Risk
Apple: Loader	10	4.5×10^{-6}	4	6.9×10^{-7}	15	1.1×10^{-5}
Sprayer	10	1.9×10^{-7}	4	2.3×10^{-8}	15	3.3×10^{-7}
Strawberries	10	2.3×10^{-8}	4	3.2×10^{-9}	20	2×10^{-7}
Home Gardens	4	1.6×10^{-9}	2	1.6×10^{-10}	6	3.5×10^{-9}
Almonds						
Pilot	2	5.9×10^{-9}	2	5.9×10^{-9}	6	1.8×10^{-8}
Mixer/loader	2	8.8×10^{-7}	2	8.8×10^{-7}	6	2.6×10^{-6}
Apple (Post - Harvest)	42	3.4×10^{-6}	42	1.1×10^{-6}	224	2.4×10^{-5}
Potatoes						
Filler/cutters	5	2×10^{-7}	2	7.8×10^{-8}	15	5.9×10^{-7}
Planters	5	5.7×10^{-8}	2	2.2×10^{-8}	15	1.7×10^{-7}
Soybean	2	1×10^{-7}	2	1×10^{-7}	3	1.5×10^{-7}

Table 6-D LADD Exposure and Assoicated Risk with Protective Clothing
($Q_1^* = 2.3 \times 10^{-3}$ when dose is in mg/kg/day)

Crop	Typical LADD No. of Days	Typical LADD Upper 95% Bound on Risk	Low LADD No. of Days	Low LADD Upper 95% Bound on Risk	High LADD No. of Days	High LADD Upper 95% Bound on Risk
Apple: Loader	10	7.4×10^{-7}	4	1×10^{-7}	15	1.8×10^{-6}
Sprayer	10	1.9×10^{-7}	4	2.2×10^{-8}	15	3.3×10^{-7}
Strawberries	10	3.4×10^{-9}	4	4.3×10^{-10}	20	3.4×10^{-8}
Home Gardens	4	4.6×10^{-10}	2	5.2×10^{-11}	6	1×10^{-9}
Almonds: Pilot	2	5.9×10^{-9}	2	6.1×10^{-9}	6	1.8×10^{-8}
Mixer/loader	2	1.4×10^{-7}	2	1.4×10^{-7}	6	4.2×10^{-7}
Apple (Post - Harvest)	42	3.6×10^{-7}	42	1.2×10^{-7}	224	2.5×10^{-6}
Potatoes:	5	2.7×10^{-8}	2	1.1×10^{-8}	15	8×10^{-8}
Filler/Cutter Planters	5	5.6×10^{-8}	2	2.2×10^{-8}	15	1.7×10^{-7}
Soybeans	2	1×10^{-8}	2	1.1×10^{-10}	3	1.6×10^{-9}

Appendix

Dermal Absorption/Interspecies Conversion Formulas

A. Dermal Absorption

Total Agent Absorbed = A (h, r, a)

$$= r\left[(h+1) - (1/a)\left(1 - (1-a)^{h+1}\right)\right]$$

when r = Arrival rate of agent in grams per hour
h = Total number of hours exposed
a = absorption rate per hour of the amount of agent present

B. Interspecies Conversion for Dietary Exposure

The extrapolation of mouse dosage to "equivalent" human dosage was done as follows:

i Mouse to Human

Human Equiv Dose in mg/kg/day = .15 (mouse dose in ppm) $\times \left(\frac{\text{wt of mouse}}{\text{wt of person}}\right)^{1/3}$

$$= .15 \text{ (mouse dose in ppm)} \times \left(\frac{25}{60000}\right)^{1/3}$$

$$= .011 \text{ (mouse dose in ppm)}$$

ii Rat to Human

Human Equiv Dose in mg/kg/day

$$= .05 \times \text{(rat dose in ppm)} \times \left(\frac{400}{60000}\right)^{1/3}$$

$$= .009 \text{ (rat dose in ppm)}$$

Human Equiv Dose when rat dose is recorded in mg/kg/day

$$= \text{(rat dose in mg/kg/day)} \times \left(\frac{400}{60000}\right)^{1/3}$$

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