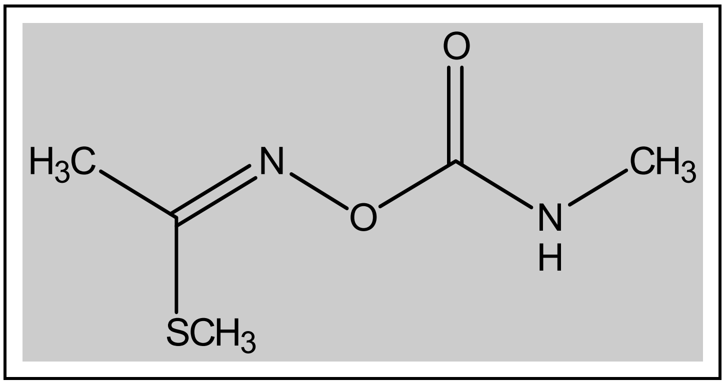
Methomyl
(S-methyl N-((methylcarbamoyl)oxy)thioacetimidate)

RISK CHARACTERIZATION DOCUMENT



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ABBREVIATIONS

AADD	annual average daily dosage
ACh	acetylcholine
AChE	acetylcholinesterase
ACGIH	American Conference of Governmental Industrial Hygienists
AIC	Akaike Information Criterion
aPAD	acute population adjusted dose
ATSDR	Agency for Toxic Substances and Disease Registry
ChE	cholinesterase
ChEI	cholinesterase inhibition
DPR	Department of Pesticide Regulation (California EPA)
EC	effective (air) concentration
ED	effective dose
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FOB	functional observational battery
FQPA	Food Quality Protection Act
gd	gestation day
GSD	geometric standard deviation
HCT	hematocrit
hdt	highest dose tested
HEC	human equivalent (air) concentration
HPLC	high pressure liquid chromatography
LADD	lifetime average daily dosage
LC_{50}	air concentration required to kill 50% of exposed animals by inhalation
LD_{50}	oral dose required to kill 50% of exposed animals
LEC	lower bound on the effective (air) concentration
LED	lower bound on the effective dose
LOEL	lowest observed effect level
ldt	lowest dose tested
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
MTD	maximum tolerated dose
NOEL	no observed effect level
OSHA	Occupational Safety and Health Administration
pnd	post natal day
PEL	permissible exposure limit
PHED	pesticide handlers exposure database
PHI	pre-harvest interval
RBC	red blood cell
RED	Reregistration Eligibility Document (US EPA)
REI	re-entry interval
RfD	reference dose
RfC	reference concentration
SADD	seasonal average daily dosage
SD	Sprague-Dawley
STADD	short-term absorbed daily dosage
TC	toxicity category

TRR	total radioactive residues
TSCA	Toxic Substances Control Act
TWA	time weighted average
USEPA	United States Environmental Protection Agency
WH&S	Worker Health and Safety Branch (DPR, California EPA)

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I. SUMMARY

Methomyl (S-methyl N-((methylcarbamoyl)oxy)thioacetimidate) is an insecticide used in a variety of crops, on turf (sod farms only), in and around livestock facilities, in refuse containers, and as a fly bait. Formulations include water-soluble powders, granules and liquids. As a carbamate, methomyl's action is based on its ability to inhibit acetylcholinesterase (AChE) in the nervous systems of the target species. Its toxicity in mammalian systems is also based on this property, though the involvement of other toxic mechanisms is not ruled out.

Methomyl was first registered in the United States in October 1968. DuPont de Nemours & Co. is the current manufacturer.

<u>Phamacokinetics</u>

Oral studies. An oral gavage dose of 5 mg/kg [1-^{14}C]methomyl in rats resulted in the detection of 53% and 2-3% of the dose in urine and feces, respectively, by 168 hours; 34-36% of the dose was in exhaled air by 120 hours; 8-9% of the dose remained associated with tissues. The predominant tissue recovery sites were red blood cells and skin (1.5-1.9% and 2.4-2.5%, respectively). A significant fraction of radiolabel was determined to be $^{14}CO_2$ and other low molecular weight compounds—these were not only exhaled, but also incorporated into other chemicals through catabolism. Identification of specific metabolites among the myriad radiolabeled compounds recovered in the urine was limited, but included the mercapturic acid derivative of methomyl (17-18%), methomyl oxime sulfate and acetic acid (5.0-5.4%), acetonitrile (6%), acetate (1.4-2.0%) and acetamide (0.2–0.4%).

An oral gavage dose of 5 mg/kg [1-^{14}C]methomyl was administered to four male cynomolgus monkeys. Thirty-nine percent of the dose was recovered in exhaled air by 48 hours, while 32% was recovered in urine (+ cage wash) and 3% in feces by 168 hours. Approximately 5% of the dose remained associated with tissues at that time. A significant proportion of the radiolabel was determined to be $^{14}CO_2$, which was found not only in exhaled air, but also incorporated into other chemicals through catabolism. Identification of specific metabolites among the myriad radiolabeled compounds recovered in the urine was limited, but included the mercapturic acid derivative of methomyl (0.8%), methomyl oxime sulfate (1.5%), acetonitrile (1.7%), acetate (0.4%) and acetamide (0.4%).

Dermal studies. One study of dermal penetration by methomyl was examined. It indicated that about 85% of a dermally-applied dose of 1 mg/kg ^{14}C-methomyl in mice penetrated the skin by 60 minutes. For several reasons, this value was considered excessive by the exposure assessor for this document. A default absorption of 50% was used to calculate dermal exposure in humans.

Inhalation studies. No studies of the pharmacokinetics of inhaled methomyl were available for this report. Rather, a default of 100% inhalation absorption in humans was assumed for this report

Methomyl in milk and tissues of lactating animals. Exposure of lactating cows and goats to oral ^{14}C-methomyl did not result in methomyl residues in milk or tissues.

Hazard identification

The acute toxicity of methomyl results largely from its ability to carbamylate, thus inhibit, acetyl cholinesterase (AChE) at synapses and neuromuscular junctions. Resultant local accumulations of acetylcholine (ACh) generate cholinergic effects. Due to the reversibility of the carbamate-AChE bond, recovery is expected when exposures are low. Other mechanisms of toxicity may also be operative.

Acute oral toxicity. Acute oral LD_{50}s for methomyl technical formulations were between 7 and 34 mg/kg (toxicity category I) for rats. Acute inhalation LC_{50}s were between 0.114 and 0.299 mg/L (toxicity category II). Methomyl did not exhibit systemic dermal toxicity in rabbits, probably because it didn't penetrate the skin. It was only slightly irritating to eyes and skin, though 10 mg of a 90% formulation was severely toxic and 15 mg lethal in rabbits by the ocular route.

The critical oral LED_{10} of **0.03 mg/kg** was based on benchmark dose analysis of dose-dependent red blood cell cholinesterase (RBC ChE) inhibition data in human males following oral exposure to a single encapsulated dose of methomyl. The doses tested were 0, 0.1, 0.2 or 0.3 mg/kg. Two clinical signs were plausibly related to methomyl exposure in the human study: (a) a headache occurring in one high dose (0.3 mg/kg) male at 1 hr 45 min after dosing and lasting about 1 hr, accompanied in the same individual by 47% inhibition of RBC cholinesterase activity at 45 min post dose; and (b) increased saliva production at 1 hr post dose (statistically significant at the high dose).

Inhibition of RBC ChE—which, like the brain enzyme, is an *acetyl*cholinesterase—is not unambiguously associated with toxicity in mammals. However, recent studies in rats show a close correspondence between RBC ChE inhibition, brain ChE inhibition and cholinergic effects for several carbamate pesticides including methomyl. Moreover, brain AChE-based LOEL values from the various rat acute studies examined for this document were similar to the doses used in the human study (0.1 - 0.3 mg/kg).

Subchronic oral toxicity. Risks from subchronic (seasonal) oral exposure to methomyl were estimated using the critical NOEL of 9.4 mg/kg/day (rounded to **9 mg/kg/day**) established in a 91-day rat dietary toxicity study. This value, calculated by the study authors from a dietary NOEL of 150 ppm, was based on reduced body weight and food consumption, tremors during the 1st four weeks and beyond, FOB signs and brain ChE inhibition at the LOEL of 1500 ppm. The enzyme inhibition and signs (clinical and FOB) were likely mechanistically related and mutually supported the establishment of 9 mg/kg/day as the critical subchronic NOEL.

Chronic oral toxicity. Risks from chronic oral exposure to methomyl were estimated using the critical NOEL of **3 mg/kg/day** established in a 2-year beagle dog dietary toxicity study. This was estimated by the author from a dietary NOEL concentration of 100 ppm. It was based on pigmentation irregularity and swelling of kidney proximal tubule cells, and pigmentation and extramedullary hematopoiesis in the spleen at the LOEL dose of 400 ppm (11 - 14 mg/kg/day).

Acute, subchronic and chronic dermal toxicity. Risks from acute, subchronic and chronic dermal exposure to methomyl were estimated using the dermal critical NOEL of **90 mg/kg/day** established in a 21-day rabbit repeat-dose dermal toxicity study. 90 mg/kg/day was the high dose employed in that study—there was no LOEL dose.

Acute inhalation toxicity. Risks from acute inhalation exposure to methomyl were estimated using a human-equivalent critical acute inhalation LEC_{10} of 0.16 mg/kg. This was established by benchmark dose modeling of brain cholinesterase inhibition data from an acute inhalation study in rats.

Subchronic inhalation toxicity. In the absence of a subchronic inhalation toxicity study, the seasonal risk from methomyl exposure was assessed using the critical subchronic oral toxicity value of **9 mg/kg/day** established in rats.

Chronic inhalation toxicity. In the absence of a chronic inhalation toxicity study, the annual risk from methomyl exposure was assessed using the critical chronic oral toxicity value of **3 mg/kg/day** established in beagle dogs.

Reproductive toxicity. Primary reproductive impacts were not indicated in the one FIFRA-compliant reproductive toxicity study available for review. For this reason, a critical reproductive NOEL was not identified in this assessment. However, several subchronic oral gavage studies in male rats indicated methomyl-induced reproductive system toxicity.

Developmental toxicity. FIFRA-compliant developmental toxicity studies in rats and rabbits did not indicate that methomyl had developmental impacts.

Genotoxicity. Two of four gene mutation studies, including a sex-linked lethality test in *Drosophila* and HGPRT forward mutation assay in Chinese hamster V79 cells were positive for gene mutation. In addition, seven of ten chromosome abnormality studies, including several *in vivo* and *in vitro* micronucleus studies, were positive, as were four of seven DNA damage studies. Based on these results, methomyl is considered to have genotoxic potential.

Oncogenicity. Oncogenicity was not observed in FIFRA-compliant chronic studies conducted in dogs, rats or mice. For this reason, a quantitative tumor analysis was not carried out for this evaluation.

Risk calculations

The potential for non-oncogenic health effects resulting from exposure to methomyl was expressed as the Margin of Exposure (MOE) ratio, which is the critical NOEL or LED divided by the estimated exposure. A MOE of >10 is generally considered to be protective of human adult health when the relevant adverse effects were observed in adult humans under controlled conditions. A MOE of >100 is considered to be protective of human adult health when the relevant adverse effects were observed in animal studies. An additional uncertainty factor of 4, based on the ~4-fold greater sensitivity of the newborn rat brain cholinesterase to inhibition by methomyl compared to the adult brain enzyme, was included when assessing acute risks to children. The product of uncertainty factors for any population / exposure scenario is the “target MOE”. Actual MOEs below the target MOE indicated that the scenario posed a potential risk to human populations.

Non-dietary exposure estimation. The exposure estimates for methomyl from non-dietary sources were developed in an accompanying DPR document. Assumptions regarding application rates, acres treated/day, dermal and inhalation absorption, and default body weight are detailed in that document. The estimates were derived from four sources: (1) surrogate data in the Pesticide Handlers Exposure Database (PHED), which predicts both dermal and inhalation exposure to handlers, (2) reentry scenarios involving dermal exposure to fieldworkers through contact with dislodgeable foliar residues, (3) air monitoring studies designed to estimate bystander exposures by the inhalation route, and (4) residue studies on food items. MOEs are summarized in Summary Table 1 and described as follows:

Occupational handler risks. Acute inhalation MOEs at or below the target MOE of 100 were noted for all handler categories (though some specific tasks within categories were above 100). There was only one acute dermal exposure category registering a MOE less than the target of 100 (pilots, 52). There were no annual exposure scenarios, either by the dermal or inhalation routes, with MOEs of less than 100.

Risks to landscape workers during turf re-entry tasks. Risks to landscape workers posed by dermal exposure to methomyl during turf re-entry tasks did not produce MOEs less than 1737 for acute, seasonal or annual scenarios.

Occupational re-entry risks. Evaluation of risk in these cases assumed exposure only by the dermal route. There was no MOE below 292 (target MOE = 100), which was recorded for acute exposure occurring during hand harvesting of sweet corn.

Risks incurred upon re-entry in "U-Pick" operations (non-occupational). Of the four "U-Pick" operations examined (sweet corn, blueberries, nectarines and peaches), sweet corn was found to generate the highest potential acute exposures (dermal, in this case). Because of this, U-Pick operations in sweet corn also posed the highest calculated risk. Seasonal and annual exposures were not considered likely. The MOE for adults was 600 for this acute scenario (target MOE = 100), while for children it was 1306 (target MOE = 400).

Risk to bystanders from exposure near application sites. Bystanders at application sites may be exposed to methomyl by the inhalation route. Using the calculated absorbed doses and the critical inhalation NOEL of 0.16 mg/kg/day, bystander acute infant MOEs, 1- and 24-hr, were 213 and 139 (target MOE = 400), while adult bystander MOEs were 1231 and 291 (target MOE = 100). Worker bystander MOEs, 1-hr and 8-hr, were 1143 and 552 (target MOE = 100). Seasonal or annual exposure scenarios were not expected.

Dietary exposure and risk. Using a probablistic distributional approach at the 99.9th percentile of exposure, the food-plus-water dietary risk for children aged 1-2 years and 3-5 years exceeded the threshold of concern, registering 159% and 160% of the acute population adjusted dose (MOEs of 25 in both cases; target MOE = 40). Inclusion of grapes resulted in even higher percent acute population adjusted doses (note: grape uses were canceled in 2010 with the exception of some uses which will remain until December 2016).

MOEs calculated for tolerances on the following commodities were below the target MOEs, which indicated a potential health concern: apple, avocado, broccoli, cantaloupe, grape, lettuce, nectarine, orange, peach, peanut, spinach, watermelon, and wheat. USEPA.should be informed of this finding. (Note: Acute exposure was calculated on a "per-user-day" basis, which includes in the distribution of exposures only those consumers who eat at least one of the assessed commodities in the consumption survey utilized by DEEM. Thus the per-user-day assumption restricts the analysis to those who actually consume the commodities in question. In contrast, USEPA calculates acute exposure on a per capita consumption basis, which factors in all members of a particular sub-population regardless of their commodity consumption.)

The results indicate that chronic dietary risk for food plus drinking water is below the threshold of concern for the general U.S. population and all population subgroups. The most highly exposed population subgroups, children 1-2 years and children 3-5 years, utilized 0.2% of the chronic population adjusted dose.

Reference doses (RfDs) and reference concentrations (RfCs). RfDs and RfCs appear in Summary Table 2. They represent methomyl dose levels or air concentration levels below which human health impacts are unlikely according to the current toxicity database. They were obtained by dividing the critical LEDs, LECs or NOELs by uncertainty factors that reflected gaps in understanding of specific toxicity issues and/or the natural variability in human populations.

Conclusion. Several handler scenarios, in addition to infant resident bystanders (1- and 24-hr) exhibited acute inhalation MOEs that were less than the relevant target MOEs. This was also the case for one handler acute dermal MOE (pilots for aerial applications). Mitigation measures should be considered for these scenarios, as they present potential health risks to the involved populations. None of the seasonal or annual scenarios evaluated for this document exhibited sub-target MOEs.

Summary Table 1. Target MOEs, actual MOEs and exposure / population scenarios exhibiting MOEs lower than the target MOE; dermal and inhalation exposure to methomyl

Exposure scenario	Target MOE	MOE range	Scenarios *below* target MOE (actual MOE)	Target MOE	MOE range	Scenarios *below* target MOE (actual MOE)
	Dermal			**Inhalation**		
Handlers **Aerial applications**						
▪ acute	100	52-2647	pilot (52)	100	5-533	M/L water sol. powder (10), M/L liquid (24), pilot (5)
▪ annual	100	145-7377	none	100	256-30,000	none
Airblast applications						
▪ acute	100	243-6383	none	100	18-800	Applicator (18)
▪ annual	100	677-17,647	none	100	909-30,000	none
Groundboom applications						
▪ acute	100	894-1277	none	100	15-145	M/L water sol. powder (59), applicator (15)
▪ annual	100	2479-3557	none	100	789-7500	none
Chemigation						
▪ acute	100	696-730	none	100	34-80	M/L water sol. powder (34), M/L liquid (80)
▪ annual	100	1944-2032	none	100	1765-4286	none

Hand spreader—bait w/gloves						
■ acute	100	165	none	100	40	Hand spreader—bait w/gloves (40)
■ annual	100	459	none	100	2143	none
Sod transplantation						
■ acute	100	1737	none			
■ seasonal	100	56,250	none			
■ annual	100	56,250	none			
<u>Occupational reentry</u> [a]						
■ acute	100	292-391,304	none			
■ seasonal	100	9358-12,676,056	none			
■ annual	100	18,716-12,676,056	none			
<u>"U-pick" reentry</u> [b]						
■ acute	400 (child) 100 (adult)	1306-4945 (child) 600-2273 (adult)	none none			
<u>Resident bystander</u>						
■ acute				400 (child) 100 (adult)	139-213 291-1231	Infant resident—1-hr (213) Infant resident—24-hr (139) none

Dietary	**Acute** [c]			**Chronic** [c]		
■ General US popln.	10	23	above target	100	100,000	above target
■ All infants <1 yr	40	53	above target	100	115,385	above target
■ Children 1-2 yr	40	25	*below target*	100	47,619	above target
■ Children 3-5 yr	40	25	*below target*	100	51,724	above target
■ Children 6-12 yr	40	43	above target	100	76,923	above target
■ Youth 13-19 yr	10	41	above target	100	120,000	above target
■ Adults 20-49 yr	10	20	above target	100	115,385	above target
■ Adults 50+ yr	10	18	above target	100	115,385	above target
■ Females 13-49 yr	10	21	above target	100	120,000	above target

Abbreviations: M/L, mixer / loader

[a] Twenty-one separate scenarios were evaluated for occupational reentry operations.
[b] Four separate scenarios were evaluated for U-pick reentry operations.
[c] For acute: food + water, except grapes; for chronic: food + water.

Summary Table 2. Uncertainty factors, reference doses and reference concentrations for methomyl by the oral, dermal and inhalation routes

	Interspecies factor	Intrahuman factor	Child protective factor	Total uncertainty factor (or target MOE)	NOEL or LED	RfD or RfC
Oral						RfD
acute, infant	1	10	4 [b]	40	0.03 mg/kg	0.75 µg/kg
acute, adult	1	10	1	10	0.03 mg/kg	3 µg/kg
subchronic [a]					n/a	n/a
chronic [a]					n/a	n/a
Dermal						RfD
acute, infant	10	10	4 [b]	400	90 mg/kg	0.2 mg/kg
acute, adult	10	10	1	100	90 mg/kg	0.9 mg/kg
subchronic	10	10	1	100	90 mg/kg/day	0.9 mg/kg/day
chronic	10	10	1	100	90 mg/kg/day	0.9 mg/kg/day
Inhalation						RfC
acute, infant	10	10	4 [b]	400	3.92 mg/m^3	9.7 µg/m^3
acute, adult	10	10	1	100	3.92 mg/m^3	39 µg/m^3
subchronic [a]					n/a	n/a
chronic [a]					n/a	n/a

[a] Calculation of RfDs and RfCs for subchronic and chronic exposures was obviated by the fact that the respective NOELs and LEC_{10}s were higher than the corresponding acute values (see text).

[b] For an explanation of the child protective factor, see main text.

II. INTRODUCTION

Methomyl (S-methyl N-((methylcarbamoyl)oxy)thioacetimidate) is a broad spectrum insecticide used in fruits, cotton, soybeans, vegetables and other field crops, on turf (sod farms only), in and around livestock facilities, in refuse containers, and as a fly bait. It is also used as a molluscicide and acaricide. There are no residential uses. Formulations include water-soluble powders, granules and liquids. Methomyl is also an intermediate of thiodicarb metabolism.

As a member of the carbamate class of pesticides, the pesticidal action of methomyl is based on its ability to inhibit acetylcholinesterase (AChE) in the nervous systems of the target species. Because insects do not have peripheral cholinergic synapses, the insecticidal action of methomyl is presumably based on cholinesterase inhibition in the central nervous system. Methomyl's toxicity in mammalian systems is also largely based on this property. However, methomyl inhibits other cholinesterases (ChEs), including the plasma-localized butyryl ChE and the red blood cell-localized AChE, which may result in toxicity. Finally, studies with organophosphate pesticides (eg., see Stotkin, 2006a and 2006b) suggest the possibility that cholinesterase-independent neurodevelopmental endpoints may be impacted by methomyl, though this must be considered speculative at this point.

Prioritization. Upon registration in California, DPR designates a priority status—high, moderate or low---for risk assessment. The priority status is based on such factors as pesticide toxicity category; nature of adverse effects; number of adverse effects; number of species affected; NOELs, LOELs and benchmark dose values; potential for human exposure; use patterns; quantity used; and USEPA evaluations and actions. Methomyl was given a high priority status for risk assessment based on the following observations (adapted and updated from http://www.cdpr.ca.gov/docs/risk/request_cmnt.pdf:)

- ♦ widespread agricultural use, primarily in lettuce, corn, onions, alfalfa, tomatoes and as a fly-bait formulation for commercial establishments

- ♦ low points of departure, particularly with respect to acute reductions in cholinesterase activity (single oral dose LED_{10}, human males: 0.03 mg/kg for decreased RBC ChE activity; oral gavage NOEL, rats: 0.25 mg/kg for decreased brain ChE activity; oral gavage LED_{10}, rat pups: 0.1 mg/kg for decreased brain ChE activity; inhalation LED_{10}, rats: 0.16 mg/kg for decreased brain ChE activity) and hematologic effects

- ♦ steepness of its acute dose-response curve (NOELs for acute oral effects are reasonably close to the LD_{50} values, which range between 7 and 34 mg/kg in rats and designate methomyl as a Toxicity Category I chemical)

- ♦ high frequencies of detections of illegal methomyl residues by DPR's Pesticide Residue Monitoring Program, which analyzes fresh produce for pesticide residues. Between 2004 and 2013, illegal resides of methomyl (exceeding the tolerance, or on foods with no established tolerances for) were found on 16 samples originating in California, Mexico and Hawaii

Background details on methomyl—including its regulatory history, technical and product formulations, California use statistics and illness reports, physico-chemical and environmental properties, and environmental fate—are discussed in the accompanying exposure assessment document (DPR, 2014) and in DPR's environmental fate document on methomyl (Van Scoy *et al.*, 2013). The following report summarizes the salient features of methomyl's toxicity, establishes the critical endpoints for risk assessment, evaluates the extent of human health risk based both on those endpoints and on the exposure estimates provided in DPR (2014), and details the inherent uncertainties in the assessment.

III. TOXICITY PROFILE

A. PHARMACOKINETICS

1. Oral route

Hawkins *et al.* (1991) investigated the metabolism of [1-^{14}C]methomyl after oral gavage dosing of 5 rats/sex at 5 mg/kg. Urine and feces were collected up to 168 hours post dose. Expired air was recovered for periods of up to 120 hours. Approximately 53% and 2-3% of the dose was detected in the urine and feces, respectively, by 168 hours; 34-36% was in exhaled air by 120 hours; 8-9% of the dose remained associated with tissues. The predominant tissue sites of recovery were red blood cells and skin (1.5-1.9% and 2.4-2.5%, respectively). A significant fraction of radiolabel was determined to be $^{14}CO_2$ and other low molecular weight compounds—these were not only exhaled, but also incorporated into other chemicals through catabolism. This was evident in the high percentage of the dose that was recovered in tissue after 168 hours and the relatively equal distribution of the radiolabel throughout the body (excluding the high levels in RBCs and skin). Identification of specific metabolites among the myriad radiolabeled compounds recovered in the urine was limited, but included the mercapturic acid derivative of methomyl (17-18%), methomyl oxime sulfate and acetic acid (5.0-5.4%), acetonitrile (6%), acetate (1.4-2.0%) and acetamide (0.2–0.4%). The metabolic pathway for methomyl in rats is outlined below in Figure 1.

This non-guideline study was considered to be supplemental.

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Hawkins *et al.* (1992) investigated the metabolism of [1-^{14}C]methomyl in four male cynomolgus monkeys after oral gavage at 5 mg/kg. Urine and feces were collected for up to 168 hours, while exhaled air was collected for up to 48 hours. 39% of the dose was recovered in exhaled air, while 32% was recovered in urine (+ cage wash) and 3% in feces. At 168 hours, ~5% of the dose remained associated with tissues. Only 79% of the dose was ultimately recovered. The reasons for this were twofold: (1) excretion via exhalation persisted beyond 48 hours, the last time this medium was analyzed; and (2) carcasses were not analyzed. A significant proportion of the radiolabel was determined to be $^{14}CO_2$, which was found not only in exhaled air, but also incorporated into other chemicals through catabolism. This was evident in the high percentage of the administered dose recovered in the tissue after 168 hours and the relatively equal distribution of the radiolabel throughout the body. Identification of specific metabolites among the myriad radiolabeled compounds recovered in the urine was limited. Tentatively identified compounds included the mercapturic acid derivative of methomyl (0.8%), methomyl oxime sulfate (1.5%), acetonitrile (1.7%), acetate (0.4%) and acetamide (0.4%). The metabolic pathway for methomyl in monkeys is outlined below in Figure 2.

This non-guideline study was considered to be supplemental.

2. Dermal route

In a report summarized in detail in the accompanying exposure assessment document (DPR, 2014), Shah *et al.* (1981) examined the dermal penetration and distribution of 14 insecticides, including ^{14}C-methomyl. Applications of 1 mg/kg were made to a 1-cm^2 shaved area of skin on the upper back of female mice followed by radioactivity measurements at timed intervals up to 48 hr in excreta and body compartments. ^{14}C from methomyl was detected within 5 minutes in blood and liver. By 60 minutes there was little compound remaining at the application site, when penetration was estimated at 85% (penetration $t_{1/2} \approx 13$ min). At 60 min, 3% of the dose appeared in blood, 5% in liver, 13% in urine / feces / CO_2 and 56% in carcass. At 8 hr, 6% of the dose appeared in blood, 3% in liver, 4% in gastrointestinal tract, 56% in urine / feces / CO_2 and 15% in carcass. The authors estimated the 8-hr dermal penetration for all of the compounds to be about 65% (*i.e.*, lower than was measured for methomyl itself), which for reasons detailed on pages 16 and 17 of DPR (2014) was considered to be excessive. As a result, a default penetration of 50% was used to estimate dermal exposure to methomyl.

3. Methomyl disposition in lactating animals

The World Health Organization reviewed studies in which a lactating cow and a lactating goat were exposed to encapsulated ^{14}C-methomyl over a 28 (cow) or 10 (goat) day period (WHO, 1996). Neither methomyl nor its metabolite MHTA (1-methyl-N-hydroxythioacetimidate) was detected in milk or in tissues

Figure 1. Methomyl metabolism in rats (from Hawkins *et al*., 1991)

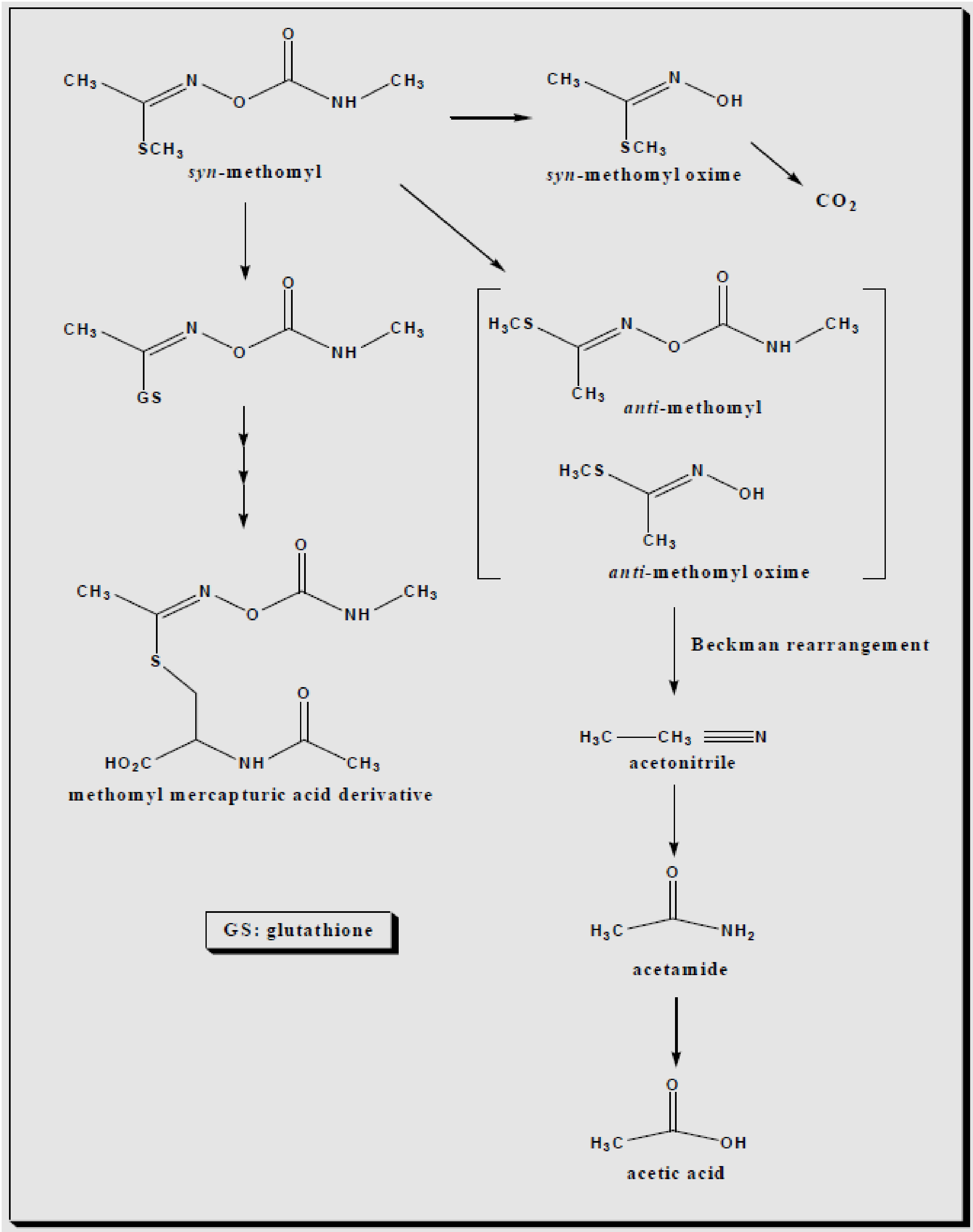
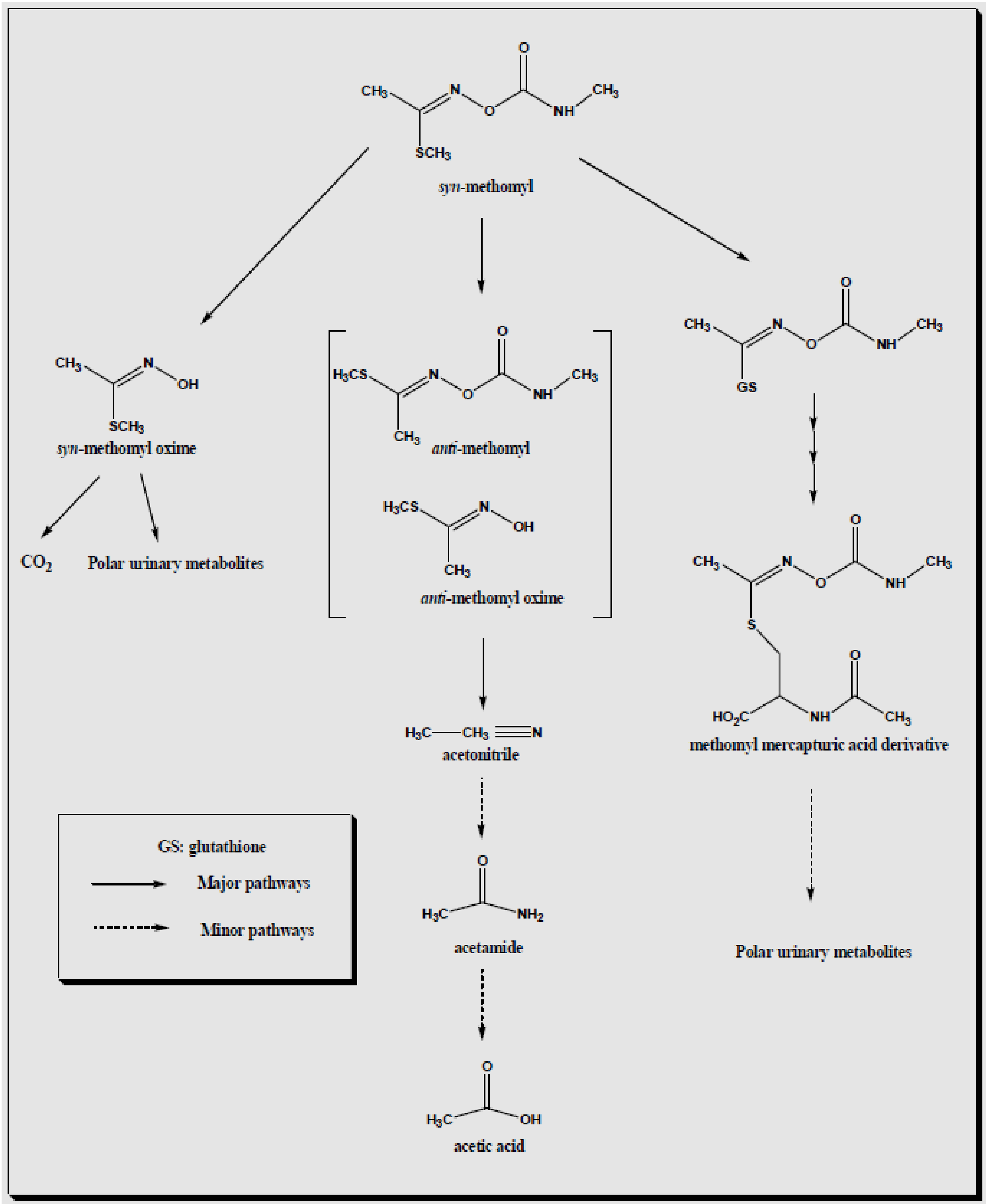


Figure 2. Methomyl metabolism in cynomolgus monkeys (from Hawkins *et al*., 1992)



B. ACUTE TOXICITY (including ACUTE NEUROTOXICITY)

1. Human studies

Lannate SP (89% methomyl) was administered by capsule to 19 human male volunteers (mean age 26 yr; all non-smokers or previous smokers) at doses of 0 (placebo control), 0.1, 0.2 or 0.3 mg/kg (McFarlane *et al.*, 1998) [1]. There were 5 subjects in each dose group and 4 subjects in the placebo group. Each individual was observed for two days, with a follow-up at 7±2 days. There were no treatment-related effects on pulse, electrocardiogram, blood pressure, respiratory rate, body temperature, hematology parameters, clinical chemistry parameters (excluding cholinesterase activities), urinalysis or pupillometry. Of the observed clinical signs, only two were plausibly related to methomyl exposure: (*a*) a headache occurring in one 0.3 mg/kg male at 1 hr 45 min after dosing and lasting about 1 hr (this individual also showed 47% inhibition of RBC cholinesterase activity at 45 min post dose); and (*b*) an increase in saliva production at 1 hr post dose (statistically significant at the high dose).

Both plasma and RBC cholinesterase (ChE) activities were inhibited by methomyl (Table III-1). Statistically significant inhibition of plasma ChE was evident at 0.3 mg/kg by the first measurement at 15 minutes post dose (9.76%, $p \leq 0.05$), reaching a maximum at 1 hr 15 min (19.67%, $p \leq 0.01$), and returning to baseline by 6 hr. Statistically significant inhibition of plasma ChE was also evident at 0.2 mg/kg, with maximal inhibition occurring between 1 hr 15 min and 1 hr 45 min (13.52%, $p \leq 0.01$), returning to baseline by 3-6 hr.

Statistically significant inhibition of RBC cholinesterase was evident at 0.3 mg/kg by the first measurement at 15 minutes post dose (18.57%, $p \leq 0.05$), reaching a maximum at 30-45 min post dose (35.25%, $p \leq 0.01$), and returning to baseline by 6 hr. Statistically significant inhibition of RBC cholinesterase was also evident at 0.2 mg/kg, with maximal inhibition occurring between 1 hr 15 min and 1 hr 30 min (27.87%, $p \leq 0.01$), returning to baseline by 3 hr. Further examination of the RBC data showed plausible, though not statistically significant, mean inhibition at 0.1 mg/kg at 1 hr (14.61%), 1 hr 15 min (19.04%) and 1 hr 30 min (10.60%). These times coincided with the peak effects seen at 0.2 and 0.3 mg/kg. Because of the apparent inhibition at 0.1 mg/kg, assignment of a LOEL or NOEL was not undertaken. However, the complete RBC cholinesterase data set was subjected to exhaustive benchmark dose-response modeling by the USEPA's National Center for Computational Toxicology , resulting in an LED_{10} (ED_{10}) of 0.03 (0.04) mg/kg (Setzer, 2006a).

Because this was not a FIFRA guideline study, it was considered to be supplemental.

Table III-1 Plasma and RBC cholinesterase activities in human males after dosing with

[1] This study was conducted in a double-blind manner. According to the study report, it "was conducted in accordance with the Declaration of Helsinki, 1964, as amended by the 29th Medical World Assembly in Venice, 1983, 41st Medical World Assembly in Hong Kong, 1989 and the 48th General Assembly, Somerset West, Republic of South Africa, October 1996." A "Good Clinical Practice Compliance Statement" was included in the study report, as well as approval of the study protocol from an Independent Inveresk Research Ethics Committee. This committee reviewed the consent form and volunteer information, letter / questionnaire to the GP, clinical protocol, investigator's brochure and toxicology review. Finally, according to a memorandum accompanying USEPA's Data Evaluation Record for this study and a parallel study on oxamyl, "both of these human studies were presented to the Human Studies Review Board (HSRB) in April 2006. The HSRB concluded that both human studies were ethically and scientifically reliable for use in risk assessment." (memo: USEPA, 2006).

methomyl (McFarlane *et al.* 1998)

	0 mg/kg, n=4	0.1 mg/kg, n=5	0.2 mg/kg, n=5	0.3 mg/kg, n=5
Plasma cholinesterase (% change from baseline [a])				
15 min post dose	-1.31 ± 5.0	-3.07 ± 3.6	-2.46 ± 2.8	-9.76 ± 2.0*
30 min	-2.87 ± 4.8	-6.64 ± 3.9	-7.87 ± 3.7	-15.85 ± 2.2**
45 min	-1.40 ± 3.8	-5.63 ± 2.1	-11.48 ± 5.5*	-21.08 ± 4.9**
1 hr	-0.31 ± 3.0	-4.52 ± 3.4	-11.03 ± 4.2*	-16.59 ± 2.2**
1 hr 15 min	-0.79 ± 4.7	-2.95 ± 5.7	-13.32 ± 5.1**	-19.67 ± 2.9**
1 hr 30 min	-2.42 ± 5.7	-5.91 ± 3.9	-12.90 ± 2.5*	-14.84 ± 4.2**
1 hr 45 min	-2.67 ± 4.8	-5.57 ± 1.8	-13.52 ± 2.0*	-15.89 ± 3.8**
2 hr	-0.99 ± 3.8	-7.22 ± 3.6	-10.34 ± 3.3*	-14.12 ± 5.6**
3 hr	-1.29 ± 4.8	-1.07 ± 4.7	-5.04 ± 4.6	-10.87 ± 3.0*
4 hr	0.02 ± 7.3	-2.51 ± 2.1	-1.26 ± 3.2	-8.11 ± 3.8*
6 hr	0.56 ± 6.4	-0.18 ± 3.8	2.06 ± 5.0	0.24 ±.3.1
8 hr	0.39 ± 8.4	-0.47 ± 3.8	0.58 ± 4.1	-0.91 ± 2.4
12 hr	-3.04 ± 8.5	0.81 ± 3.9	-0.69 ± 1.7	8.38 ± 17.2
24 hr	1.25 ± 8.2	2.26 ± 4.0	0.45 ± 5.3	3.36 ± 7.8
RBC cholinesterase (% change from baseline [a])				
15 min post dose	5.83 ± 9.8	3.15 ± 17.5	-1.19 ± 9.3	-18.57 ± 12.4*
30 min	-1.78 ± 5.6	-9.20 ± 13.0	-12.42 ± 5.6	-31.96 ± 3.6**
45 min	-2.93 ± 14.9	-2.45 ± 12.1	-19.98 ± 14.1*	-35.25 ± 10.4**
1 hr	-3.98 ± 17.3	-14.61 ± 11.6	-24.71 ± 9.4*	-27.28 ± 7.5*
1 hr 15 min	-4.26 ± 5.8	-19.04 ± 9.3	-27.59 ± 10.7*	-26.79 ± 7.3*
1 hr 30 min	-0.30 ± 5.6	-10.60 ± 10.6	-27.87 ± 7.4**	-23.20 ± 7.4*
1 hr 45 min	1.82 ± 5.9	3.67 ± 11.5	-22.19 ± 4.9*	-22.41 ± 10.7*
2 hr	5.84 ± 14.0	-8.91 ± 11.2	-16.20 ± 5.6*	-16.02 ± 8.7*
3 hr	12.06 ± 12.7	-2.13 ± 12.5	-1.34 ± 7.4	-12.90 ± 16.5*
4 hr	11.35 ± 10.1	4.97 ± 12.3	-2.28 ± 8.8	-5.05 ± 8.5*
6 hr	6.22 ± 12.8	-5.89 ± 16.3	14.75 ± 6.4	-1.99 ± 6.7
8 hr	-4.35 ± 14.8	-8.73 ± 25.1	9.02 ± 5.6	-0.47 ± 4.8

12 hr	-5.66 ± 16.8	-15.33 ± 17.0	14.42 ± 8.5	-5.57 ± 11.7
24 hr	-4.91 ± 15.9	-3.74 ± 20.0	9.97 ± 10.8	-1.43 ± 5.9

*,**: p<0.05, 0.001 compared with controls, respectively (with outliers)
[a] "Baseline is defined as the mean of two predose values (16h and 30 min pre-dose) for each individual of the dose group. If one of the pre-dose values was missing for an individual, baseline was taken as the non-missing assessment. The mean baseline for the group was used to determine the % change from baseline." (quoted directly from the USEPA Data Evaluation Report for this study)

2. Laboratory animal studies

a. LD_{50}, LC_{50} and primary eye and skin irritation studies

Formulations of methomyl that contain either 98% (the technical grade) or 90-92% active ingredient show high acute toxicity by the oral or inhalation routes and slight acute toxicity by the dermal route (Table III-2). Symptoms of toxicity after oral dosing included salivation, tremors, and convulsions, with death occurring within one day of dosing. Animals exposed by inhalation showed salivation, diarrhea, abnormal gait, tremors, muscle fasciculations, hyperactivity, hyperreactivity, and abnormal posture. Rapid breathing and slight loss of body weight were observed after dermal exposure. These formulations showed no or slight dermal irritation. Ocular exposure to 15 mg of a 90% formulation caused systemic toxicity and death in rabbits. There was no mortality when the dose was reduced to 10 mg, but the animals exhibited severe systemic toxicity and mild eye irritation including transient corneal opacity.

Formulations that contain 29% methomyl caused moderate-to-high acute toxicity after oral exposure and slight-to-moderate toxicity after inhalation exposure. No toxicity was observed in an acute dermal limit test. Slight dermal irritation was observed. Application to the eye caused low grade but persistent corneal opacity and clinical signs consistent with cholinesterase inhibition.

A fly bait formulation containing 1% methomyl showed slight acute toxicity after oral exposure. Exposure by inhalation to the maximum generatable air concentration (1.75 mg/L) resulted in no toxic signs. No toxicity was observed in an acute dermal limit test. Slight dermal and eye irritation were observed.

Table III-2. Acute toxicity of methomyl-containing formulations

Study type, species	Gender	Results, g or mg formulation (Toxicity Category)	References
TGAI (98%)			
Acute Oral			
Rat	M	LD_{50} = 34 mg/kg (TC I)	Sarver, 1991a*
Rat	F	LD_{50} = 30 mg/kg (TC I)	Sarver, 1991a*
Acute Dermal			
Rabbit	M	LD_{50} > 2 g/kg (TC III)	Sarver, 1991b*
Rabbit	F	LD_{50} > 2 g/kg (TC III)	Sarver, 1991b*
Acute Inhalation			
Rat	M	LC_{50} = 0.273 mg/L (TC II)	Panepinto, 1991*
Rat	F	LC_{50} = 0.243 mg/L (TC II)	Panepinto, 1991*
Eye Irritation		no studies available	
Dermal Irritation			
Rabbit	-	no irritation (TC IV)	Sarver, 1991d
Rabbit	-	no irritation (TC IV)	Sarver, 1993a*
90-92% formulations			
Acute Oral			
Rat	M	LD_{50} = 14.2 mg/kg (TC I)	Kuhn, 1996a*
Rat	F	LD_{50} = 7.14 mg/kg (TC I)	Kuhn, 1996a*
Acute Dermal			
Rat	M	LD_{50} > 5 g/kg (TC III)	Kuhn, 1996b*
Rat	F	LD_{50} > 5 g/kg (TC III)	Kuhn, 1996b*
Acute Inhalation			
Rat	M	LC_{50} > 0.114 < 0.299 mg/L (TC II)	Bennick, 1996*
Rat	F	LC_{50} > 0.114 < 0.299 mg/L (TC II)	Bennick, 1996*
Eye Irritation			
Rabbit	-	corneal opacity (TC III)	Kuhn, 1996c*
Rabbit	-	slight irritation, systemic toxicity (not determined)	Sarver, 1991c
Dermal Irritation			
Rabbit	-	slight irritation (TC IV)	Kuhn, 1996d*
Rabbit	-	no irritation (TC IV)	Sarver, 1993b*
29% formulation			
Acute Oral			
Rat	F	LD_{50} = 0.103 g/kg (TC II)	Durando, 2007a*
Rat	M	LD_{50} = 88.7 mg/kg (TC II)	Sarver, 1996*
Rat	F	LD_{50} = 48.9 mg/kg (TC I)	Sarver, 1996*
Acute Dermal			
Rat	M	LD_{50} > 2 g/kg (TC III)	Durando, 2007b*
Rat	F	LD_{50} > 2 g/kg (III)	Durando, 2007b*
Acute Inhalation			
Rat	M	LC_{50} > 0.053, < 0.35 mg/L (TC II)	Durando, 2007c*
Rat	F	LC_{50} > 0.053, < 0.35 mg/L (TC II)	Durando, 2007c*
Rat	M/F	LC_{50} = 1.1 mg/l (TC III)	O'Neill, 1997*

Eye Irritation Rabbit	-	corneal opacity (TC I)	Durando, 2007d*
Rabbit	-	corneal opacity, systemic toxicity (TC I)	Finlay, 1997a*
Dermal Irritation Rabbit	-	slight irritation (TC IV)	Durando, 2007e*
1% formulation (fly bait)			
Acute Oral Rat	M	LD_{50} = 2.455 g/kg (TC III)	Robbins, 1987a*
Rat	F	LD_{50} = 3.236 g/kg (TC III)	Robbins, 1987a*
Acute Dermal Rat	M	LD_{50} > 2 g/kg (TC III)	Robbins, 1987b*
Rat	F	LD_{50} > 2 g/kg (TC III)	Robbins, 1987b*
Acute Inhalation Rat	M	LC_{50} > 1.75 mg/L (TC III)	Robbins, 1987c*
Rat	F	LC_{50} > 1.75 mg/L (TC III)	Robbins, 1987c*
Eye Irritation Rabbit	-	slight irritation (TC IV)	Robbins, 1987d*
Dermal Irritation Rabbit	-	slight irritation (TC IV)	Robbins, 1987e*

Abbreviation: TC, toxicity category
* Acceptable by FIFRA guidelines.

b. Full acute toxicity studies

i. Oral exposure

Malley (1997) treated SD rats with 0 (vehicle: ionized water) or 3 mg/kg of methomyl (purity 98.6%), or with 0 or 1 mg/kg of oxamyl (purity 98.6%) by oral gavage. Ten animals/sex/time point were sacrificed at 0.5, 2, 3 and 4 hours for measurements of plasma, RBC and brain ChE activities.

For methomyl, RBC ChE was reduced to 44 and 59% of controls at 0.5 hours in males and females, respectively. Return to control levels required 3 hours in males and 2 hours in females. Brain ChE was reduced to 54% (♂) and 61% (♀) of controls at 0.5 hours. Return to control levels required 3-4 hours in males and 2-4 hours in females. Plasma ChE was reduced to 73 (♂) and 90% (♀) of controls at 0.5 hours in males and females, respectively. Return to control level was difficult to determine in view of the low level of peak inhibition.

For oxamyl, RBC ChE was reduced to 42 and 39% of controls at 0.5 hours in males and females, respectively. Return to control levels required about 2 hours in both sexes. Brain ChE was reduced to 55 (♂) and 52% (♀) of controls at 0.5 hours, requiring 2-3 (♂) or 2-4 (♀) hours to return to control levels. Plasma ChE was reduced to 43 (♂) and 50% (♀) of controls at 0.5 hours. Return to control levels required 2 hours in males and 3 hours in females.

Neither a LOEL nor a NOEL were determined in this study, which was considered to be supplemental and preliminary.

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Mikles (1998a) examined the neurotoxic effects of a single oral gavage dose of methomyl (98.6%) in young adult SD rats. Fifty-two/sex/group were treated with 0, 0.25, 0.5, 0.75 or 2 mg/kg. Functional observational batteries (FOB) and motor activity assessments were conducted on 12/sex/group on the dosing day (*i.e.*, day 1, both prior to and 30 minutes after dosing), and on study days 8 and 15. Six/sex/group from this cohort were also examined for muscle and nervous system histopathology. RBC and plasma ChE activities were determined in 10/sex/group from the remaining 40 animals at one day prior to dosing, 30 minutes post dose (day 1) and 1 day post dose (day 2). Brain ChE was determined at the latter two time points.

There were no treatment-related deaths. At 2 mg/kg, 5/40 males and 5/40 females exhibited tremors at 30 minutes post dose. In the FOB group, tremors were observed in 4/12 males and lacrimation in 1/12 males at 30 minutes at 2 mg/kg. Incidence of other signs was not significantly different from controls. There were no clinical signs by 24 hours post dose. Females at 2 mg/kg gained significantly less weight than controls between days 2 and 8. Neither gross lesions nor treatment-related neuropathology were evident.

Statistically significant plasma ChE inhibition occurred at 30 minutes post dose at 0.75 and 2 mg/kg (77 and 58% of control in males; 60 and 64% of control in females). Statistically significant RBC ChE inhibition occurred at 30 minutes in males at 2 mg/kg (54% of control) and in females at 0.5, 0.75 and 2 mg/kg (75,62 and 43% of control). Statistically significant brain ChE inhibition occurred at 30 minutes at 0.5, 0.75 and 2 mg/kg in both sexes (81, 75 and 53% of control in males; 80, 70 and 49% of control in females). All cholinesterase activities returned to control levels by 24 hours post dose.

The NOEL for this study was 0.25 mg/kg based on statistically significant brain ChE inhibition at 0.5 mg/kg and above in both sexes. The study was considered to be acceptable under FIFRA guidelines.

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Malley (2005) measured RBC and brain ChE activities in post natal day 11 (pnd-11) and young adult (pnd-42) rats after exposure to methomyl by the oral route. An initial study was designed to determine the time to peak inhibition. Thirty-five pnd-11 Sprague-Dawley pups/sex were treated by gavage with 0.3 mg/kg methomyl (purity 98.08%). RBC and brain ChE were measured after sacrifice in 5/sex/time point at 30, 60, 120, 180 and 360 minutes post dose. A control group consisting of 15/sex was dosed with distilled water, with 5/sex/time point assayed at 60, 120 and 240 minutes post dose. Maximal inhibition of both enzymes was noted at 30 minutes. Subsequent assays were thus conducted at that time.

A second study examined the dose responsiveness of pnd-11 pups. Ten/sex/dose were dosed with 0, 0.1, 0.2, 0.3 or 0.4 mg/kg methomyl and euthanized after 30 minutes. Maximal inhibition of both RBC and brain ChE was observed at 0.4 mg/kg (RBC: 49% in both sexes; brain: 41% in males, 42% in females), with less inhibition at 0.3 mg/kg (RBC: 40% in males, 42% in females; brain: 36% in males, 33% in females), 0.2 mg/kg (RBC: 19% in males, 36% in females; brain: 26% in males, 20% in females) and 0.1 mg/kg (RBC: 14% in males, 19% in females; brain: 12% in both males and females). These results are summarized in Table III.3.a.

A third study examined the dose responsiveness of pnd-42 adults. Twenty/sex/dose were exposed to 0, 0.3, 0.5 or 0.75 mg/kg, with 10/sex/dose assayed at 30 and at 240 minutes. Inhibition of RBC ChE at 0.75 mg/kg was 41% and 25% at 30 minutes in males and females, respectively, and 19% and 12% at 0.3 mg/kg. Inhibition of brain ChE at 0.75 mg/kg was 19% and 29% in males and females, respectively, and 2% and 14% at 0.3 mg/kg. RBC ChE remained somewhat inhibited at 240 minutes, though brain ChE activities had returned to control levels by that time. These results are summarized in Table III.3.b.

These data suggested that brain ChE from pnd-11 pups was more sensitive to the inhibitory effects of oral methomyl than the same enzyme from pnd-42 adults. Dose-response modeling of the data from the whole dose range by US EPA's National Center for Computational Toxicology confirmed this (Setzer, 2006b). Pnd-11 pups showed an LED_{10} of 0.1 mg/kg, while the LED_{10} for day 42 adults was 0.36 mg/kg.

This study was considered to be supplemental.

Table III.3.a. Dose dependence of RBC and brain cholinesterase inhibition in pnd-11 rats (Malley, 2005)

	Methomyl (mg/kg) - 30-minutes post-exposure				
	0	0.1	0.2	0.3	0.4
Males					
RBC ChE (U/L)	3060±709 (0%)	2636±463 (14%)	2478±661 (19%)	1848±521 (40%)	1574±389 (49%)
Brain ChE (U/g)	5.7±0.4 (0%)	5.0±0.6 (12%)	4.2±0.7 (26%)	3.6±0.5 (36%)	3.3±0.5 (41%)
Females					
RBC ChE (U/L)	3473±333 (0%)	2802±550 (19%)	2234±531 (36%)	2000±824 (42%)	1768±445 (49%)
Brain ChE (U/g)	5.5±0.3 (0%)	4.9±0.7 (12%)	4.4±0.5 (20%)	3.7±0.9 (33%)	3.2±0.6 (42%)

Table III.3.b. Dose dependence of RBC and brain cholinesterase inhibition in pnd-42 rats (Malley, 2005)

	Methomyl (mg/kg)							
	30 minutes post-exposure				240 minutes post-exposure			
	0	0.3	0.5	0.75	0	0.3	0.5	0.75
Males								
RBC ChE (U/L)	2230±506 (0%)	1806±422 (19%)	1272±453 (43%)	1326±546 (41%)	2156±488 (0%)	2068±726 (4%)	1480±349 (31%)	1700±489 (21%)
Brain ChE (U/g)	9.5±0.9 (0%)	9.3±0.8 (2%)	8.4±0.8 (12%)	7.7±0.8 (19%)	10.0±0.6 (1%)	10.0±0.4 (0%)	9.5±0.9 (6%)	10.1±0.7 (-1%)
Females								
RBC ChE (U/L)	1942±476 (0%)	1712±460 (12%)	1526±799 (21%)	1456±452 (25%)	1890±551 (0%)	2426±396 (-28%)	1710±1123 (10%)	1486±373 (21%)
Brain ChE (U/g)	10.2±0.5 (0%)	8.7±0.9 (14%)	7.9±0.6 (23%)	7.2±1.1 (29%)	9.6±0.9 (0%)	9.7±0.6 (-1%)	10.0±0.8 (-5%)	9.9±0.8 (-3%)

ii. Inhalation exposure

Panepinto (1991) exposed 5 Sprague-Dawley rats/sex/dose to aerosolized methomyl (97.7% purity) for a single 4-hour period in an LC_{50} study. Nose-only devices were used. The gravimetrically-determined doses were 0.137, 0.181, 0.182, 0.232 and 0.326 mg/L. There was no control group. A period of 14 days followed the exposure in which the animals were weighed and observed for toxic signs. At the end of that period, they were sacrificed and subjected to gross pathological examination. Cholinesterase activities were not determined.

The death rate among males at ascending doses was 0/5, 0/5, 0/5, 3/5 and 3/5. Among females it was 0/5, 0/5, 1/5, 3/5 and 4/5. All deaths occurred during the exposure period, though the precise times-to-death were not provided in the study report. Despite body weight losses on the first postexposure day, all survivors gained weight during the observation period. Toxic signs during the exposure period included nasal discharge and salivation. Toxic signs noted upon removal from the nose-only devices (*i.e.*, following exposure) included diarrhea, lethargy and ocular and-or nasal discharge. If the air concentrations were high enough to cause death, signs included abnormal gait or mobility, tremors, hyperactivity, hyperreactivity, muscle fasciculations and hunched and/or low posture in survivors. Methomyl-related abnormalities were not apparent upon necropsy.

The LC_{50} for males and females was 0.273 and 0.243 mg/L, respectively. As signs were noted at all doses, a NOEL was not assigned. The LOEL was set at the low dose of 0.137 mg/L.

This study was considered to be acceptable by FIFRA guideline standards.

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Weinberg (2014) evaluated toxic signs and dose and time dependencies of RBC and brain ChE inhibition and recovery following single nose-only inhalation exposures to methomyl (99.4%) in Sprague-Dawley rats. The study was conducted in 3 phases.

Phase I subjected males and females—3/sex/dose----to doses of 100-195 mg/m^3 for 6 hours. All doses elicited salivation, lacrimation, tremors, coolness to touch, wet / clear material on head / face, and dried material on face or other areas.

In Phase II, males and females (5/sex/dose/exposure time) were exposed to 0 or 136 mg/m^3 and assayed for brain and RBC ChE at 1, 3 and 6 hr during the 6-hr exposure period and at 1, 2 and 4 hours post exposure. Thus a fixed dose of 136 mg/m^3 achieved maximal brain and RBC ChE inhibition by 1 hr, with no subsequent change over the 6-hr exposure period (65-69% inhibition in brain, 73-84% in RBCs of either sex). Inhibition began to diminish within 1-2 hr of exposure cessation for both enzymes. By 4 hr post-exposure, inhibition was reduced to 16-25% for both brain and RBCs (Table III.4).

Since gender differences were not evident and maximum RBC and brain ChE inhibition occurred within 3 hr, phase III evaluated the dose-response relationship in males (10/dose) following 3 hours of exposure. Brain ChE inhibition at this point ranged from 13% at 5.6 mg/m^3 to 66% at 105 mg/m^3, while RBC ChE inhibition ranged from 16% at 5.6 mg/m^3 to 93% at 105 mg/m^3 (Table III.5). Salivation and lacrimation were noted even at the low dose of 5.6 mg/m^3.

Benchmark dose analysis using the Hill model at a default 10% response rate—adopted even in the presence of clinical signs at the low dose due to their mildness and lack of dose responsiveness—yielded an LEC_{10} (EC_{10}) of 3.92 (4.37) mg/m^3. The modeling output for this analysis appears in Appendix I. Because inhibition was maximal at 1 hr at the higher dose of 136 mg/m^3 used in phase II of the study, a 1-hr rat inhalation rate was used to calculate the rat internal dose. This calculation, detailed in section IV.A.1.e. below, yielded an internal dose LEC_{10} of 0.16 mg/kg.

As this was not a FIFRA guideline study, it was classified as supplemental. Nonetheless, the data were sufficient to support a critical acute inhalation LEC_{10} determination.

Table III.4. RBC and brain ChE inhibition in rats as a function of time during and after inhalation exposure to a single air concentration—136 mg/m^3---of methomyl (Weinberg, 2014)

			Cholinesterase activity (U/L)			
			Males		Females	
Exposure time	**Methomyl (mg/m^3)**	**n**	**RBC**	**Brain**	**RBC**	**Brain**
1 hr	**0** **136**	**5** **5**	4476 1212** (27%)	49907 17606** (35%)	4810 1294** (27%)	51804 18184** (35%)
3 hr	**0** **136**	**5** **5**	5469 904** (17%)	51035 16012** (31%)	5591 876** (16%)	49655 15527** (31%)
6 hr	**0** **136**	**5** **5**	4898 1144** (23%)	49404 16897** (34%)	4918 1220** (25%)	51940 16555* (32%)
1 hr post exposure	**0** **136**	**5** **5**	4949 1684** (34%)	51161 24083** (47%)	5099 1246** (24%)	51697 20334** (39%)
2 hr post exposure	**0** **136**	**5** **5**	5240 2572** (49%)	49876 28717** (58%)	5163 2500** (48%)	50901 22354** (44%)
4 hr post exposure	**0** **136**	**5** **5**	5020 4200 (84%)	49468 40135** (81%)	4265 3400 (80%)	50793 38150* (75%)

Note: Numbers in parentheses indicate the percentage of concurrent control values.
*, **: p≤0.05, 0.01 using a two-sample t-test.

Table III.5. Effect of 3-hr inhalation exposure to methomyl on RBC and brain cholinesterase activities in male rats (Weinberg, 2014)

		Cholinesterase activity (U/L)			
		Phase IIIA		Phase IIIB	
Methomyl (mg/m^3)	n	RBC	Brain	RBC	Brain
0	10	3357±708.8	53,448±1843.6	4541±407.5	52,257±1339.3
5.6	9			3835±802.7 (16%)	45,539±2176.6** (13%)
14	10			3274±964.1** (28%)	39,050±3691.6** (25%)
19	10			2983±478.3** (34%)	35,616±3668.1** (32%)
31	10			2199±333.5** (52%)	28,598±4842.6** (45%)
36	10	814±348.6** (76%)	24,145±2431.0** (55%)		
68	10	542±237.3** (84%)	20,834±2352.6** (61%)		
105	10	231±160.9** (93%)	18,336±2211.6** (66%)		

*, **: p≤0.05, 0.01 using a two-sample t-test.

Table III-6. NOEL and LOEL values for acute toxicity studies on methomyl

Species, strain	Study type & exposure regimen	Effects at LOEL	NOEL (or LED)	LOEL	Reference
human males	single capsular dose: 0, 0.1, 0.2 or 0.3 mg/kg	↓ RBC & plasma ChE	0.03 mg/kg (LED_{10} for RBC ChE inhibition) [a]	not determined [a]	McFarlane *et al.*, 1998; Setzer, 2006a *Supplemental*
rat, Sprague-Dawley	single gavage dose: 0 or 0.3 mg/kg	↓ RBC, plasma and brain ChE	not determined	not determined [b]	Malley, 1997 *Supplemental*
rat, Sprague-Dawley	single gavage dose: 0, 0.25, 0.5, 0.75 or 2 mg/kg	↓ brain ChE	0.25 mg/kg	0.5 mg/kg	Mikles, 1998a *Acceptable*
rat, Sprague-Dawley	single gavage dose: 0 - 0.75 mg/kg in pnd-11 pups and pnd-42 adults (3 studies)	↓ brain ChE	0.1 mg/kg (LED_{10}, pnd-11 pups) [c] 0.36 mg/kg (LED_{10}, pnd-42 adults) [c]	not determined not determined	Malley, 2005 *Supplemental*
rat, Sprague-Dawley	4-hr inhalation at 0.137, 0.181, 0.182, 0.232 & 0.326 mg/L	cholinergic signs	not determined	not determined [d]	Panepinto, 1991 *Acceptable*
rat, Sprague-Dawley (♂)	3-hr inhalation at 0, 5.6, 14, 19, 31, 36, 68 & 105 mg/m^3	↓ brain ChE and cholinergic signs	3.92 mg/m^3 (LEC_{10}) (≈0.16 mg/kg) [e]	5.6 mg/m^3	Weinberg, 2014 *Supplemental*

Abbreviation: pnd, post natal day

[a] As there was a plausible, though not statistically significant, inhibition of RBC ChE at the low dose of 0.1 mg/kg, USEPA's benchmark dose analysis (Setzer, 2006a) was relied upon for determination of the LED_{10}.
[b] Preliminary study
[c] Benchmark dose analysis for this study was done by Setzer (2006b).
[d] This was an acute LC_{50} study that was not designed to determine LOELs and NOELs.
[e] For calculation of the human equivalent LEC_{10}, see section IV.A.1.e. This value was considered to apply to 1, 8 and 24-hr exposures (see discussion in section IV.A.1.e.

C. SUBCHRONIC TOXICITY (including SUBCHRONIC NEUROTOXICITY)

1. Oral exposure

Two three-month feeding studies conducted in the 1960s, one in rats (Sherman, 1967) and one in dogs (Kundzin and Paynter, 1966) were reviewed for this assessment. Treatment effects were discerned neither in rats at levels as high as 500 ppm (23-32 mg/kg/day) nor in dogs at levels as high as 400 ppm (12.5-14.7 mg/kg/day). As these studies predated FIFRA guidelines, they were considered to be supplemental.

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Mikles (1998b) subjected 42 Sprague Dawley rats/sex/dose to 0, 20, 50, 150 or 1500 ppm methomyl (98.6% purity) in the diet for up to 91 days. The mean daily intakes over the entire exposure period were 0, 1.29, 3.14, 9.42 and 94.9 mg/kg/day in males and 0, 1.48, 3.85, 11.2 and 113 mg/kg/day in females. Three sets of 10/sex/dose were used in cholinesterase studies—these animals were sacrificed at weeks 4, 8 and 13 for assays of RBC, plasma and brain ChE. The other 12/sex/dose underwent neurobehavioral testing (FOB and motor activity) pre-test and at weeks 4, 8 and 13. Of these, 6/sex/dose were perfused *in situ*. Neuropathology was performed on control and high dose central and peripheral nervous system preparations.

Body weights and food consumption were markedly reduced at 1500 ppm in both sexes throughout the study, with a substantially milder consumption decline in females at 150 ppm. The most prominent of the clinical observations were tremors in most 1500 ppm males and females during the first 4 weeks and occasionally thereafter. Common FOB observations included increased resistance to handling and removal from the cage, ptosis [2] and absent pupillary response in both sexes. In addition, females exhibited increased urination during open field observations and decreased urination and defecation during motor activity assessment, though the toxicologic significance of such observations was unclear. None of these findings was progressive over time. Histopathology was negative. Brain ChE was marginally inhibited at 1500 ppm (significant for each sex at one of three assay times). Plasma and RBC ChE activites were unaffected. Highlights of these observations are provided in Table III-7.

The NOEL of 150 ppm (~9.4 mg/kg/day) was based on reduced body weight and food consumption, tremors, FOB signs and brain ChE inhibition at 1500 ppm. This study was acceptable according to FIFRA guidelines.

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[2] Ptosis: "drooping of the upper eyelid from paralysis of the third nerve or from sympathetic innervation" (Dorland's Illustrated Medical Dictionary, 26th Edition, p. 1093)

Table III-7. Selected body weights, clinical signs, FOB data and brain ChE activities in rats during and after 91 days of dietary exposure to methomyl (Mikles, 1998b)

Parameter	Methomyl (ppm) [a]									
	0		20		50		150		1500	
	M	F	M	F	M	F	M	F	M	F
Body wt. (grams)										
day 0	184	148	184	148	185	149	183	148	182	147
day 7	236	172	236	171	238	170	232	168	180*	139*
day 91	520	293	508	286	506	275	518	276	395*	237*
Food consumption (g/rat/day)										
day 0-7	22.4	17.1	22.2	16.4	22.3	16.7	21.5	16.1*	11.1*	8.7*
days 84-91	24.6	17.1	24.3	17.0	23.2	17.3	24.5	16.5	20.3*	14.7*
Clinical observations										
Tremors										
d. 0-27 (M) or 0-28 (F)	0/42	0/42	0/42	0/42	0/42	0/42	0/42	0/42	32/42*	23/42*
d. 28-49 (M) or 29-55 (F)	0/32	0/32	0/32	0/32	0/32	0/32	0/32	0/32	2/32*	2/32*
d. 86-93 (M) or 87-93 (F)	0/12	0/12	0/12	0/12	0/11	0/12	0/12	0/12	0/12	0/12
Hyperreactivity										
d. 0-27 (M) or 0-28 (F)	0/42	0/42 [b]	0/42	0/42	0/42	0/42	0/42	0/42	1/42	0/42
d. 50-85 (M) or 56-86 (F)	0/22	0/22 [b]	0/22	0/22	0/21	0/22	0/22	0/22	5/22*	0/22
Aggressiveness										
d. 0-27 (M) or 0-28 (F)	0/42	0/42 [b]	0/42	0/42	0/42	0/42	0/42	0/42	0/42	0/42
d. 50-85 (M) or 56-86 (F)	0/22	0/22 [b]	0/22	0/22	0/21	0/22	1/22	0/22	4/22*	0/22
Alopecia										
d. 0-27 (M) or 0-28 (F)	0/42	2/42	0/42	3/42	0/42	3/42	0/42	3/42	0/42	4/42
d. 28-49 (M) or 29-55 (F)	0/32	2/32	0/32	4/32	0/32	2/32	0/32	1/32	0/32	14/32*
d. 50-85 (M) or 56-86 (F)	0/22	2/22	0/22	2/22	0/21	0/22	0/22	2/22	0/22	12/22*
Functional observational battery—males										
Difficult cage removal										
Week 4	0/12		0/12		0/12		0/12		3/12*	
Week 8	0/12		0/12		0/12		0/12		1/12	
Week 13	0/12		0/12		0/12		0/12		1/12	
Difficult handling										
Week 4	0/12		0/12		0/12		1/12		4/12*	
Week 8	0/12		0/12		0/12		0/12		3/12*	
Week 13	0/12		0/12		0/12		0/12		1/12	
Ptosis[b] (home cage)										
Week 4	0/12		0/12		1/12		0/12		1/12	
Week 8	0/12		0/12		0/12		0/12		2/12*	
Week 13	0/12		0/12		0/12		0/12		0/12	

No pupillary response										
Week 4	0/12		0/12		0/12		0/12		5/12*	
Week 8	0/12		0/12		0/12		0/12		6/12*	
Week 13	0/12		0/12		0/12		0/12		5/12*	
Functional observational battery—females										
Palpebral closure										
Week 4		1/12		1/12		1/12		3/12		3/12
Week 8		0/12		0/12		0/12		0/12		2/12*
Week 13		0/12		0/12		0/12		0/12		0/12
Difficult cage removal										
Week 4		0/12		0/12		0/12		0/12		1/12
Week 8		0/12		0/12		0/12		0/12		2/12*
Week 13		0/12		0/12		0/12		0/12		0/12
Difficult handling										
Week 4		0/12		0/12		0/12		0/12		1/12
Week 8		0/12		0/12		0/12		1/12		2/12*
Week 13		0/12		0/12		0/12		0/12		0/12
Ptosis (home cage)										
Week 4		0/12		0/12		0/12		1/12		2/12*
Week 8		0/12		0/12		0/12		0/12		2/12*
Week 13		0/12		0/12		0/12		0/12		0/12
Abnormal gait (dragging limbs, hopping)										
Week 4		0/12		1/12		0/12		0/12		1/12
Week 8		0/12		2/12		0/12		1/12		4/12*
Week 13		0/12		0/12		0/12		0/12		0/12
Low arousal level										
Week 4		0/12		0/12		1/12		1/12		3/12*
Week 8		3/12		1/12		3/12		2/12		2/12
Week 13		1/12		1/12		1/12		0/12		0/12
Urination (present)										
Week 4		0/12		0/12		0/12		2/12		3/12*
Week 8		2/12		0/12		1/12		0/12		0/12
Week 13		3/12		0/12		2/12		0/12		2/12
Defecation (present)										
Week 4		4/12		3/12		1/12*		1/12*		1/12*
Week 8		4/12		4/12		2/12		2/12		0/12*
Week 13		5/12		3/12		2/12		3/12		0/12*
Pupillary response (absent)										
Week 4		1/12		0/12		0/12		0/12		4/12*
Week 8		0/12		0/12		0/12		0/12		2/12*
Week 13		0/12		0/12		0/12		0/12		4/12*
Brain cholinesterase activity (U/g)										
Week 4	11.3	12.0	11.3	11.5	11.3	11.6	11.4	11.2	10.4	10.8*
Week 8	11.2	11.6	10.9	11.2	11.0	11.4	10.8	11.6	9.1*	11.2

Week 13	10.6	11.2	10.4	10.7	10.5	10.9	10.8	10.7	10.1	10.8

*p<0.05

[a] Calculated mean internal doses: 0, 1.29, 3.14, 9.42 and 94.9 mg/kg/day in males and 0, 1.48, 3.85, 11.2 and 113 mg/kg/day in females

[b] Clinical observational data for hyperreactivity and aggressiveness (both in males) and alopecia (females) were not reported, prompting a conclusion by the risk assessor that the incidence was nil throughout the dose curve. Need to clarify this statement!!

2. Dermal exposure

Brock (1989) applied a methomyl paste (purity: 98.4%) constituted in deionized water to the scapular-to-lumbar back region of New Zealand White rabbits. Five rabbits/sex/dose received 0, 5, 50 or 500 mg/kg for 6 hr/day on 21 consecutive days, with an additional 5/sex/dose (0 and 500 mg/kg only) acting as recovery groups for 14 further days. Body weight determinations, food consumption, clinical chemistry and pathology were carried out after sacrifice.

There was no compound-related mortality. A statistically significant rise in hyperreactivity (*i.e.*, increased reaction to stimuli) in males, along with a similar, but non-statistically significant, rise in females, occurred at the high dose (incidence in males at ascending doses: 3/10, 3/5, 3/5, 9/10*; females: 7/10, 3/5, 3/5, 9/10; p<0.05) . This was considered as plausibly due to methomyl exposure. However, this conclusion was not definitive due to the high incidence in controls.

Plasma ChE activities were significantly decreased in 50 and 500 mg/kg males (36% and 77% of control, respectively; p<0.05). Statistical significance in females occurred only at the high dose (55% of controls; p<0.05). RBC ChE decreased at the high dose, but statistical significance was not achieved (80% and 85% of controls in males and females, respectively; p>0.05). Brain ChE was statistically decreased at 500 mg/kg in both sexes (48% and 68% of controls in males and females, respectively; p<0.05). Some non-statistically significant inhibition may have been present at 50 mg/kg, though this was not definitive (91% and 86% of controls in males and females, respectively). Examination of individual animal brain ChE data raised the possibility that methomyl-based inhibition was present at 50 mg/kg, especially in females, where 4/5 animals registered activities lower than the control mean. Because the cholinesterase assay details were not provided in the report, it was assumed that the standard Ellman assay was used. This may underestimate the degree of cholinesterase inhibition. Consequently, the female brain data at 50 mg/kg were considered to reflect possible inhibition at that dose.

The NOEL for this study was set at 5 mg/kg based on non-statistically significant brain cholinesterase inhibition in females at the LOEL dose of 50 mg/kg. The absence of statistical significance prevented a definitive conclusion, however. Statistically significant inhibition of plasma ChE at 50 mg/kg was also noted at this dose in males. The high dose of 500 mg/kg was associated with statistically increased hyperreactivity in males and decreased brain and plasma ChE activities in both sexes. This study was considered to be acceptable according to FIFRA guidelines.

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Finlay (1997b) applied methomyl technical (purity: 98.6%) to the shaved skin of 6 New Zealand White rabbits/sex/group at 0 (deionized water), 15, 30, 45 or 90 mg/kg/day for 6 hr/day on 21 consecutive days. There were no deaths, no clinical signs, no effects on body weights or food consumption and no treatment-related lesions noted upon necropsy. Although the mean cholinesterase activities in plasma, RBCs and brain of treated animals were slightly less than controls, statistical significance was not achieved at any dose, nor was dose-responsiveness clearly evident. For example, brain ChE activities at ascending doses in males were 100%, 99%, 90%, 88% and 90% of controls, while in females they were 100%, 101%, 100%, 94% and 94% of controls.

A NOEL was not determined for this study since definitive effects were not observed even at the high dose of 90 mg/kg/day (*i.e.*, the NOEL was >90 mg/kg/day). However, because a "modified Ellman" spectrophotometric procedure was used to assay cholinesterases, it does not appear that measures were taken to minimize carbamate-ChE dissociation. This raised the possibility that actual ChE inhibition was underestimated in this study. It is noted that all males at 30 mg/kg/day and above exhibited brain ChE activities that were lower than control means.

The study was considered to be supplemental since clinical chemistry, hematology, ophthalmology and histopathology—all of which are required under FIFRA guidelines—were not carried out.

Table III-8. NOEL and LOEL values for subchronic toxicity studies on methomyl

Species, strain	Study type & exposure regimen	Effects at LOEL	NOEL	LOEL	Reference
rat (strain not identified)	3-month dietary	no effects detected	n/a [a]	n/a [a]	Kundzin & Paynter, 1966 *Supplemental*
rat, SD	91-day dietary	reduced body weight and food consumption, tremors during the 1st four wks and beyond, FOB signs and “marginal” brain ChEI (RBC & plasma ChE unaffected)	150 ppm (♂, ♀: 9.4, 11.2 mg/kg/day)	1500 ppm (♂, ♀: 94.9, 113 mg/kg/day)	Mikles, 1998b *Acceptable*
dog, beagle	3-month dietary	no effects detected	>400 ppm (♂,♀: 14.7, 12.5 mg/kg/day)	>400 ppm (♂,♀: 14.7, 12.5 mg/kg/day)	Sherman, 1967 *Supplemental*
rabbit, NZW	21-day dermal	brain ChEI in females [b]	5 mg/kg/day	50 mg/kg/day	Brock, 1989 *Acceptable*
rabbit, NZW	21-day dermal	n/a	>90 mg/kg/day (hdt)	>90 mg/kg/day (hdt)	Finlay, 1997b *Supplemental*

[a] Neither a NOEL nor LOEL were assigned due to the limited number of tests conducted in this study.
[b] Inhibition of brain ChE did not achieve statistical significance in the Brock (1989) study. Judgment of an effect at the LOEL of 50 mg/kg/day was based on (1) the observation that enzyme activities in 4/5 females were lower than controls at that dose, and (2) the assumption that special precautions were not taken to minimize carbamate-enzyme dissociation in the assay. Statistically significant brain ChE inhibition was, however, noted at 500 mg/kg/day.

D. CHRONIC TOXICITY AND ONCOGENICITY

Busey (1968) exposed 4 beagle dogs/sex/dose to dietary methomyl (purity: 90-100%) for 2 years at 0, 50, 100, 400 or 1000 ppm (mean intakes, ♂: 0, 1.39, 2.96, 10.94 and 31.13 mg/kg/day; ♀: 0, 1.45, 3.42, 13.90 and 33.67 mg/kg/day). An interim sacrifice of 1 dog/sex/group was conducted after 1 year of exposure. Daily observations were made for clinical signs, appearance, behavior, appetite and elimination. Body weight and food consumption were recorded on a weekly basis. Clinical laboratory determinations were made at 0, 3, 6, 12, 18 and 24 months. These included hematolgy (hematocrit, hemoglobin, RBCs and total and differential leukocytes; also, leukocyte determinations were done at termination on femoral bone marrow), serum chemistry (glucose, urea nitrogen, alkaline phosphatase, glutamic-pyruvic transaminase, glutamic-oxaloacetic transaminase and prothrombin time; electrolytes, protein and albumin were determined at 18 and 24 months only), and urinalysis (appearance, pH, specific gravity, glucose, acetone, protein, bilirubin, occult blood and microscopic analysis of sediment). Plasma and RBC cholinesterase levels were determined at 0 (all animals), 9 (controls and high dose only) and 13 weeks (high dose only). Gross necropsies and organ weight determinations were done on all sacrificed animals. Histopathology was performed on an extensive array of tissues. Terminal analyses were also performed on animals that died during the study.

Mortality and clinical signs. Two high-dose females died during the study. The first died at 9 weeks. The second, which was put on study to replace the first decedent, died 17 days after the beginning of treatment. Both deaths were attributed to methomyl exposure. Two high-dose males showed “tremors, salivation, incoordination and circling movements” on a single day during week 13, returning to normal behavior by the following morning. Another high-dose male (dog #10468) showed severe anemia and was taken off treatment during weeks 85-94. This animal also showed diarrhea and emesis during the week 73-81 period.

Body weight and food consumption. It was difficult to identify a treatment effect on body weight due to the small sample sizes and individual variability of weights. However, most of the animals gained weight during the treatment period, even at the high dose. A systematic effect on food consumption was not evident.

Hematology. Exposure to methomyl at the high dose produced consistently lower values for all three RBC-related hematologic parameters beginning with the first measurement at 3 months and extending throughout the 2-year study (Table III-9). As noted above, anemia was particularly severe in one high-dose male—removal of data from that male (#10468) decreased the apparent mean effect at 1000 ppm but did not abolish it (censored data not shown) [3]. Hematologic effects were not observed at the other doses. It is noted that both rats and mice exposed to methomyl also sustained reductions in RBC-related hematologic parameters (Kaplan, 1981; Serota, 1981).

Serum chemistry. Overt effects on serum chemistry were not observed. Even RBC and plasma cholinesterase levels did not appear to vary significantly from controls, though the latter enzyme was reduced at 3 months at the high dose in one male and one female.

Organ weights. Due to the small number of animals, it was difficult to determine if organ weights were affected by exposure. However, the investigators pointed out that the kidney weight relative to body weight was moderately increased in one 400-ppm male and two 1000-ppm males.

Gross pathology. Necropsies on the two female high-dose decedents revealed

[3] This animal also may have shown effects on platelet and reticulocyte counts, as well, though these data were not clearly presented by the investigators.

abnormalities in many organ systems. Interpretation of these observations was unclear. Necropsies on the 1-yr sacrifices revealed one high-dose male liver with a pale yellow-brown color that was considered to be treatment-related. Necropsies on the 2-yr sacrifices revealed one high-dose male with an enlarged liver and an enlarged spleen containing white deposits at the capsular surface. Both observations were likely related to the profound anemia experienced by that animal. One high-dose female exhibited scattered ecchymoses [4] in the jejunal mucosa. A test article relation was plausible.

Histopathology. Histopathologic alterations were noted particularly in the kidney and spleen of animals exposed to 400 and 1000 ppm methomyl. The splenic observations might be interpreted as secondary to impacts on hematology noted particularly at 1000 ppm (see above). Specific methomyl-related observations were as follows: (1) 400- and 1000-ppm males showed increased pigment in the renal epithelial cells of the proximal tubule; (2) renal proximal tubular epithelial cells were slightly swollen in 1000-ppm animals of both genders; (3) an abnormally high level of extramedullary hematopoiesis was noted in the spleens of animals at 1000 ppm; (4) spleens also exhibited moderate or moderate-to-severe pigmentation at 400 and 1000 ppm; (5) minimal or slight bile duct hyperplasia was noted at 400 and 1000 ppm; and (6) severe bone marrow hematogenic activity increased at 1000 ppm. These findings are summarized below in Table III-10.

The NOEL for this study was set at 100 ppm (~3 mg/kg/day) based on the histopathologic findings at 400 ppm in the kidney, spleen and liver detailed in the preceding paragraph. This study was considered acceptable according to FIFRA guidelines.

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[4] Ecchymosis: "a small hemmorrhagic spot, larger than a petechia, in the skin or mucous membrane forming a nonelevated rounded or irregular, blue or purplish patch." (Dorland's Illustrated Medical Dictionary, 26th Edition, 1985. p. 417

Table III-9. RBC-related hematologic parameters after various time intervals of dietary methomyl exposure (Busey, 1968)

	Methomyl in feed (ppm)									
	Males [a]					Females [a]				
Parameter	**0**	**50**	**100**	**400**	**1000**	**0**	**50**	**100**	**400**	**1000**
Hematocrit (%)										
0 months	44.25	45.00	46.13	46.25	44.50	46.75	48.75	46.63	50.13	47.67
3	47.38	43.75	46.38	46.50	35.81	46.50	45.25	46.38	49.63	40.92
6	46.75	44.00	45.13	47.00	38.88	48.13	43.38	47.00	46.25	45.33
12	49.50	46.63	46.75	50.75	38.63	48.25	45.75	49.75	51.00	45.83
18	50.17	46.67	41.00	49.67	35.42	46.67	48.33	48.33	49.33	49.50
24	50.00	48.00	43.00	49.00	37.33	52.33	50.67	46.33	50.33	43.00
Hemoglobin (g/100 ml)										
0 months	14.90	14.85	15.50	15.30	14.65	15.38	16.08	15.30	16.28	15.73
3	17.28	16.18	16.58	16.63	12.11	17.03	16.93	16.93	17.28	13.57
6	16.85	15.20	16.23	17.50	13.10	17.23	16.65	16.65	16.55	15.67
12	17.38	16.15	16.35	17.65	12.55	16.73	17.03	17.03	18.08	15.77
18	18.40	16.47	14.50	17.45	12.18	16.73	17.50	17.50	17.00	16.80
24	17.33	16.67	14.83	17.10	12.63	18.37	16.37	16.37	17.33	14.75
RBC counts ($x10^6/mm^3$)										
0 months	6.62	6.70	6.60	6.89	6.64	6.61	6.80	6.94	7.23	6.64
3	7.43	6.62	6.25	6.23	4.61	7.03	6.47	6.53	7.06	5.40
6	7.21	6.84	6.70	7.04	5.40	7.20	6.38	6.93	6.82	6.44
12	6.85	6.76	6.85	6.50	4.84	6.49	6.24	6.73	6.70	5.64
18	7.86	7.30	6.34	7.24	5.03	7.12	6.97	7.21	7.25	6.92
24	7.09	7.04	6.14	7.05	4.94	7.15	6.94	6.62	7.17	5.61

Note: These mean data were calculated by the DPR reviewer from individual data presented in the study reporth.

[a] Mean intake, ♂: 0, 1.39, 2.96, 10.94 and 31.13 mg/kg/day; ♀: 0, 1.45, 3.42, 13.90 and 33.67 mg/kg/day

Table III-10. Splenic and renal histopathology in beagle dogs after a 2-yr exposure to dietary methomyl (Busey, 1968)

	Methomyl in feed (ppm)									
	Males[a]					Females[a]				
Parameter	**0**	**50**	**100**	**400**	**1000**	**0**	**50**	**100**	**400**	**1000**
Spleen pigmentation										
minimal	0/3	0/3	0/3	0/3	0/3	0/3	1/3	0/3	0/3	0/2
slight	1/3	1/3	2/3	0/3	0/3	0/3	1/3	1/3	0/3	0/2
moderate	2/3	2/3	0/3	0/3	1/3	3/3	1/3	1/3	2/3	0/2
moderate-to-severe	0/3	0/3	1/3	3/3	2/3	0/3	0/3	1/3	1/3	2/2
Splenic extramedullary hematopoiesis										
minimal	2/3	3/3	2/3	2/3	0/3	1/3	2/3	3/3	1/3	0/2
slight	0/3	0/3	0/3	1/3	1/3	1/3	0/3	0/3	2/3	0/2
moderate	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	1/2
moderate-to-severe	0/3	0/3	0/3	0/3	1/3	0/3	0/3	0/3	0/3	1/2
severe	0/3	0/3	0/3	0/3	1/3	0/3	0/3	0/3	0/3	0/2
Renal pigmentation[b]										
minimal	0/3	0/3	2/3	0/3	0/3	1/3	1/3	1/3	1/3	0/2
slight	2/3	1/3	1/3	1/3	0/3	0/3	0/3	0/3	1/3	0/2
moderate	0/3	0/3	0/3	1/3	1/3	0/3	0/3	0/3	0/3	2/2
moderate-to-severe	0/3	0/3	0/3	1/3	2/3	0/3	0/3	0/3	0/3	0/2
Renal epithelial swelling or irregularity										
minimal	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/2
slight	0/3	0/3	0/3	1/3	1/3	0/3	0/3	0/3	0/3	1/2
moderate	0/3	0/3	0/3	0/3	2/3	0/3	0/3	0/3	0/3	1/2
moderate-to-severe	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/2
Bone marrow hematogenic activity										
minimal	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/2
slight	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/2
moderate	1/3	2/3	2/3	1/3	0/3	1/3	2/3	1/3	0/3	0/2
moderate-to-severe	2/3	1/3	0/3	2/3	0/3	2/3	1/3	2/3	2/3	0/2
severe	0/3	0/3	1/3	0/3	3/3	0/3	0/3	0/3	1/3	2/2
Bile duct hyperplasia										
minimal	1/3	0/3	0/3	0/3	0/3	0/3	0/3	1/3	1/3	1/2
slight	0/3	0/3	0/3	1/3	1/3	0/3	0/3	1/3	0/3	1/2[e]
moderate	0/3	0/3	0/3	0/3	2/3	0/3	0/3	0/3	0/3	0/2
moderate-to-severe	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/2

Note: When the investigators graded an effect as *between* minimal and slight or between any of the other categories, the more severe category was enumerated in the table

[a] Mean intake, ♂: 0, 1.39, 2.96, 10.94 and 31.13 mg/kg/day; ♀: 0, 1.45, 3.42, 13.90 and 33.67 mg/kg/day

[b] Proximal tubule

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Kaplan (1981) exposed Sprague-Dawley rats, 70/sex/dose, to dietary methomyl (purity: 99+%) at 0, 50, 100 or 400 ppm for 2 years. An additional 10/sex/dose were subjected to interim sacrifice at 1 year. Mild reductions in RBC parameters (RBC counts, hemoglobin concentration and hematocrit) may have occurred at 12 and 24 months in 400 ppm males and females, though these were not sufficiently robust for LOEL determination. Both sexes experienced 10% body weight gain decrements at 400 ppm by the end of the study. Histopathologic observations in males suggested mild treatment-induced increases at the high dose in focal hepatic hematopoiesis, bone marrow and adrenal medullary hyperplasia, and adrenal cortical focal degeneration / angiectasis [5]. These increases did not preclude effects at lower doses, but their extent even at the high dose called into question their toxicologic import. While some spontaneous tumors were detected, there was no evidence that methomyl induced tumors. The NOEL was set at 100 ppm (3.5-15.20 mg/kg/day, depending on gender and study phase).

This study was considered acceptable according to FIFRA guidelines.

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Serota (1981) exposed CD-1 mice, 80/sex/dose, to dietary methomyl (purity: 99+%) at 0, 50, 100 (reduced to 75 ppm at week 39) and 800 (reduced to 400 at week 28, then reduced to 200 ppm at week 39) ppm for 104 weeks. The dose reductions were carried out because of unexpected deaths that had become statistically significant at the high dose by week 26. There was no apparent mortality effect at 75 ppm or lower. Body weights were unaffected by treatment at any dose. Group mean compound consumption over the entire study was 0, 8.7, 15.4 and 93.4 mg/kg/day in males and 10.7, 19.1 and 118.6 mg/kg/day in females. There were no treatment-related clinical signs. Modest reductions in RBC parameters were observed at the mid and high doses at weeks 13 and 26 (though dose reductions had been instituted by the wk. 52 measurements). Necropsies and histopathologic observations did not reveal methomyl-induced tumors or other lesions. The NOEL was set at 75 ppm (15-19 mg/kg/day) based on mortality and RBC parameter reductions at 100 ppm and above.

This study was considered acceptable according to FIFRA guidelines.

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[5] Angiectasis: "gross dilatation and often lengthening of a blood vessel" (Dorland's Illustrated Medical Dictionary, 26th edition, page 74) .

Table III-11. NOEL and LOEL values for chronic toxicity studies on methomyl

Species, strain	Study type & exposure regimen	Effects at LOEL	NOEL	LOEL	Reference
rat, SD	2-yr dietary (chronic onco)	body weight decrements and mild anemia	100 ppm (3.5-15.20 mg/kg/day depending on gender & study phase)	400 ppm	Kaplan, 1981 *Acceptable*
dog, beagle	2-yr dietary	pigmentation irregularity, swelling of kidney proximal tubule cells, pigmentation and extramedullary hematopoiesis of spleen, and bile duct hyperplasia	100 ppm (~3 mg/kg/day)	400 ppm	Busey, 1968 *Acceptable*
mouse, CD	104-wk (chronic onco)	modest anemia, increased mortality	75 ppm (15-19 mg/kg/day)	100 ppm	Serota, 1981 *Acceptable*

E. GENOTOXICITY

Two of four gene mutation studies, including a sex-linked lethality test in *Drosophila* and HGPRT forward mutation assay in Chinese hamster V79 cells were positive for gene mutation. In addition, seven of ten chromosome abnormality studies, including several *in vivo* and *in vitro* micronucleus studies, were positive, as were four of seven DNA damage studies. These results are summarized in Table III-12 below. Methomyl is, accordingly, considered to have genotoxic potential.

Table III-12. Genotoxic effects of methomyl

Test type / system	Species / strain / culture	Dose or concentration	S9 [a]	Result	Reference
Gene mutation:					
HGPRT forward mutation assay (*in vitro*)	Chinese hamster ovary cells	0, 10, 20, 40, 50 or 55 mM, positive control: EMS 0, 100, 150, 200, 250 or 350 mM, postive control: DMBA	- +	no effect on mutation frequency to 6-TG resistance; ↓ survival @ higher conc.	Haskell Laboratories, 1983 *Acceptable*
Ames test (*in vitro*)	*Salmonella typhimurium* strains TA 100, 1535, 1537, 1538	0, 1, 10, 50, 100, 500 or 1000 µg/plate	-&+	no effect on reversion rate	SRI, 1977a *Unacceptable*
Sex-linked recessive lethal test	*Drosophila melanogaster*	0, 0.2, 0.4 or 0.6 µl/100 ml of Lannate 20 (20% methomyl)	n/a	↑ recessive lethals	Hemavathy & Krishnamurty, 1987a *Supplemental*
HGPRT forward mutation assay (*in vitro*)	Chinese hamster V79 cells	0, 63, 125, 250 & 500 µg/ml 0, 0.5, 1, 2 or 4 µg/ml N-nitroso-methomyl	- +	no effect on mutation frequency to 6-TG resistance ↑ mutation frequency to 6-TG resistance	Wang *et al.*, 1998 *Supplemental*
Chromosomal aberration:					
Chromosome aberrations (*in vivo*)	Rat, gavage exposure	0, 2, 6 or 20 mg/kg	n/a	no effect on aberration rate	Hazleton, 1984 *Acceptable*
Micronucleus induction (*in vitro*)	Chinese hamster ovary cells	0, 2, 4, 8, 16 or 32 µg/ml	-	↑ micronuclei/ 1000 binucleated cells	Wei *et al.*, 1997 *Supplemental*
Micronucleus induction (*in vivo*)	BALB/c mice, *ip* and oral gavage	0, 1, 3 or 6 mg/kg	n/a	↑ micronucleated reticulocytes	Wei *et al.*, 1997 *Supplemental*
Micronucleus induction (*in vivo*)	Swiss CD1 mouse, *ip* injection	10 mg/kg methomyl or Lannate 25	n/a	↑ micronuclei/ 1000 binucleated cells (both test articles)	Bolognesi *et al.*, 1994 *Supplemental*

Chromosome aberrations (*in vitro*)	human lymphocytes	0, 0.02, 0.06, 0.18 or 0.54 mM methomyl 0, 0.25, 05 or 1 mM Lannate 25	-	↑aberration rate (both test articles)	Bonatti *et al.*, 1994 *Supplemental*
Sister chromatid exchange (*in vitro*)	human lymphocytes	0, 0.02, 0.06 or 0.18 mM	-	no effect on SCE rate	Bonatti *et al.*, 1994 *Supplemental*
Micronucleus induction (*in vitro*)	human lymphocytes	0, 0.01, 0.03 or 0.09 mM methomyl 0, 0.01, 0.03 or 0.1 mM Lannate 25	-	↑micronuclei/ 1000 cells (both test articles)	Bonatti *et al.*, 1994 *Supplemental*
Chromosome aberrations (*in vivo*)	Swiss albino mouse, oral gavage`	0, 20, 40 or 60 mg/kg, administered in 5 divided doses separated by 24 hr	n/a	↑abnormal sperm,↑ sperm chromosome abnormalities	Hemavathy & Krishnamurty, 1987b *Supplemental*
Chromosome aberrations (*in vivo*)	Mouse (strain not stated), *ip* injection	0 or 1 mg/kg	n/a	↑ spleen chromosome aberrations,↑ aberrant metaphases	Amer *et al.*, 1996 *Supplemental*
Micronucleus induction (*in vivo*)	Swiss CD1 mouse, oral gavage	0, 3 or 6 mg/kg	n/a	no effect on micronucleated polychromatic erythrocytes	Bentley, 1995
<u>DNA damage</u>:					
Unscheduled DNA synthesis (*in vitro*)	Primary rat hepatocytes	0, 1, 10, 100, 1000, 5000, 75,0000 µM for 18 hr	-	no increase in net grain counts	Vincent, 1985 *Acceptable*
Mitotic recombination	*Saccharomyces* cervisiae	2 & 3%, w/v	-	increased mitotic recombinants	SRI, 1977b *Unacceptable*
DNA breaks & alkali labile sites (*in vivo*)	Swiss CD1 mice, *ip* injection	5 mg/kg methomyl or 25 mg/kg Lannate 25 (equiv. to 5 mg/kg methomyl)	n/a	↑elution rate constant for both test articles	Bolognesi *et al.*, 1994 *Supplemental*
Oxidative damage to DNA (*in vivo*)	Swiss CD1 mice, *ip* injection	55 mg/kg (either pure or contained in Lannate 25)	n/a	↑ 8-hydroxy deoxyguanosine for both test articles	Bolognesi *et al.*, 1994 *Supplemental*
DNA adduct formation–^{32}P postlabelling (*in vivo*)	Swiss CD1 mice, *ip* injection	5 mg/kg methomyl or 2.5, 5 10 mg/kg Lannate 25	n/a	no effect for methomyl, ↑ adduct formation for Lannate 25	Bolognesi *et al.*, 1994 *Supplemental*
DNA breaks & alkali labile sites (*in vitro*)	human lymphocytes	0, 0.06, 0.18, 0.54, 1 or 2 mM methomyl 0, 0.015, 0.045, 0.13, 0.5, 1 or 2 mM Lannate 25	-	↑elution rate constant for both test articles	Bonatti *et al.*, 1994 *Supplemental*
Oxidative damage to DNA (*in vitro*)	human lymphocytes	0, 0.25, 0.5 or 1 mM methomyl 0, 0.25, 0.5 or 1 mM Lannate 25	-	no effect for methomyl,↑ 8-hydroxy deoxyguanosine for Lannate 25	Bonatti *et al.*, 1994 *Supplemental*

[a] S9 refers to the microsomal activating system that is added in some *in vitro* assays to determine if relevant metabolites are genotoxic.

F. REPRODUCTIVE TOXICITY

Lu (1982) exposed Sprague-Dawley rats over two generations to dietary methomyl (identified as methomyl technical; no purity provided). There was one litter per generation. Dosages were 0, 75, 600 and 1200 ppm. Group sizes were 13 males and 26 females for F0 parents, and 20 males and 40 females for F1 parents. Premating treatment times were 100 and 120 days for F0 and F1 parentals, respectively. Mean daily intakes during premating periods were 5, 37, and 74 mg/kg/day (F0 males); 5, 39, and 76 mg/kg/day (F0 females); 7, 56, and 117 mg/kg/day (F1 males); and 7, 59, and 128 mg/kg/day (F1 females), though doses as low as 3.4 and 2.4 mg/kg/day in males and females, respectively, were achieved during certain weeks in the low dose group (Table III.13). Treatment of F0 mothers was terminated after weaning the F1 pups; F1 mothers were terminated at week 30. Treatment of fathers was continuous until termination; F2 rats were terminated at weaning.

Parental observations*.* One 75-ppm F0 dam and one 600-ppm F1 dam died from causes unrelated to treatment. Clinical signs were not reported in a detailed manner, though the following is quoted from page 7 of the study:

> “Increased activity, piloerection, depressed righting reflex and myoclonic body tics were more frequent and prominent in the F0 rats as the dosage level increased. This increase was initially noted during study week one through week three, thereafter this incidence was infrequent and sporadic. There were no apparent dose related clinical observations in the F0 [*sic*: the investigators probably meant F1] rats.”

Due to the summary nature of this reporting, parental NOELs based on clinical signs were not assigned, though it is likely that low dose consumption was associated with at least some overt maternal toxicity.

Statistical decrements in parental body weights were apparent at the top two doses (600 and 1200 ppm) before gestation in both sexes and in both generations (Table III.14). Weight decrements at the low dose (75 ppm) were more apparent in gestational F1 parentals, particularly the females. After gestation, body weight decrements were maintained at the top two doses. Food consumption was also reduced, though statistical significance was not evident at the low dose (data not shown). Hematologic parameters---RBC counts, hematocrit and hemoglobin---measured only at week 13 in the F0 parentals, were unaffected by dosing.

Reproductive and pup observations. The number of live litters was unaffected by dosing in both the F1 and F2 generations (Tables III.15 and III.16). The mean live litter size was similar to controls at all doses for the F1 pups, though slight reductions were evident for F2 pups at all doses. Toxicologic significance at the low and mid doses was unclear. At the high dose there was a statistically significant rise in the number of dead pups per F2 litter, though not for the F1 litter. The mean live litter size on days 4, 7, 14 and 21 was statistically reduced at the high dose in both generations and at the mid dose in the F2 generation. Mean pup weights were statistically reduced at the mid and high doses on days 1, 4, 7, 14 and 21 in both generations, and in the F1 generation at the low dose on days 14 and 21. The effect on pup weights, including at 75 ppm in F1 pups, was likely due to increased maternal feeding during lactation (resulting in higher test article exposure of the pups), as well as to direct pup exposure due to increasing feed consumption. It is unlikely that these effects were a result of specifically reproductive impacts.

Toxicologic impacts were noted in both dams (possible clinical signs and maternal weight decrements) and pups (reduced weights during the last week of weaning) at the low dose of 75 ppm. In addition, there was a slight decrease in live F2 litter size at that dose, though this was of unclear toxicologic significance. Consequently, 3.5 mg/kg/day, which approximated the compound intake of 75 ppm males during the weeks just before mating (*i.e.*, before the period of heavy maternal feeding), was established as the NOEL for parental rats (corresponding female food consumption was just over 4 mg/kg/day). In light of the heavy feeding during the late phase of lactation—amounting to about 18 mg/kg/day—when pup weight effects were observed at 75 ppm, 3.5 mg/kg/day was also considered to be a NOEL for reproductive and pup effects. LOELs for both maternal and reproductive effects were set at 18 mg/kg/day.

This study was considered to be acceptable by FIFRA standards.

Table III.13. Pre-mating methomyl consumption in the 2-generation reproductive toxicity study of Lu (1982)

	Males (ppm)			Females (ppm)		
	75	600	1200	75	600	1200
F0 parentals	mg/kg/day					
Week 1	9.39	59.83	94.90	8.17	69.77	82.52
Week 2	7.22	55.90	114.16	6.42	52.42	111.91
Week 4	5.38	45.35	90.73	5.86	44.28	86.21
Week 7	4.22	33.74	67.10	4.36	38.34	76.60
Week 10	3.42	27.47	58.88	4.22	33.01	66.29
Week 15	3.80	32.73	64.39	2.44	19.24	41.57
F1 parentals						
Week 1	18.64	156.79	268.88	18.44	151.25	300.00
Week 2	16.08	122.39	265.10	14.04	115.42	259.26
Week 4	8.89	69.91	144.35	8.08	67.42	152.83
Week 7	5.71	52.55	106.99	6.64	54.00	116.02
Week 10	4.56	39.00	79.88	5.46	41.64	98.65
Week 15	3.82	34.99	71.14	4.53	41.40	84.51

Table III14. Parental body weights as a function of dietary methomyl exposure in the 2-generation reproductive toxicity study of Lu (1982)

	Males (ppm)				Females (ppm)			
	0	75	600	1200	0	75	600	1200
F0 parentals	grams				grams			
Week -1	107.2	107.5	107.5	107.5	98.8	98.9	99.2	99.2
Week 1	167.5	169.3	171.5	167.8	138.0	140.4	139.3	139.6
Week 2	223.7	227.6	209.3**	187.0**	163.6	168.1	156.8*	146.9**
Week 4	323.1	337.3	303.0*	275.1**	208.9	211.1	199.2	190.7*
Week 7	407.1	435.9*	389.4	355.9**	255.1	254.4	237.9**	230.3**
Week 10	465.1	500.9*	439.0	405.8**	284.3	278.6	263.7**	254.7**
Week 15 [b]	536.0	570.1	489.4**	456.6**	308.6	301.4	286.9*	277.1**
Week 20 [c]	a	a	a	a	338.3	315.4*	298.4**	282.0**
Week 22	a	a	a	a	352.3	351.0	330.2	290.1**
F1 parentals								
Week 0	61.4	54.5	50.4	47.8*	59.2	54.9	48.6**	45.4**
Week 1	102.4	84.4	83.9	67.9**	93.5	87.1	75.9**	64.8**
Week 2	165.8	140.4*	126.8**	108.5**	139.3	128.2	112.9**	98.8**
Week 4	279.0	252.9	218.0**	188.9**	194.7	176.9**	163.6**	150.4**
Week 7	401.5	376.4	317.7**	284.1**	246.3	226.2**	206.5**	195.3**
Week 10	470.6	441.1*	371.7**	333.1**	272.1	255.6**	227.8**	221.5**
Week 15	494.9	458.4	404.4**	371.4**	292.8	280.9	248.4**	240.6**
Week 18 [b]	525.4	484.2	425.9**	389.7**	307.1	290.5*	257.8**	248.1**
Week 22 [c]	a	a	a	a	330.7	314.5	259.8**	245.3**
Week 30	a	a	a	a	328.6	323.0	274.2**	273.0**

*,**: p,0.05, 0.01 (Dunnett's test)
[a] F1 parental males were sacrificed after week 17, F2 after week 20
[b] Final week before mating
[c] First week for females after gestation

Table III15. Effect of dietary methomyl exposure on reproductive indices and pup weights and survival, F0 parental → F1 offspring (Lu, 1982)

	Dose (ppm)			
	0	75	600	1200
# F0 males on study	13	13	13	13
# F0 males FD + KE	0	0	0	0
# F0 females on study	26	26	26	26
# F0 females FD + KE	0	0	1 [a]	0
# F0 females pregnant	17	15	20	21
# F1 live litters (day 1)	17	15	17 [b]	19 [b]
Mean dead pups per litter (day 1)	0.6	0.3	0.4	0.4
# F1 live litters (day 21)	17	14	17	14
Mean live litter size (day 1) [c]	11.9	13.4	12.1	11.5
Mean live litter size (day 4)	11.8	12.9	11.4	7.8**
Mean live litter size (day 7) [d]	9.7	9.1	9.5	6.3**
Mean live litter size (day 14)	9.6	9.1	9.2	6.1**
Mean live litter size (day 21)	9.6	9.1	9.2	5.9**
Mean pup weight (day 1)	6.5	6.2	6.0**	5.6**
Mean pup weight (day 4)	9.4	8.5	7.9**	6.7**
Mean pup weight (day 7)[4]	14.5	13.5	11.6**	10.0**
Mean pup weight (day 14)	29.5	26.5**	22.7**	20.2**
Mean pup weight (day 21)	43.2	39.3*	34.2**	30.4**

Abbreviations: FD, found dead; KE, killed *in extremis*

*, ** $p < 0.05$ and $p < 0.01$, respectively (analysis by investigators)

[a] Section B, pages 7-8, and page 2 of Table 17.

[b] Two F0 females in each of these groups (600 and 1200 ppm) did not show signs of pregnancy, and were sacrificed. All four of these females were determined to be pregnant at autopsy. Thereafter females were not killed before allowing ample time to demonstrate gravid condition.

[c] Mean litter survival data are based on numbers of litters surviving on day 1 (compare summary data in Table 9 with individual data in Appendix L).

[d] Litters were culled to 10 pups after the day 4 litter evaluations (p. 5).

Table III.16. Effect of dietary methomyl exposure on reproductive indices and pup weights and survival, F1 parental → F2 offspring (Lu, 1982)

	Dose (mg/kg/day)			
	0	**75**	**600**	**1200**
# F1 males on study	20	20	20	20
# F1 males FD + KE	0	0	0	0
# F1 females on study	40	40	39 [b]	38 [c]
# F1 females FD + KE	0	1 [a]	0	0
# F1 females pregnant	31	31	31	31
# F2 live litters (day 1)	31	30	31	31
Mean dead pups per litter (day 1)	0.4	0.6	0.3	1.6**
# F2 live litters (day 21)	31	30	31	27
Mean live litter size (day 1)	12.8	11.0*	10.7*	10.1**
Mean live litter size (day 4)	12.5	10.6	9.7**	6.8**
Mean live litter size (day 7) [d]	9.6	8.9	8.6	6.3**
Mean live litter size (day 14)	9.6	8.9	8.6	6.2**
Mean live litter size (day 21)	9.5	8.9	8.6	6.2**
Mean pup weight (day 1)	6.3	6.3	5.7**	5.3**
Mean pup weight (day 4)	8.9	9.1	7.8**	6.9**
Mean pup weight (day 7)	14.0	13.9	11.5**	10.0**
Mean pup weight (day 14)	26.8	26.9	23.0**	19.9**
Mean pup weight (day 21)	40.2	40.2	34.7**	31.7**

Abbreviations: FD, found dead; KE, killed *in extremis*
*, ** $p < 0.05$ and $p < 0.01$, respectively (analysis by investigators).
[a] See p. 8 and Table 18, p. 2.
[b] One sibling mating was eliminated (Table 8). Although it does not appear to be stated in the report, it is probable that this was Dam #364, which no longer had pups by study day 4. Individual data for such parameters as body weight and food consumption typically did not censor this animal, however.
[c] Only 38 females were available at time of selection (p. 3).
[d] Litters were culled to 10 pups after the day 4 litter evaluations (p. 5).

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Shalaby *et al.* (2010) investigated the effects of methomyl (purity not stated; referred to as "a pure white crystal powder") and folic acid—alone and in combination—on reproductive capacity, testicular histopathology, sexual organ weights, semen status and serum testosterone levels in male Sprague-Dawley rats. The animals were exposed for 65 consecutive days—one spermatogenic cycle—to methomyl by oral gavage at 0.5 or 1 mg/kg/day. The doses, 1/40th and 1/20th of the acute LD_{50} of 20 mg/kg (determined by the authors), were associated with muscle tremors, abdominal cramps, sweating, muscle incoordination, irregular respiration and heart rate during the first 24 hr. The effects of folic acid (1.1 mg/kg/day; the acceptable daily intake) were examined because it is required for normal male fertility; it was thus of interest to see if it might counteract any adverse effects of methomyl on reproduction.

The authors observed dose-dependent declines in fertility index [6], testis and accessory male reproductive gland weights, serum testosterone levels, sperm motility and sperm counts (Table III-17). With the exception of fertility index, all of these effects were statistically significant[7]. Methomyl exposure also may have increased the incidence of sperm abnormalities, though statistical significance was not achieved. Finally, moderate-to-severe histopathology of the seminiferous tubules was observed at both doses. These effects were ameliorated by co-exposure to folic acid. The authors speculated that “the protective effect of folic acid against methomyl induced reproductive toxicity in male rats could be attributed to its positive role on homocysteine metabolism which is necessary for nomal spermatogenesis” (p. 3225). Partial reversal of the effects was evident after an additional 65-day methomyl-free period (data not summarized here).

The reproductive LOEL was 0.5 mg/kg/day (lowest dose tested), with a NOEL not observed. Lack of similar effects in the Lu (1982) study may be attributable to their use of dietary (as opposed to gavage) exposure, with resultant lower blood and tissue concentrations, and to its lack of specific concentration on spermatogenic toxicity. However, there were technical aspects of this study that were inadequately explained, particularly relating to the serial mating technique, as well as lack of clarity regarding the numbers of animals used. A letter was sent to Dr. Shalaby requesting clarifications (Appendix II). No response was forthcoming.

The Shalaby study was classified as supplemental.

Table III-17. Effects of oral methomyl (ML) and folic acid (FA) exposure for 65 days on reproductive parameters in male rats (Shalaby *et al.*, 2010)

	Control	0.5 mg/kg ML	1 mg/kg ML	1.1 mg/kg FA	0.5 mg/kg ML + 1.1 mg/kg FA	1 mg/kg ML + 1.1 mg/kg FA
Fertility index [a]	9/9 (100%)	7/9 (77.8%)	5/9 (55.6%)	9/9 (100%)	8/9 (88.9%)	6/9 (66.7%)
Testis weight (g)	2.69±0.01	2.09±0.02**	1.86±0.03**	2.67±0.07**	2.29±0.05**	2.25±0.03**
Semin. vesicle wt. (g)	1.82±0.03	1.11±0.04**	1.86±0.01**	1.85±0.03**	1.42±0.05**	1.37±0.01**
Prostate wt. (g)	0.564±0.02	0.458±0.01**	0.348±0.03**	0.563±0.02*	0.465±0.01**	0.43±0.01**
Sperm count, $10^{6/}$ per epididymis	71.67±0.40	64.67±0.33**	51.0±0.0**	73.67±0.18**	69.0±0.31**	65.0±0.31**
Sperm motility (%)	90.0±0.0	64±2.44**	50.0±0.0**	90.0±0.0	78.0±2.0**	70.0±0.0**
Sperm abnormalities (%)	2.66±0.17	3.33±0.18	3.67±0.16	2.33±0.15	2.53±0.20	3.33±0.28
Serum testosterone (ng/dl)	6.73±0.05	4.08±0.11**	3.30±0.04**	7.13±0.15**	5.64±0.09**	4.46±0.04**

[6] Fertility index = number of pregnant females ÷ number of mated females

[7] The absence of statistical significance for fertility index may be due to the fact that only nine males were exposed per dose, which decreased the statistical power of the observation.

*,**: $p<0.05$, 0.01
[a] Fertility index = number of pregnant females ÷ number of mated females

****

In an earlier open-literature study, Mahgoub and El-Medany (2001) noted extensive hormonal and histopathologic changes to the male Wistar rat reproductive tract after 60 days of daily oral exposure to 17 mg/kg methomyl (purity not stated; referred to as a "pure compound"). Three groups, each containing 8 males, were tested: (1) controls—1 ml saline/kg/day orally for 60 days; (2) 17 mg/kg methomyl in saline for 60 days, and (3) same as group 2, except those animals were left for 30 days after methomyl withdrawal. The hormonal and histopathologic changes included statistically significant decreases in testosterone and increases in FSH, LH and prolactin, as well as degenerative histopathology and histochemistry in male reproductive structures. These effects continued even after the exposure regimen was discontinued for a month, attesting to their relative permanence.

This study was considered to be supplemental.

****

Further evidence for toxic impacts of methomyl on male reproductive tissues was forthcoming from the study of Hemavathy and Krishnamurthy (1987b). Swiss albino mice were exposed by gavage to total doses of 20, 40 or 60 mg/kg Lannate 20 (20% methomyl administered as 5 divided doses separated by 24 hours). There were 5 males/dose. The LD_{50} was stated to be 80 mg/kg.

Statistically significant increases in percent abnormal sperm and sperm chromosome aberrations were noted at all three doses. Thus the LOEL for this study was 20 mg/kg Lannate 20. It was not clear from the text of the study whether this value represented the dose of methomyl or of the formulation as a whole. Nonetheless, the reproductive system impacts were sufficiently important to merit reporting in this document.

This study was considered to be supplemental.

Table III-18. NOEL and LOEL values for reproductive toxicity studies on methomyl

Species, strain	Study type & exposure regimen	Effects at LOEL	NOEL	LOEL	Reference
rat, CD	2-generation dietary	Parental: clinical signs & maternal wt. decrements Reproductive: reduced pre- & post-weaning pup wts	Parental: 75 ppm (~3.5 mg/kg/day during premating) Reproductive: 75 ppm (~3.5 mg/kg/day during premating)	Parental: 75 ppm (~18 mg/kg/day during late gestation) Reproductive: 75 ppm (~18 mg/kg/day during late gestation & pup growth)	Lu, 1982 *Acceptable*
rat, Wistar	2-month male dietary exposure	↓ testosterone, ↓ FSH, ↓ LH, ↓ prolactin, degenerative histopathology & histochemistry in male repro. tract	not determined	17 mg/kg/day (only dose tested)	Mahgoub & El-Medany, 2001 *Supplemental*
rat, SD	2-month male dietary exposure	↓ fertility index, ↓ testicular and male sex organ weights, ↓testosterone, ↓ sperm motility & count, ↑ sperm abnormalities, histopathology of seminiferous tubules	not determined	0.5 mg/kg/day (lowest dose tested)	Shalaby *et al.*, 2010 *Supplemental*
mouse, Swiss albino	acute administration of Lannate 20 (20% methomyl), 5 divided doses separated by 24-hr intervals	↑ abnormal sperm, ↑ sperm chromosome abnormalities	not determined	20 mg/kg [a]	Hemavathy & Krishnamurty, 1987b *Supplemental*

[a] It was not clear from the text of the study whether this value represented the dose of methomyl or of the formulation as a whole. Nonetheless, the reproductive system impacts were sufficiently important to merit reporting in this document.

G. DEVELOPMENTAL TOXICITY

Rogers and Culick (1978) fed methomyl (purity 99%) through the diet to 25 pregnant female Sprague-Dawley rats/group at 0, 50, 100 or 400 ppm on gestation days 6-15. These doses corresponded to average intakes of 0, 4.9, 9.4 and 33.9 mg/kg/day. Body weights, feed consumption and toxic signs were monitored throughout the study. The rats were euthanized on day 21, after which corpora lutea, implantation sites, live / dead fetuses, resorptions (early and late), fetal weights and crown-rump lengths and gross anomalies were recorded. Approximately half of the fetuses from each litter were preserved and stained for skeletal examination; the remaining fetuses were fixed and sectioned for visceral and neural anomalies.

All rats survived treatment. There were no clinical signs of toxicity during the study. Maternal weight gains were significantly curtailed at the high dose (average weight gain at ascending doses, days 6-15: 78, 78, 77 and 61 g; days 6-21: 156, 156, 157 and 143 g). Less food was consumed by the 100 and 400 ppm dose groups between days 6 and 16 (average food consumption, days 6-16: 24.0, 23.5, 22.5 and 19.6 g). There were no gross pathological changes that could be attributed to treatment. Pregancy outcomes, fetal development and presence of fetal malformations and major anomalies were also unaffected. While minor anomalies and variants in pups were noted throughout the dose range, none were related to treatment.

The maternal NOEL was determined to be 100 ppm (9.4 mg/kg/day) based on impacts on body weight and food consumption. The developmental NOEL was >400 ppm (>33.9 mg/kg/day). There was no evidence for teratogenicity in this study, which was considered to be acceptable by FIFRA standards.

^^^^^^^^^^^^^^^^^^^^

Feussner (1983) exposed 20 artificially-inseminated New Zealand White female rabbits by gavage to methomyl (purity: 98.7%) at 0, 2, 6 and 16 mg/kg/day (water vehicle, 5 ml/kg/day), gestation days 7-19. Does were sacrificed on gestation day 29. Clinical signs, body weights, feed consumption, corpora lutea, resorptions, live / dead fetuses, implantations (early and late), fetal weights, gross external / internal and skeletal fetal alterations, and soft tissue and skeletal histopathology were monitored.

One doe at 6 mg/kg/day and seven at 16 mg/kg/day were found dead during the study (a seventh high-dose animal died on gestation day 2, before commencement of dosing). The 6-mg/kg/day death may not have been treatment related—it occurred on day 27 (eight days after dose termination) and a pattern of signs indicative of severe methomyl toxicity was not observed. Clinical observations in does were restricted to the high dose. These included impaired or lost righting reflex (3/19), ataxia (3/19), convulsions (4/19*), hyperpnea (6/19**), aggressive behavior (7/19**), excessive salivation (7/19**), body jerks (8/19***), hyperactivity (11/19***) and tremors (13/19***); p<0.05, 0.01, 0.001. Neither reproductive nor developmental toxicity were evident.

The maternal NOEL was set at 6 mg/kg/day (deaths and clinical signs). The developmental NOEL was >16 mg/kg/day. This study was considered acceptable according to FIFRA guidelines.

Table III-19. NOEL and LOEL values for developmental toxicity studies on methomyl

Species, strain	Study type & exposure regimen	Effects at LOEL	NOEL	LOEL	Reference
rat, SD	dietary exposure, gestation days 6-15	maternal: body weight and food consumption impacts developmental: none	maternal: 100 ppm (9.4 mg/kg/day) developmental: >400 ppm (33.9 mg/kg/day)	maternal: >400 ppm (33.9 mg/kg/day) developmental: >400 ppm (33.9 mg/kg/day)	Rogers & Culick, 1978 *Acceptable*
rabbit, NZW	gavage exposure, gestation days 7-19	maternal: 7 deaths and tremors, hyperactivity, body jerks, salivation, convulsions and ataxia at the hdt of 16 mg/kg/day developmental: none	maternal: 6 mg/kg/day developmental: >16 mg/kg/day (hdt)	maternal: 16 mg/kg/day developmental: >16 mg/kg/day	Feussner, 1983 *Acceptable*

IV. RISK ASSESSMENT

A. HAZARD IDENTIFICATION

1. Non-oncogenic effects

a. Acute oral toxicity

The risk of toxicity from acute oral exposure to methomyl was estimated using a benchmark dose derived LED_{10} of **0.03 mg/kg**, which was calculated using RBC ChE inhibition data from the study of McFarlane *et al.* (1998). In that study, human males were exposed by capsule to a single dose containing 0, 0.1, 0.2 or 0.3 mg/kg methomyl. The theoretical basis for the analysis, which was performed by USEPA's National Computational Toxicology Center (Setzer, 2006a), is found in USEPA's cumulative carbamate risk assessment (USEPA, 2007b). The benchmark response level was set at 10% because that was the lowest level for which cholinesterase inhibition could be reliably measured. Setzer's empirical modeling utilized a dose-time mathematical response model, *i.e.*, one which took into account both the dose dependence and time dependence of cholinesterase inhibition. As noted in the cumulative assessment (USEPA, 2007b; p. 34):

> Several features of the dose-time response for the N-methyl carbarmates were to be captured in an empirical model:
>
> ❑ The rapid decline of ChE activity with increasing dose, perhaps after a "shoulder" at the low-dose end of the dose-response curve;
>
> ❑ A potential minimum level below which ChE activity will not drop, regardless of dose;
>
> ❑ The rapid decline of ChE activity after dosing to a minimum level which depends upon dose, then returns to the background level over a period of minutes to hours, at a rate that may also depend upon dose;
>
> ❑ Lack of early time points in most of the time course studies to accurately estimate the time of maximum effect, but instead start collecting data around a previously estimated time of maximum effect.
>
> The model described is the result of multiplying a dose-response model for inhibition that is closely related to the model that was successful at characterizing OP dose-response curves and a time-course model for inhibition. Transformations of parameters were used to enforce constraints, since the statistical software used for estimating model parameters does not incorporate bounded estimation (for example, to require that half-life estimates remain positive).

The equations used in the benchmark dose analysis are found on pages 35-37 of the cumulative assessment (USEPA, 2007b).

Inhibition of RBC ChE—which, like the brain enzyme, is an *acetyl*cholinesterase—is not unambiguously associated with toxicity in mammals. However, recent studies in rats show a close correspondence between RBC ChE inhibition, brain ChE inhibition and cholinergic effects for several carbamate pesticides including methomyl (Padilla *et al.*, 2007; McDaniel *et al.*, 2007). RBC ChE inhibition was thus considered a credible surrogate for more direct, though unobtainable, markers of cholinergic toxicity in humans. Moreover, the brain enzyme-based LOEL values from the various rat acute studies examined for this document were similar to the doses used in the human study (0.1 - 0.3 mg/kg) (Table III-1).

b. Subchronic oral toxicity

Risks from subchronic (seasonal) oral exposure to methomyl were estimated using the critical NOEL of 9.4 mg/kg/day—rounded to **9 mg/kg/day**—established in the 91-day rat dietary toxicity study of Mikles (1998b). This value, calculated by the study authors from a dietary NOEL of 150 ppm, was based on reduced body weight and food consumption, tremors during the first four weeks and beyond, FOB signs and brain ChE inhibition at the LOEL of 1500 ppm (♂, ♀: 94.9, 113 mg/kg/day). The enzyme inhibition and signs (clinical and FOB) were likely mechanistically related and mutually supported the establishment of 9 mg/kg/day as the critical subchronic NOEL.

The implications of, and possible reasons for, the 300-fold difference between the critical acute LED_{10} and the critical subchronic NOEL appear below in Section V. of this document.

c. Chronic oral toxicity

Risks from chronic (annual) oral exposure to methomyl were estimated using the critical NOEL of **3 mg/kg/day** established in the 2-year beagle dog dietary toxicity study of Busey (1968). This was estimated by the author from a dietary NOEL concentration of 100 ppm. It was based on pigmentation irregularity and swelling of kidney proximal tubule cells, pigmentation and extramedullary hematopoiesis in the spleen and bile duct hyperplasia at the LOEL dose of 400 ppm (11 - 14 mg/kg/day). Hematologic effects (reduction of RBC-related parameters) were noted at the high dose of 1000 ppm, which may have a relation to the extramedullary hematopoiesis noted at 400 ppm.

d. Acute, subchronic and chronic dermal toxicity

Risks from acute, subchronic and chronic dermal exposure to methomyl were estimated using the dermal critical NOEL of **90 mg/kg/day** established in the 21-day rabbit repeat-dose dermal toxicity study of Finlay (1997b). 90 mg/kg/day was the high dose employed in that study—there was no LOEL dose. Neither signs nor cholinesterase inhibition of any type were noted. The 21-day rabbit repeat-dose dermal study of Brock (1989) noted statistically significant increases in hyperreactivity incidence (*i.e.*, responsiveness to external stimuli) in males and decreased brain cholinesterase activity in both sexes at the 500 mg/kg/day, but not at 50 mg/kg/day. While the NOEL for that study was set at 5 mg/kg/day based on statistically significant plasma ChE inhibition and a suggestion of brain ChE inhibition (not statistically significant) at 50 mg/kg/day, those observations were considered inadequate to support a critical NOEL designation.

e. Acute inhalation toxicity

Risks from acute and short term inhalation exposures to methomyl were estimated using the acute LEC_{10} of **3.92** mg/m^3 (EC_{10} = 4.37 mg/m^3) from phase III of the rat inhalation study of Weinberg (2014) (air concentration dependence of RBC and brain cholinesterase inhibition). This value emerged from benchmark concentration modeling of brain cholinesterase inhibition following a single 3-hr inhalation exposure (Appendix I). The 10% benchmark response level was chosen based on USEPA's contention that "the 10% level is generally at or near the limit of sensitivity for discerning a statistically significant decrease in ChE activity in the brain compartment and is a response level close to the background brain ChE level" (USEPA, 2014; p. 56). This is supported by a power analysis performed by USEPA in conjunction with their organophosphate cumulative analysis that showed that a 10% level of brain cholinesterase inhibition was "at or near the limit of sensitivity for discerning a statistically significant decreasase in ChE activity in the [rat] brain compartment..." (USEPA, 2002b). Mild cholinergic signs—salivation and lacrimation---in addition to brain cholinesterase inhibition, were noted even at the lowest dose tested (5.6 mg/m^3), though these did not demonstrate pronounced dose responsivity and were not sufficient to change the default BMR.

The internal dose was estimated by multiplying the 3-hr LEC_{10} by the default rat inhalation rate of 0.04 m^3/kg/hr. A 1-hr rate was used despite the 3-hr exposure time because brain cholinesterase inhibition was shown to be stable at a single—albeit higher—air concentration (136 mg/m^3) between 1 and 6 hours during the 6-hr exposure period employed in phase II of the study. This suggested that an equilibrium was present by 1 hour.

$$(3.92 \text{ mg/m}^3) \times (0.04 \text{ m}^3\text{/kg/hr}) = \mathbf{0.16 \text{ mg/kg}}$$

We assumed the estimated internal dose of 0.16 mg/kg to be applicable to 1- and 8-hr human exposure scenarios. As there were no laboratory animal data for 24-hr exposures (which were applicable to resident bystanders), stable inhibition was assumed for that exposure length, as well.

Panepinto (1991) also evaluated the effects of inhalation exposure to methomyl in rats. As with Weinberg (2014), toxic signs were noted at the low dose. However, a much higher dose range was tested by Panepinto—0.137-0.326 mg/L, equivalent to 137-326 mg/m^3—compared to that used by Weinberg—5.6-105 mg/m^3—who also noted mild signs at the low dose. The markedly lower sensitivity of the Panepinto study (which appears to have been designed to determine an LC_{50}), combined with its lack of FOB or cholinesterase analyses, resulted in its exclusion from consideration as a critical study.

f. Subchronic inhalation toxicity

In the absence of a subchronic inhalation toxicity study, the seasonal risk from methomyl exposure will be assessed using the critical subchronic oral toxicity value of **9 mg/kg/day** established in rats by Mikles (1998b).

g. Chronic inhalation toxicity

In the absence of a chronic inhalation toxicity study, the annual risk from methomyl exposure will be assessed using the critical chronic oral toxicity value of **3 mg/kg/day** established in beagle dogs by Busey (1968).

h. Reproductive toxicity

The only FIFRA-compliant reproductive toxicity study, that of Lu (1982), did not indicate primary reproductive impacts. For this reason, a critical reproductive NOEL was not identified for this assessment. However, several subchronic oral gavage studies in male rats indicated methomyl-induced toxicity to the reproductive system. These are summarized in section III.F (Toxicity Profile: Reproductive Toxicity) and discussed further in section V.B.8 (Risk Appraisal).

i. Developmental toxicity

Neither of the two available FIFRA-compliant developmental toxicity studies—Rogers and Culick

(1978) in rats and Feussner (1983) in rabbits—indicated that methomyl had developmental impacts. A developmental neurotoxicity study was not identified.

g. Genotoxicity

One of four gene mutation studies on methomyl—the sex-linked lethality test in *Drosophila* (Hemavathy and Krishnamurty, 1987a)—was positive for gene mutation. In addition, a study using N-nitroso-methomyl was positive for increased mutation to 6-thioguanine resistance in Chinese hamster V79 cells (Wang *et al.*, 1998).

Seven of ten chomosome abnormality studies (Wei *et al*., 1997 [two different tests]; Bolognesi *et al.*, 1994; Bonatti *et al.*, 1994 [two different tests]; Hemavathy and Krishnamurty, 1987b; Amer *et al.*, 1996), including several *in vivo* and *in vitro* micronucleus studies, were positive, as were five of seven DNA damage studies (SRI, 1977b; Bolognesi *et al.*, 1994 [two different tests]; Bonatti *et al.*, 1994).

Based on these results, methomyl is considered to have genotoxic potential.

h. Immunotoxicity

No immunotoxicity studies have been reviewed for this document. Consequently, the risk of immune system impacts have not been estimated for this assessment.

2. Oncogenicity

Oncogenicity was not observed in FIFRA-compliant chronic studies conducted in dogs, rats or mice. For this reason, a quantitative tumor analysis was not carried out for this evaluation.

B. EXPOSURE ASSESSMENT

1. Introduction

Estimates of exposure to methomyl resulting from various occupational and bystander scenarios were developed by the Worker Health and Safety Branch (WH&S) of DPR. These, along with all of the calculations and assumptions that underlay those calculations, are contained in a companion document to this report entitled Estimation of Exposure of Persons in California to the Pesticide Products that Contain Methomyl (DPR, 2014). Exposure estimates from that document are summarized below and in the ensuing tables. In addition, this document estimates the potential for dietary exposure. That assessment is found in section 7 below.

2. Occupational handler exposure

Occupational handler exposure estimates—including acute absorbed daily dosages (acute ADDs),and long-term (annual) average daily dosages (AADDs)—are summarized in Table IV-1. Seasonal average daily dosages (SADDs) were not calculated for handlers because individuals were assumed to have been exposed throughout the year, in effect making a year into the seasonal exposure value and equating the SADD and AADD values (DPR, 2014; pp. 54-55). The handler exposure data were calculated by WH&S using surrogate data from the Pesticide Handlers Exposure Database (PHED). Assumptions made by PHED regarding application rates, acres treated/day, dermal and inhalation absorption and default body weights are detailed in the exposure assessment document (DPR, 2014).

Table IV-1. Occupational handler exposure to methomyl by the dermal and inhalation routes—short-term and annual estimates (DPR, 2014: Table 14)

Exposure scenario	Acute ADD (µg/kg/day) [a]		Long term (annual) ADD (µg/kg/day) [b]	
	Dermal	Inhalation	Dermal	Inhalation
Aerial applications [c]				
Mixer/loader, water soluble powder	422.7	16.2	152.0	5.9
Mixer/loader, liquid	443.6	6.8	159.7	2.5
Pilot	1728.0	32.7	621.0	11.7
Flagger	34.0	0.3	12.2	0.1
Airblast applications [d]				
Mixer/loader, water soluble powder	14.1	0.5	5.1	0.2
Mixer/loader, liquid	14.8	0.2	5.3	0.1
Applicator	370.3	9.1	132.9	3.3
Groundboom applications [e]				
Mixer/loader, water soluble powder	70.5	2.7	25.3	1.0
Mixer/loader, liquid	73.9	1.1	26.6	0.4
Applicator	100.7	10.6	36.3	3.8
Chemigation [f]				
Mixer/loader, water soluble powder	123.3	4.7	44.3	1.7
Mixer/loader, liquid	129.4	2.0	46.6	0.7
Hand spreader, bait [g]				
With gloves	546.6	4.0	196.2	1.4

Note: For details concerning the calculations of the values in this table, including the source of the raw data and the scenario-dependent requirements for personal protective equipment, see the indicated tables and text in DPR (2012). Assumptions: dermal absorption = 50%; inhalation rate = 16.7 L/min; inhalation absorption = 100%; body weight = 70 kg (mean for adult [♂ and ♀], U.S. population).

[a] Acute ADD [*i.e.*, acute absorbed daily dosage] = [(acute exposure) x (absorption) x (acres treated/day) x (application rate)] ÷ 70 kg bw. The acute exposure values are in Table 14 of DPR (2014). The absorption and acres treated/day values are in footnotes c-g below.

[b] Long-term ADD [*i.e.*, annual average daily dosage] = [long-term exposure x (absorption) x

(acres treated/day) x (application rate)] ÷ 70 kg. The long-term values are in Table 14 of DPR (2014). The absorption and acres treated/day values are in footnotes c-g below.

[c] Area treated was 1200 acres/day for mixer/loaders and 350 acres/day for pilots. The maximum application rate was 0.9 lb. methomyl/acre.

[d] Area treated was 40 acres/day. The maximum application rate was 0.9 lb. methomyl/acre.

[e] Area treated was 200 acres/day. The maximum application rate was 0.9 lb. methomyl/acre.

[f] Area treated was 350 acres/day. The maximum application rate was 0.9 lb. methomyl/acre.

[g] Formulations with 1% fly baits were considered. Area treated was 1 acre/day. The maximum application rate was 0.218 lb. methomyl/acre.

3. Exposure to landscape workers transplanting sod

Exposure to methomyl of landscape workers transplanting sod was evaluated using a surrogate study performed after a broadcast application of oxadiazon (DPR, 2014). The application rate was adjusted to the maximal rate of 0.9 lb/acre for methomyl. The presence of clothing representing a 90% protection factor was also assumed. Amortization calculations were carried out for exposures at 2 days (the REI; used for short-term exposures) and 7 days (the REI + 5 days; used for long-term exposures). Because it was assumed that turf can be transplanted on a year-round basis in California, annual use was set at 12 months/year. This equalized the seasonal and long-term ADDs.

The exposure values appear in Table IV-2.

Table IV-2. Exposure to methomyl by the dermal route in landscape workers transplanting sod—acute, seasonal and long-term (annual) estimates (DPR, 2014: Table 15)

Exposure scenario	Acute ADD (μg/kg/day) [a]	Seasonal ADD (μg/kg/day) [a]	Annual ADD (μg/kg/day) [b]
Sod transplantation	51.8	1.6	1.6

[a] Acute and seasonal ADD in μg/kg/day = [(DA) x (DFR) x (TC) x (ED)] ÷ BW

- DA, dermal absorption, assumed to be 50%
- DFR, dislodgeable foliar residue in $\mu g/cm^2$
- TC, transfer coefficient in cm^2/hr
- ED, exposure duration, assumed to be 8 hr/day
- BW, default body weight of 70 kg (mean of adult male and female population)

[b] Annual ADD in μg/kg/day = SADD x (annual use months/yr) (12 months in a year)

4. Occupational re-entry exposure

Occupational re-entry exposures were calculated by WH&S using dislodgeable foliar residue data (determined for methomyl in several studies), default transfer coefficients for surrogate chemicals and annual use estimates, as noted in DPR (2014). These exposures are summarized below in Table IV-3.

Table IV-3. Occupational re-entry exposure to methomyl by the dermal route—acute, seasonal and long-term (annual) estimates (DPR, 2014: Tables 16 and 17)

Exposure scenario	Acute ADD (µg/kg/day) [b]	Seasonal ADD [b] (µg/kg/day)	Annual ADD (µg/kg/day) [c]
alfalfa scouting, REI=2 days [a]	36.68	1.1486	0.5743
anise hand harvesting, PHI=7 days [a]	1.91	0.0571	0.0286
anise scouting, REI=2 days [a]	36.68	1.1486	0.5743
apple thinning, REI=3 days [a]	24.43	0.7714	0.3857
asparagus scouting, REI=2 days [a]	6.82	0.2143	0.1071
bean hand harvesting, REI=2 days [a]	34.10	1.0714	0.5357
blueberry hand harvesting, PHI=3 days [a]	12.21	0.3857	0.1929
cabbage hand harvesting, REI=2 days [a]	46.34	1.4571	0.7286
sweet corn hand harvesting, REI=2 days [a]	308.23	9.6171	4.8086
cotton scouting, REI=3 days [a]	8.18	0.1714	0.0857
cucumber thinning, REI=2 days [a]	34.10	1.0714	0.5357
lettuce hand harvesting, PHI=10 days [a]	0.23	0.0071	0.0071 [d]
lettuce scouting, REI=2 days [a]	34.01	1.0629	1.0629
green onion thinning, REI=2 days [a]	34.10	1.0714	0.5357
potato scouting, REI=2 days [b]	20.46	0.6429	0.3214

tomato hand harvesting, REI=2 days [a]	13.64	0.4286	0.2143

Abbreviations: REI, re-entry interval; PHI, pre-harvest interval.

[a] Data for all reentry tasks came from dislodgeable foliar residue values determined for methomyl in several studies and default transfer coefficients for surrogate chemicals. These details appear in DPR (2014), Tables 16 and 17.

[b] Acute and seasonal ADD in µg/kg/day = [(DA) x (DFR) x (TC) x (ED)] ÷ BW

- DA, dermal absorption, assumed to be 50%
- DFR, dislodgeable foliar residue in $\mu g/cm^2$
- TC, transfer coefficient in cm^2/hr
- ED, exposure duration, assumed to be 8 hr/day
- BW, default body weight of 70 kg (mean of adult male and female population)

[c] Annual ADD in µg/kg/day = SADD x (annual use months/yr) (12 months in a year). The annual use for lettuce is 12 months/yr. For all other crops it is 6 months/yr.

[d] Since the annual use on lettuce is 12 months (footnote c), the seasonal and annual ADDs are the same.

5. Non-occupational re-entry exposure: "U-Pick" re-entry operations

One set of non-occupational re-entry exposure scenarios that DPR (2014) considered to pose exposure risks were "U-Pick" operations, in which members of the general public enter commercial orchards to pick fruit. DPR (2014) chose four such operations in its examination of the methomyl exposure potential: sweet corn, blueberries, nectarines and peaches. Based on determinations of dislodgeable foliar residues at the designated re-entry interval or pre-harvest interval, half-lives and transfer coefficients, sweet corn U-Pick operations were expected to result in the highest acute absorbed doses, both for adults and for children (Table IV-4). Longer-term exposures were not expected in U-Pick operations.

Table IV-4. Acute dermal exposure to methomyl in U-Pick re-entry operations (DPR, 2014: Table 18)

Crop	Application rate (lb ai/acre)	REI or PHI (days)	Acute ADD (µg/kg/day) [a]
Sweet corn	0.45	2 (REI)	150.1 (adult) 68.9 (child)
Blueberries	0.9	2 (PHI)	39.6 (adult) 18.2 (child)
Nectarines	0.9	3 (REI)	64.6 (adult) 29.7 (child)
Peaches	0.9	4 (REI)	46.5 (adult) 21.4 (child)

Abbreviation: REI, re-entry interval; PHI, pre-harvest interval

[a] Acute ADD in µg/kg/day = [(DA) x (DFR) x (TC) x (ED)] ÷ BW

- DA, dermal absorption, assumed to be 50%
- DFR, dislodgeable foliar residue in $\mu g/cm^2$ (see DPR, 2014; Table 18)
- TC, transfer coefficient in cm^2/hr (see DPR, 2014; Table 18)
- ED, exposure duration, assumed to be 4 hr for adults and 2 hr for children
- BW, default body weight of 71.8 kg was assumed for adults, 39.1 kg for children

6. Bystander exposure at application sites

Workers or non-workers proximal to specific methomyl applications may be exposed to this pesticide by the inhalation route. One-hr and 24-hr exposure estimates for such individuals were calculated from field measurements made during a potato field application in San Diego County in August 1996 (DPR, 2014).

The 1-hr calculated dosages assumed that exposure occurred during periods of heavy physical activity and used the highest methomyl concentration detected during the first monitoring period (*i.e.*, 2 hours 45 minutes). The particular monitoring station receiving the highest detected air levels was located 40 meters northwest of the field. Short-term default breathing rates consistent with heavy activity were utilized in the dosage calculation.

In contrast to the 1-hr dosages, the 24-hr dosages assumed "a typical mixture of activity levels throughout the day [resulting in lower default breathing rates] and are based on the highest 24-hour and 14-hour time-weighted average (TWA) air concentrations for residential and occupational exposure, respectively". Both the 24-hr and 14-hr TWA concentrations came from measurements at a monitoring station located 10 meters to the west of the field.

Bystander exposure estimates appear in Table IV-5.

Table IV-5. Bystander inhalation exposure to methomyl near application sites (DPR, 2014: Table 19)

	Air concentration (μg/m^3)	Inhalation rate	Absorbed dose [a]
1-hr determinations (heavy activity)			
Infant resident	3.0082	0.250 m^3/kg/hr	0.75 μg/kg/hr [a]
Adult resident	3.0082	0.045 m^3/kg/hr	0.13 μg/kg/hr [a]
Worker bystander	3.0082	0.046 m^3/kg/hr	0.14 μg/kg/hr [a]
8-hr (worker) or 24-hr (resident) determinations			
Infant resident (24 hr)	1.9479	0.59 m^3/kg/24 hr	1.15 μg/kg/24 hr [b]
Adult resident (24 hr)	1.9479	0.28 m^3/kg/24 hr	0.55 μg/kg/24 hr [b]
Worker bystander (8 hr)	2.2377	0.13 m^3/kg/8 hr work day	0.29 μg/kg/8 hr work day [b]

[a] 1-hr absorbed dosage = (highest air concentration during application) x (inhalation rate)
[b] Acute ADD for 8-hr and 24-hr determinations = (TWA air concentration) x (inhalation rate)

7. Dietary exposure

Under the California Food Safety Act (AB-2161; Bronzan and Jones (1989)), the Department of Pesticide Regulation conducts acute and chronic dietary exposure assessments to evaluate the risk of human exposure to a pesticide in food. Two separate approaches are used to estimate the risk: (1) risk is determined for the total dietary exposure based on measured residue levels on all commodities with established tolerances, and (2) risk is estimated for exposure to an individual commodity at the tolerance level (see section VI. Tolerance Assessment).

Dietary exposure is the product of the amount of food that is consumed and the concentration of the pesticide residue in that food. The total exposure in an individual's diet for a defined time period is the sum of exposure from all foods consumed within that period, in various forms and as ingredients in processed food items.

Two distinct pieces of information were required to assess dietary exposure: (1) the amount of the pesticide residue in food, and (2) the food consumption (including drinking water). For estimating the acute exposure, either the highest residue values at or below the tolerance or the distribution of residues are considered. In contrast, for chronic exposure the mean residue values were considered. Acute exposure was calculated on a "per-user-day" basis, which includes in the distribution of exposures only those consumers who eat at least one of the assessed commodities in the consumption survey utilized by DEEM. (Note: USEPA calculates acute exposure on a per capita consumption basis, which factors in all members of a particular sub-population regardless of their commodity consumption. Per-user-day is, consequently, inherently more health conservative because it restricts the analysis to those who actually consume the commodities in question.) Chronic exposure to pesticides was calculated using per-capita mean consumption estimates.

Acute and chronic dietary (food and drinking water) exposure and risk assessments were conducted for methomyl using the Dietary Exposure Evaluation Model, DEEM-FCID™, Version 3.18, which uses food consumption data from the NHANES 2003-2008 survey. The complete analysis, including exposure and risk estimates for the general U.S. population and several population subgroups, appears below in Appendix IV. Results of both the acute and chronic dietary analyses are summarized in section IV.C.3.a. and IV.C.3.b. below.

C. RISK CHARACTERIZATION

1. Introduction

The potential for non-oncogenic health effects resulting from methomyl exposure is expressed as the margin of exposure (MOE). The MOE is the ratio of the critical NOEL or LED value, as derived from the definitive acute, subchronic or chronic studies, divided by the estimated exposure.

$$\text{Margin of Exposure (MOE)} = \frac{\text{NOEL or LED (mg/kg)}}{\text{Exposure dose (mg/kg)}}$$

In general, MOEs of 10 or more are considered protective of human health if the relevant adverse effects were observed in human experimental toxicity studies, as was this case with methomyl for acute oral and inhalation exposures. This reflects the default assumption that a 10-fold range of sensitivity exists between average and highly sensitive humans (the “intrahuman” factor).

On the other hand, MOEs of 100 are considered protective of human health if the relevant toxicologic effects were observed in experimental animal studies. The default assumptions in these cases include: (1) the intrahuman 10x factor, and (2) an interspecies 10x factor reflecting the assumption that average humans are 10-fold more sensitive than animals. The 100x factor applied to all adult exposure scenarios considered for this document *except* acute oral and inhalation. An additional 4x factor was relevant in scenarios in which children might be exposed. This factor was based on the observation of Malley (2005) that LED_{10}s for rat brain ChE were 0.1 and 0.36 mg/kg, a 3.6-fold difference.

Risks from acute, seasonal (subchronic) and annual (chronic) exposures were calculated. As there was no evidence from chronic toxicity studies that methomyl is an oncogen, estimation of oncogenic risk was not further pursued.

2. Worker and resident / bystander risk

As noted in the accompanying exposure assessment document (DPR, 2014) and summarized above in section IV.B., the exposure estimates for methomyl from non-dietary sources came from four places: (1) surrogate data in the Pesticide Handlers Exposure Database (PHED), which predicts both dermal and inhalation exposure to handlers, (2) reentry scenarios involving dermal exposure to fieldworkers through contact with dislodgeable foliar residues, (3) air monitoring studies designed to estimate bystander exposures by the inhalation route, and (4) residue studies on food items. The following sections provide the MOE values generated by those exposure scenarios for various categories of workers and bystanders.

a. Occupational handler and occupational reentry exposure risks

MOEs for occupational handler exposure scenarios appear in Table IV-6. Acute inhalation exposures posed higher risks (*i.e.*, had lower MOEs) than dermal exposures despite exhibiting lower exposure values due to the much lower acute value used to gauge inhalation risk. In fact, the majority of the analyzed scenarios exhibited MOEs lower than the target MOE of 100, including for aerial applications (mixer / loaders for both water-soluble powders and liquids, as well as pilots), for airblast applications (applicators), for groundboom applications (mixer / loaders for water-soluble powders, as well as applicators), for chemigation (mixer / loaders for both water-soluble powders and liquids), and for bait spreaders by hand (with gloves). All of the long term inhalation MOEs exceeded the target of 100.

All acute and long term dermal MOEs exceeded the target of 100 except for the acute exposure of aerial application pilots (MOE = 52).

Table IV-6. Risks from occupational handler exposure to methomyl by the dermal and inhalation routes—short-term and annual estimates

Exposure scenario	Acute MOE		Long term (annual) MOE	
	Dermal [a]	Inhalation [b]	Dermal [c]	Inhalation [d]
Aerial applications				
Mixer/loader, water soluble powder	213	10	592	508
Mixer/loader, liquid	203	24	564	1200
Pilot	52	5	145	256
Flagger	2647	533	7377	30,000
Airblast applications				
Mixer/loader, water soluble powder	6383	320	17,647	15,000
Mixer/loader, liquid	6081	800	16,981	30,000
Applicator	243	18	677	909
Groundboom applications				
Mixer/loader, water soluble powder	1277	59	3557	3000
Mixer/loader, liquid	1218	145	3383	7500
Applicator	894	15	2479	789
Chemigation				
Mixer/loader, water soluble powder	730	34	2032	1765
Mixer/loader, liquid	696	80	1944	4286
Hand spreader, bait				
With gloves	165	40	459	2143

Note: Exposure values appear in Table IV-1 and in Table 14 of DPR (2014). Details for each exposure scenario also appear in the latter reference.

[a] Acute dermal NOEL = 90 mg/kg, highest dose tested in rabbit 21-day study (Finlay, 1997b).

[b] Acute inhalation LEC_{10} = 0.16 mg/kg based on brain ChE inhibition in rats, inhalation route (Weinberg, 2014).

[c] Chronic dermal NOEL = 90 mg/kg/day (Finlay, 1997b).

[d] Chronic inhalation NOEL = 3 mg/kg/day (Busey, 1968).

b. Risks to landscape workers during sod transplantation

Risks to landscape workers posed by dermal exposure to methomyl during sod transplantation tasks are presented in Table IV-7 below. All MOEs were far above the relevant target MOE of 100.

Table IV-7. Risks to landscape workers from exposure to methomyl by the dermal route during sod transplantation—acute, seasonal and long-term (annual) estimates

	Acute MOE [a]	Seasonal MOE [a]	Annual MOE [a]
Sod transplantation	1737	56,250	56,250

See Table IV-2 and DPR (2014), Table 15, for references, details and calculations.

[a] Acute, seasonal and annual dermal NOEL = 90 mg/kg (Finlay, 1997b).

c. Occupational re-entry risks

MOEs for occupational acute, seasonal and long-term (annual) re-entry exposure scenarios appear in Table IV-8. Evaluation of risk in these cases assumed exposure only by the dermal route. All MOEs exceeded the target MOE of 100. In fact, there was no MOE below 292, recorded for acute exposure incurred during hand harvesting of sweet corn (REI=2 days).

Table IV-8. Risks from occupational re-entry exposure to methomyl by the dermal route—acute, seasonal and long-term (annual) estimates

	Acute MOE [a]	Seasonal MOE [a]	Annual MOE [a]
alfalfa scouting, REI=2 days	2454	78,356	156,713
anise hand harvesting, PHI=7 days	47,120	1,576,182	3,146,853
anise scouting, REI=2 days	2454	78,356	156,713
apple thinning, REI=3 days	3684	116,671	233,342
asparagus scouting, REI=2 days	13,196	419,972	843,336
bean hand harvesting, REI=2 days [b]	2639	84,002	168,004
blueberry hand harvesting, PHI=3 days	7371	233,342	466,563
cabbage hand harvesting, REI=2 days	1942	61,767	123,525
sweet corn hand harvesting, REI=2 days	292	9358	18,716
cotton scouting, REI=3 days	11,002	525,088	1,050,175
cucumber thinning, REI=2 days	2639	84,002	168,004
lettuce hand harvesting, PHI=10 days	391,304	12,676,056	12,676,056
lettuce scouting, REI=2 days	2646	84,674	84,674
green onion thinning, REI=2 days	2639	84,002	168,004
potato scouting, REI=2 days	4399	139,991	280,025
tomato hand harvesting, REI=2 days	6598	209,986	419,972

Abbreviations: REI, re-entry interval; PHI, pre-harvest interval; nd, not determined. See Table IV-3 and DPR (2014), Tables 16 and 17 for details of the exposure scenarios and calculations.

[a] Acute, seasonal and annual dermal NOEL = 90 mg/kg (Finlay, 1997b).

d. Risks incurred by participation in "U-Pick" operations (non-occupational)

Of the four "U-Pick" operations examined (sweet corn, blueberries, nectarines and peaches), sweet corn was found to generate the highest potential exposures and the highest calculated risk. MOEs for children were about half of those for adults. Seasonal and annual exposures were not considered likely for any of these U-Pick scenarios. The range MOEs of appears below in Table IV-9. Target MOEs (adults: 100; children: 400) were exceeded in each case.

Table IV-9. Acute exposure to methomyl in U-Pick re-entry operations

Crop	Application rate (lb ai/acre)	REI or PHI (days)	Acute MOE [a]
Sweet corn	0.45	2 (REI)	600 (adult) 1306 (child)
Blueberries	0.9	2 (PHI)	2273 (adult) 4945 (child)
Nectarines	0.9	3 (REI)	1393 (adult) 3030 (child)
Peaches	0.9	4 (REI)	1935 (adult) 4206 (child)

Abbreviation: REI, re-entry interval; PHI, pre-harvest interval. See Table IV-4 and DPR (2014), Table 18, for references, details and calculations.

[a] Acute dermal NOEL = 90 mg/kg (Finlay, 1997b).

e. Risk to bystanders from exposure at application sites

Bystanders at application sites may be exposed to methomyl by the inhalation route. Using the calculated absorbed doses and the critical inhalation LEC_{10} of 0.16 mg/kg/day, bystander MOEs ranged between 213 and 1231 for 1-hr determinations (heavy activity) and between 139 and 552 for 8-hr (worker bystander) or 24-hr (resident bystander) determinations. Both infant resident bystander exposure scenarios (1-hr and 24-hr) exhibited MOEs that were less than the infant inhalation target MOE of 400. The adult bystander 1- and 24-hr MOEs were greater than the adult inhalation target MOE of 100.

Seasonal or annual exposure scenarios were not expected.

Table IV-10. Risk to bystanders from inhalation exposure to methomyl near application sites.

	Absorbed dose	MOE [a]
1-hr determinations (heavy activity)		
Infant resident	0.75 µg/kg/hr	213
Adult resident	0.13 µg/kg/hr	1231
Worker bystander	0.14 µg/kg/hr	1143
8-hr (worker bystander) or 24-hr (resident bystander) determinations		
Infant resident (24 hr)	1.15 µg/kg/24 hr	139
Adult resident (24 hr)	0.55 µg/kg/24 hr	291
Worker bystander (8 hr)	0.29 µg/kg/8 hr work day	552

Note: Data in this table came from Table IV-5 above and from DPR (2014), Table 19. Details of application rates and other assumptions can be found there.

[a] Acute inhalation LEC_{10} = 0.16 mg/kg (Weinberg, 2014).

3. Dietary risk

a. Acute dietary, food-only and food-plus-drinking-water

A refined acute probabilistic exposure assessment was conducted for the general U.S. population and various population subgroups. The full assessment appears as Appendix IV of this report. It used primarily U. S. Department of Agriculture (USDA) Pesticide Data Program (PDP) monitoring data for 2000 through 2011 combined with percent crop treated (PCT) estimates provided in U.S. EPA's 2009 screening level usage analysis for methomyl. For a few commodities or food forms, tolerances or anticipated residues calculated by U.S. EPA were used as residue estimates. Exposures were aggregated by eating occasion rather than over 24 hours due to the specific mechanism of action of methomyl.

Exposure was calculated with and without drinking water, which was included as a point estimate at the limit of detection (LOD), 5.3 ppt, and with and without grape. (Methomyl use on grape was cancelled in December 2010, with some use allowed until December 2016 (Federal Register, 2012).)

The results indicate that at the 99.9th percentile of exposure, food-only dietary risk for children aged 1-2 years and 3-5 years exceeds the threshold of concern even when grape is excluded from the assessment. Exposure without grape was 163% of the aPAD (acute population adjusted dose) for children 1-2 years and 157% of the aPAD for children 3-5 years, corresponding to MOEs of 25 in both cases (target MOE for infants and children = 40). Inclusion of grapes resulted in much higher percent acute population adjusted doses.

When drinking water exposure is included in the assessment as a point estimate of 5.3 ppt, a concentration that appears to be quite conservative compared to the results of surface water monitoring and drinking water modeling studies, food-plus-water (excluding grape) dietary risk exceeds the threshold of concern for children aged 1-2 years and 3-5 years. Exposure was 159% of the aPAD for children 1-2 years and 160% of the aPAD for children 3-5 years, again corresponding to MOEs of 25 in both cases (target MOE = 40).

The commodities that contribute the most to exposure of children age 1-5 years are grape, apple (juice), cantaloupe, peanut, and lettuce. Federal tolerances for the following commodities were found to be health protective (calculated MOE > target MOE) for all populations: bell pepper, field corn, and peanut. Tolerances for the following commodities were not health protective (calculated MOE < target MOE) for one or more population groups: apple, avocado, broccoli, cantaloupe, grape, lettuce, nectarine, orange, peach, peanut, spinach, watermelon, and wheat. Thus the highest legal methomyl residues for these commodities do not exhibit health protective MOEs. Because DPR has measured methomyl residues at or near the tolerance for some of these commodities, USEPA should be informed of these results (see comment in section IV.B.7 regarding differences in acute exposure calculations between USEPA and DPR).

b. Chronic dietary, food and drinking water

A refined chronic dietary exposure assessment was conducted for the general U.S. population and various population subgroups using the same data sources described for the acute exposure assessment. Drinking water was included in the assessment as a point estimate at the limit of detection (LOD), 5.3 ppt.

The results indicate that dietary risk for food plus drinking water is below the threshold of concern for the general U.S. population and all population subgroups. The most highly exposed population subgroups, children 1-2 years and children 3-5 years, utilized only 0.2% of the cPAD.

As noted, the complete dietary exposure assessment appears as Appendix IV of this document.

V. RISK APPRAISAL

A. INTRODUCTION

Risk assessment is the process by which the toxicity of a compound is compared to the potential for human exposure under specific conditions in order to estimate the risk to human health. Every risk assessment has inherent limitations relating to the relevance and quality of the available toxicity and exposure data. Assumptions and extrapolations are incorporated into the hazard identification, dose-response assessment and exposure assessment processes. This results in uncertainty in the risk characterization, which integrates the information from the preceding three processes. Qualitatively, risk assessments for all chemicals have similar uncertainties. However, the extent of the uncertainty varies with the availability and quality of toxicity and exposure data, and with the relevance of that data to the anticipated exposure scenarios.

In the following sections, the specific areas of uncertainty associated with the characterization of health risks from dietary, inhalation and dermal exposure of both workers and the general public to methomyl are described.

B. HAZARD IDENTIFICATION

Selection of the appropriate laboratory animal toxicity studies to characterize human risk is a central task of pesticide risk assessment. Two factors influence the selection process: (1) the scientific quality of the studies in question, including the reliability of the data used to support the selection of critical LOELs, NOELs and LEDs, and (2) the relevance of the routes of exposure employed in those studies to the anticipated routes of human exposure in the field. These factors are discussed in the following sections as they relate to acute (short-term), subchronic (seasonal) and chronic (annual) exposure to methomyl. As noted above, an oncogenic assessment was not carried out because oncogenicity was not evident in the studies reviewed for this document.

Both the acute oral and acute inhalation endpoints are dependent on inhibition of cholinesterase activities (RBC cholinesterase in the case of acute oral and brain cholinesterase in the case of acute inhalation). In contrast to organophosphates, carbamates do not form irreversible inhibitory bonds with ChE molecules. Because of the relatively fast decarbamylation and enzymic re-activation reactions, standard methods of sample preparation for enzyme assay may underestimate the extent of peak inhibition. This is because such assays utilize extended incubation times at 37°C and large dilutions in buffer, both of which favor the decarbamylation-reactivation process. Efforts launched in the 1990s were directed toward ChE assay techniques that take into account the carbamate dissociation problem (Padilla and Hooper, 1992; Nostrandt *et al.,* 1993), though such techniques do not appear to have been utilized in most analyses of methomyl-exposed tissues examined for this document. This methodological conundrum is viewed as a limitation in the present risk evaluation. Even so, assessments of carbamate-ChE interactions by the USEPA support the validity of the standard Ellman assay for most carbamate pesticides examined(USEPA, 2005, 2007b).

1. Acute oral toxicity

Inhibition of RBC ChE in human males exposed to methomyl through a single capsular dose was the basis for the critical acute LED_{10} determination of 0.03 mg/kg (McFarlane *et al.*, 1998; Setzer, 2006a). Statistically significant inhibition of this enzyme occurred both at the high dose of 0.3 mg/kg (achieving a maximum of 35.25% at 30-45 min post dose) and at the mid dose of 0.2 mg/kg (maximum of 27.87% between 1 hr 15 min and 1 hr 30 min). Inhibition at 0.1 mg/kg, while not statistically significant, reached 19.04% at 1 hr 15 minutes, roughly coinciding with the peak inhibition seen at 0.2 and 0.3 mg/kg. Because inhibition was plausibly present at the low dose, benchmark dose modeling was conducted by the US EPA's Center for Computational Toxicology, establishing the 0.03 mg/kg LED_{10} (Setzer, 2006a).

The major uncertainty associated with use of RBC ChE inhibition as a critical endpoint is that it is not unambiguously associated with toxicity. Rather, RBC ChE inhibition is used here primarily as a surrogate for brain ChE inhibition, which underlies cholinergic neurotoxicity in the central nervous system but is not subject to measurement in humans. Because both the RBC and brain ChEs are *acetyl*cholinesterases, this document assumes that inhibition of one signifies inhibition of the other. Such appears to be the case in recent studies conducted in rats—a correspondence between RBC ChE inhibition, brain ChE inhibition and cholinergic effects is evident for several carbamate pesticides including methomyl (Padilla *et al.*, 2007; McDaniel *et al.*, 2007). Even so, a 2005-2006 Department of Pesticide Regulation internal analysis of registrant-submitted acute oral studies on organophosphates did not indicate a consistent relationship between the NOELs established for RBC and brain ChE. Five of those 12 chemicals exhibited equivalent NOELs for the two enzymes, while 4 showed a lower NOEL for RBC ChE and 3 showed a lower NOEL for brain ChE. Similar inconsistencies were evident when NOELs for RBC ChE and neurobehavioral endpoints were compared.

Despite designating RBC ChE inhibition as a surrogate for brain ChE inhibition, there are several proposed physiological roles for the RBC enzyme that may point to modes of toxicity independent of the brain enzyme. These include (1) a protective role (along with butyryl ChE) as a scavenger for circulating ChE inhibitors (Wills, 1972; Jimmerson, 1989), (2) a role in hematopoiesis (Silver, 1974), and (3) a role in membrane permeability (Silver, 1974). However, these remain speculative at present.

Uncertainty was also inherent in the use of benchmark dose (BMD) modeling to determine the acute value. BMD modeling avoids the pitfalls associated with setting LOEL and NOEL values (which were, in any case, irrelevant in the McFarlane study since inhibition was noted at the low dose), allowing more of the dataset to be used to determine the critical value. But there was major uncertainty associated with the chosen benchmark response level of 10%, since the actual toxicity, or even the meaning, of RBC ChE inhibition was unclear. As DPR opted to depend on USEPA's analysis (see section IV.A.1.a. for a detailed discussion), the 10% response level they adopted was maintained for this document.

Uncertainty was introduced into the critical oral study and several of the support studies by utilization of gavage as the oral dosing technique. Gavage dosing is likely to result in a more precipitous rise in blood pesticide levels than dietary intake over a single eating occasion or single day. Depending on the pharmacokinetics of methomyl toxicity, in particular whether acute toxicity is more influenced by the highest achieved concentration or the total concentration over a finite time span (*i.e.*, the area under the time-*vs.*-concentration curve), gavage dosing may generate a more severe response than acute dietary exposure. Also, decarbamylation of impacted cholinesterases may be more prominent under dietary than under gavage dosing scenarios due to the more gradual pesticide-enzyme interaction. Reactivation of cholinesterases over the exposure period would probably act to lessen the dietary response more than the gavage response.

Finally, uncertainty in the acute, subchronic and chronic designations derived from a lack of measurements of more subtle neurologic and developmental impacts (USEPA, 2012), some of which may be independent of cholinesterase inhibition and have long-term consequences. These are mentioned below under Developmental Toxicity (section 9).

2. Subchronic oral toxicity

A major uncertainty with respect to the critical subchronic oral NOEL designation of 9 mg/kg/day (Mikles, 1998b) resided in the observation that it is 300 times higher than the acute value of 0.03 mg/kg (McFarlane *et al.*, 1998; Setzer, 2006a). For most chemicals, longer exposure times are expected to yield lower LOELs and NOELs. However, this is less the case for cholinergic compounds, where longer exposures result in adaptation with respect to cholinergic endpoints. In addition, the acute endpoint, RBC cholinesterase inhibition, was derived from a human study, while the subchronic study was conducted in rats, which may be less sensitive to this compound. This also meant that an additional 10-fold uncertainty factor was applied to the target MOEs in the subchronic and chronic oral cases, reducing the effective gulf between those endpoint values and the acute value. In any case, it was assumed that regulation based on the acute endpoint will accordingly protect from effects requiring longer exposure times.

Because of the ~10-fold difference between the LOEL and NOEL doses, BMD modeling may be an option to arrive at a more refined—and perhaps higher---critical regulatory value. However, the data were not amenable to modeling since the major effects (reduced body weight and food consumption, tremors during the first four weeks and beyond, FOB signs and brain ChE inhibition) were noted only at the high (*i.e.*, the LOEL) dose.

It might be argued that the 3.5 mg/kg/day NOEL from the rat reproductive toxicity study of Lu (1982) better represented the potential for subchronic toxicity. However, the pup weight deficits noted at the LOEL of 14 mg/kg/day were marginal (<10%) and may have been acutely induced. Similarly, the LOEL of 0.5 mg/kg/day (ldt) determined in the male reproductive toxicity study of Shalaby *et al.* (2012), which was based on spermatogenic toxicity, might also be considered a critical subchronic value. However, technical questions in that open-literature study precluded it from consideration as a critical study (see detailed summary in section III.F., as well as in Appendix II).

3. Chronic oral toxicity

The primary uncertainty associated with the critical chronic oral toxicity endpoint of 3 mg/kg/day (Busey, 1968) was that it was based on histopathologic signs of uncertain toxicity and meaning[8]. In particular, since the study did not measure brain ChE, it was plausible that there were effects at chronic doses that were lower than those necessary to produce toxic signs.

[8] These signs included pigmentation irregularity and swelling of kidney proximal tubule cells, and pigmentation and splenic extramedullary hematopoiesis.

Like the subchronic value, the chronic value was much higher (100-fold) than the acute value. Thus there was a likelihood that protection from acute toxicity would also protect from chronic toxicity.

4. Acute, subchronic and chronic dermal toxicity

The major uncertainty with the 90 mg/kg/day critical dermal NOEL designation lay with the fact that this concentration was the high dose in the critical 21-day dermal study of Finlay (1997b). This precluded LOEL identification and suggested that the applied doses were not sufficiently high to allow appreciable dermal penetration. A similar study by Brock (1989) noted increases in hyperreactivity and decreased brain cholinesterase activity 500 mg/kg/day. Brock also noted a slight, though nonstatistically significant, inhibition of brain ChE at 50 mg/kg/day, raising the possibility of unobserved toxicity at that concentration. While Brock's data were not inconsistent with an effect at 50 mg/kg/day, Finlay's observation of no toxicity—including no brain ChE inhibition—even at 90 mg/kg/day minimized the possibility that the critical NOEL was too high.

5. Acute inhalation toxicity

The most prominent uncertainty associated with the acute inhalation critical LEC_{10} of 0.16 mg/kg was the use of 1 hour as the time of maximal brain cholinesterase inhibition. This was based on Weinberg's observation in study phase II that a fixed exposure at 136 mg/m^3 resulted in maximal brain and RBC ChE inhibition by 1 hr, with no subsequent change over the 6-hr exposure period (65-69% inhibition in brain, 73-84% in RBCs of either sex) (Weinberg, 2014). The importance of this observation resided in the fact that the LEC_{10} air level, determined in phase III of the study, was actually 3.92 mg/m^3 (section IV.A.I.e.), much lower than the concentrations used in phase II. Thus if the kinetics of enzyme inhibition at low doses is different than at higher doses, the human-equivalent LEC_{10} would also be proportionately different. For example, were the maximal inhibition time at low doses actually 4 hours instead of 1 hour, the resultant equivalent dose would be 0.64 mg/kg, 4-fold higher than the calculated critical value.

Another uncertainty attached to the 0.16 mg/kg critical inhalation value was the use of 10% as the benchmark response level. This was a default based on USEPA's contention that 10% was at the low end of detectability in standard rat brain cholinesterase inhibition studies (USEPA, 2014). However, mild clinical signs—salivation and lacrimation—were present in addition to brain cholinesterase inhibition at all doses employed in the Weinberg (2014) study, including the low dose of 5.6 mg/m^3, albeit at low incidence rates. This suggested that the degree of inhibition at that dose was sufficient to have an overt toxicologic effect in some animals, which is not always observed at low brain cholinesterase inhibition levels. A benchmark response level of 5%—which generated an LED_{05} of 1.85 mg/m^3 (0.07 mg/kg) using Hill modeling—would decrease all of the acute inhalation MOEs by ~2-fold.

Finally, there was minor uncertainty associated with the choice of the Hill algorithm to model the brain cholinesterase results. Hill was chosen from among 8 algorithms because it exhibited the lowest AIC number and scaled residual, as well as the highest *p* value (see tabulated comparison at the end of Appendix I). Nonetheless, it is possible that inhibition at very low doses (*i.e.*, below the lowest dose employed in this study) might not be well characterized by Hill-generated kinetics.

6. Subchronic inhalation toxicity

As was the case for estimation of acute and chronic inhalation risk, subchronic inhalation risk was estimated using the critical oral subchronic value of 9 mg/kg/day (Mikles, 1998b). Uncertainty was inherent in the route extrapolation.

7. Chronic inhalation toxicity

As was the case for estimation of acute and subchronic inhalation risk, chronic inhalation risk was estimated using the critical oral chronic value of 3 mg/kg/day (Busey, 1968). Uncertainty was inherent in the route extrapolation.

8. Reproductive toxicity

Despite the apparent absence of overt reproductive toxicity in the FIFRA-acceptable study of Lu (1982), three subchronic oral gavage studies in male rats indicated methomyl-induced toxicity to the reproductive system. The most prominent in this regard was the study of Shalaby (2010), which demonstrated decreased fertility index (though low sample numbers precluded definitive conclusions on this parameter), decreased testicular and male sex organ weights, decreased testosterone, decreased sperm motility and count, increased sperm abnormalities, and histopathological changes in the seminiferous tubules at gavage doses as low as 0.5 mg/kg/day. In addition, both Mahgoub and El-Medany (2001) and Hemavathy and Krishnamurthy (1987b) showed male reproductive system impacts in rats, though at higher doses. Finally, recent human health risk assessments by the Department of Pesticide Regulation on two other carbamate insecticides, carbofuran (DPR, 2006) and carbaryl (DPR, 2010), provided evidence for toxic reproductive system impacts.

9. Developmental toxicity

No evidence for developmental toxicity emerged from the rat or rabbit developmental toxicity studies reviewed for this document (rat: Rogers and Culick, 1978; rabbit: Feussner, 1983). However, an epidemiologic study in California that used a hierarchical multiple-pesticide model suggested an association between neural tube defects in offspring and ambient maternal exposure, which was ascertained by linking maternal addresses with records of pesticide applications (Rull *et al*., 2006). In addition, there is growing awareness that fetal or early-life exposure to cholinesterase inhibitors may have neurodevelopmental consequences in humans. This was most clearly demonstrated in the case of the organophosphate insecticide chlorpyrifos (*eg*., Rauh *et al.,* 2006 and 2012). Impacts on behavior, intelligence and/or brain structure may be independent of cholinesterase inhibition and occur at doses too low to induce overt clinical signs, making them difficult to detect in standardized animal testing. Thus the lack a specific developmental neurotoxicity study on methomyl in laboratory animals constitutes an uncertainty in the present context.

10. Genotoxicity

With two of five gene mutation studies, 7/10 chomosome abnormality studies and 5/7 DNA damage studies registering positive, methomyl is considered to have genotoxic potential.

11. Immunotoxicity

In the absence of an immunotoxicity study, no risk estimates were made regarding the possibility of immune system impacts. While this is an uncertainty in the current context, it is worth noting that USEPA waived the immunotoxicity study requirement for methomyl.

C. RISK CHARACTERIZATION

Non-oncogenic risk was evaluated by use of the margin of exposure (MOE) ratio, equivalent to the critical NOEL or LED divided by the anticipated exposure. The MOE approach was described above in secion IV.C.1. Uncertainties were introduced into MOE calculations by uncertainties in both the NOEL and exposure terms. These were documented in the preceding sections and in the accompanying exposure assessment document (DPR, 2014).

It is worth reemphasizing the uncertainty inherent in MOEs that employ RBC ChE inhibition as the toxicity endpoint. Such was the case in this document with respect to the calculation of acute oral and inhalation risk (for full discussion, see section IV.C.1.a.). Without an overt connection to toxicity, such MOEs may over- or underestimate risk depending on the degree of correlation between RBC and brain ChE inhibition, and between RBC ChE inhibition and toxicity endpoints (particularly neurodevelopmental) that were not measurable.

Furthermore, this assessment recognizes the possibility that neurodevelopmental endpoints that are mechanistically *independent* of cholinesterase inhibition may be relevant to any of the exposure scenarios examined here, particularly if they involve pregnant women, infants or young children.

D. CRITICAL TOXICITY ENDPOINTS—USEPA vs. DPR

USEPA first identified its critical toxicologic endpoints for methomyl in a Reregistration Eligibility Decision document (RED) dated December 1998 (USEPA, 1998). In an update of the dietary risk assessment (USEPA, 2007), the critical acute oral endpoint was revised to take into account the analysis of the McFarlane (1998) human study, as well as to establish time courses for effects on rat RBC and brain cholinesterases and a child protective (FQPA) factor. In the following paragraphs, as well as in Table V-1, these values are compared to DPR values established in the present document.

1. Acute oral toxicity

USEPA and DPR use the same critical oral LED_{10} value of 0.03 mg/kg based on RBC ChE inhibition in human males following a single capsular dose (McFarlane, 1998; Setzer, 2006a).

2. Subchronic oral toxicity

USEPA did not discuss the possibility of risk from seasonal exposure to methomyl in its 1998 RED or in its 2007 revised dietary assessment. For its part, DPR used the subchronic NOEL of 9 mg/kg/day established in the 91-day rat dietary toxicity study of Mikles (1998b) to estimate seasonal risk. This value, which was calculated from a NOEL concentration of 150 ppm in the feed, was based on reduced body weight and food consumption, tremors (first four wks and later), FOB signs and brain ChE inhibition at the LOEL of 1500 ppm.

3. Chronic oral toxicity

USEPA and DPR used the same dog study (Busey, 1968) and histopathologic endpoints (pigmentation irregularity and swelling of kidney proximal tubule cells, and pigmentation and extramedullary hematopoiesis in the spleen) to establish critical chronic oral NOELs of 2.5 mg/kg/day (USEPA) and 3 mg/kg/day (DPR). The reason for the slight difference in assigned NOELs is that USEPA determined internal doses by converting the dietary concentrations (expressed in the study in ppm) using a standard dog conversion ratio, while DPR calculated mean doses from the monthly methomyl intakes provided in the study.

4. Acute, subchronic and chronic dermal toxicity

Though not explicitly stated in their RED, USEPA appears to consider dermal risk to arise only from short- and intermediate-term occupational exposure scenarios (USEPA, 1998). For these, USEPA used the NOEL of 90 mg/kg/day established in the 21-day dermal toxicity study of Finlay (1997b). In this document, DPR also uses 90 mg/kg/day from the Finlay study to gauge acute, seasonal and annual risk.

5. Acute inhalation toxicity

USEPA used the NOEL of 0.137 mg/L from Panepinto (1991) after transformation to an internal dose of 37 mg/kg/day to estimate acute inhalation risk. The calculation underlying this transformation is, however, unclear and possibly incorrect (see page 50 of the EPA document (USEPA, 1998)).

In any case, the lack of FOB and cholinesterase data in the Panepinto study, combined with the much higher doses used in that study (0.137-0.326 mg/L, equivalent to 137-326 mg/m^3) compared to the critical Weinberg (2014) study (5.6-105 mg/m^3), made it inadequate to assess inhalation risk in the present assessment [9]. Instead, we chose the LEC_{10} of 3.92 mg/m^3 (0.16 mg/kg) from the Weinberg study (2014) to estimate acute inhalation risk.

6. Subchronic and chronic inhalation toxicity

As with acute inhalation toxicity, USEPA used the NOEL of 0.137 mg/L from Panepinto (1991) after transformation to an internal dose of 37 mg/kg/day to estimate "intermediate" and "long-term" inhalation risk. DPR, after rejecting Panepinto as inadequate to support critical NOEL designations, opted to use the subchronic oral value of 9 mg/kg/day (Mikles, 1998b) to estimate seasonal inhalation risk and the chronic oral value of 3 mg/kg/day (Busey, 1968) to estimate annual inhalation risk.

7. Oncogenicity

USEPA and DPR agree that the chronic studies on methomyl do not suggest an oncogenic risk.

8. Reproductive and developmental toxicity

In its 2007 dietary risk assessment on methomyl, USEPA adopted a 2x FQPA child protection factor based on the observation by Malley (2005) that RBC and brain cholinesterases in postnatal day (pnd) 11 (newborn) rats were more sensitive to orally administered methomyl than similar enzymes in adult rats (USEPA, 2007a). USEPA used newborn and adult BMD_{10} values derived by Setzer's analysis of the RBC ChE data, which they favored over brain because the RBC enzyme was more sensitive (*i.e.*, had lower BMDs) to methomyl-induced inhibition (Setzer, 2006b and 2006c) [10], to arrive at the 2x value. Even so, the BMD_{10} for the adult RBC ChE was actually 3.3-fold greater than the pnd11 BMD_{10}, raising the question as to why they adopted a child protection factor of only 2. For the current analysis, we have adopted a factor of 4 based on the 3.6-fold greater sensitivity of the pnd11 *brain* ChE to methomyl compared to the adult enzyme. For further discussion of this issue, see section VII.A. below.

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[9] The USEPA did not have access to the Weinberg study at the time of their 1998 assessement.

[10] USEPA's reason for choosing RBC ChE inhibition data over that of the brain enzyme—that the "RBC compartment was also more sensitive than brain AChE activity" (USEPA, 2007; p. 5)—is not clear, particularly as the sensitivity difference between pnd11 and adult animals is actually greater for the brain enzyme.

Table V-1. Critical toxicity endpoints for methomyl: USEPA *vs*. DPR

Study type	USEPA (USEPA, 1998 & 2007)	DPR
Acute oral toxicity	**McFarlane *et al.* (1998); Setzer (2006a)** **Acute oral toxicity—human** LOEL not determined (RBC ChEI) LED_{10} = 0.03 mg/kg	**McFarlane *et al.* (1998); Setzer (2006a)** **Acute oral toxicity—human** LOEL = 0.1 mg/kg (ldt, RBC ChEI) LED_{10} = 0.03 mg/kg
Subchronic oral toxicity	Not determined	**Mikles (1998b)** **Subchronic oral toxicity—rat** LOEL = 1500 ppm (⇓ body weight and food consumption, tremors, FOB signs and brain ChEI) NOEL = 150 ppm (~9 mg/kg/day)
Chronic oral toxicity	**Busey (1968)** **Chronic oral toxicity—dog** LOEL = 400 ppm (pigmentation irregularity and swelling of kidney proximal tubule cells, and pigmentation and extramedullary hematopoiesis in the spleen) NOEL = 100 ppm (~2.5 mg/kg/day) [a]	**Busey (1968)** **Chronic oral toxicity—dog** LOEL = 400 ppm (pigmentation irregularity and swelling of kidney proximal tubule cells, and pigmentation and extramedullary hematopoiesis in the spleen, bile duct hyperplasia) NOEL = 100 ppm (~3 mg/kg/day) [a]
Acute, subchronic and chronic dermal toxicity	**Finlay (1997b)** **21-day dermal toxicity—rabbit** LOEL > 90 mg/kg/day (hdt) NOEL = 90 mg/kg/day	**Finlay (1997b)** **21-day dermal toxicity—rabbit** LOEL > 90 mg/kg/day (hdt) NOEL = 90 mg/kg/day
Acute inhalation toxicity	**Panepinto (1991)** **Acute inhalation toxicity—rat** LOEL = 0.182 mg/L (death and toxic signs) NOEL = 0.137 mg/L (~37 mg/kg) [b]	**Weinberg (2014** **Acute inhalation toxicity—rat** LOEL = 5.6 mg/m^3 (brain ChEI) (ldt) LEC_{10} = 3.92 mg/m^3 (0.16 mg/kg)
Subchronic inhalation toxicity	**Panepinto (1991)** **Acute inhalation toxicity—rat** LOEL = 0.182 mg/L (death and toxic signs) NOEL = 0.137 mg/L (~37 mg/kg) [b]	**Mikles (1998b)** **Subchronic oral toxicity—rat** LOEL = 1500 ppm (⇓ body weight and food consumption, tremors, FOB signs and brain ChEI) NOEL = 150 ppm (~9 mg/kg/day)
Chronic inhalation toxicity	**Panepinto (1991)** **Acute inhalation toxicity—rat** LOEL = 0.182 mg/L (death and toxic signs) NOEL = 0.137 mg/L (~37 mg/kg) [b]	**Busey (1968)** **Chronic oral toxicity—dog** LOEL = 400 ppm (pigmentation irregularity and swelling of kidney proximal tubule cells, and pigmentation and extramedullary hematopoiesis in the spleen) NOEL = 100 ppm (~3 mg/kg/day) [a]
Oncogenicity	No evidence for oncogenicity	No evidence for oncogenicity

Abbreviations: hdt, highest dose tested; ldt, lowest dose tested
[a] The reason for the slight difference in calculated NOELs is that USEPA determined internal doses by converting the dietary concentrations (expressed in the study in ppm) using a standard dog conversion ratio, while DPR calculated mean doses from the monthly methomyl intakes provided in the study.

[b] The US EPA calculation that resulted in the establishment of the 37 mg/kg internal dose was unclear. Using the same air concentration NOEL of 0.137 mg/L, DPR calculated the internal dose to be 0.3 mg/kg.

VI. ISSUES RELATED TO THE FOOD QUALITY PROTECTION ACT

The Food Quality Protection Act (FQPA) of 1996 mandated the USEPA to "upgrade its risk assessment process as part of the tolerance setting procedures" (USEPA, 1997a and b). The improvements to risk assessment were based on recommendations made in the 1993 National Academy of Sciences report, "Pesticides in the Diets of Infants and Children" (NRC, 1993). The Act required an explicit finding that tolerances are safe for children. USEPA was required to use an extra 10-fold safety factor to take into account potential pre- and post-natal developmental toxicity and the completeness of the data, unless USEPA determined, based on reliable data, that a different margin was warranted. Based on the analysis provided in DPR's dietary assessment of methomyl (Appendix IV), which showed MOEs of less than 20 for infant and age 1-2 yr subpopulations (distributional analysis, 99.9th percentile), it appears that the extra 10-fold factor should be considered.

FQPA also requires the USEPA to consider available information on: 1) aggregate exposure from all non-occupational sources; 2) effects of cumulative exposure to the pesticide and other substances with common mechanisms of toxicity; 3) the effects of *in utero* exposure; and 4) the potential for endocrine disrupting effects.

A. AGGREGATE EXPOSURE AND RISK

When considered together, the dietary assessment (Appendix IV) and DPR's exposure assessment (DPR, 2014) suggest a potential for simultaneous exposure to methomyl by the oral, dermal and/or inhalation routes. Since toxicologic impacts are plausible at least by the oral and inhalation routes, an aggregate health evaluation would seem to be in order to gauge the possibility of even greater impacts. However, the ability to do a valid aggregate analysis was, in the acute case, impeded by the fact that the critical oral LED_{10} derived from a human study, while the critical dermal NOEL and critical inhalation LEC_{10} came from laboratory animal studies. As noted in Table VII.1 below, the target MOEs were different because an interspecies uncertainty factor was not required for acute oral exposure, while it was for dermal and inhalation. Thus an aggregate risk calculation that includes oral exposure with either dermal or inhalation exposure is of uncertain meaning because it is not clear which target MOE is appropriate. Moreover, the critical toxicologic endpoints for the three exposure routes—*oral*: RBC cholinesterase inhibition; *dermal*: no LOEL (therefore no actual toxicologic endpoint); *inhalation*: brain cholinesterase inhibition—were different, rendering an aggregate risk calculation effectively impossible. Nonetheless, there is a possibility that acute risk is underestimated in this document due to the lack of an aggregate analysis.

It was theoretically possible to aggregate both the subchronic and the chronic oral and inhalation risk numbers, since they relied on the same critical studies. However, as with the acute, the subchronic / chronic dermal lacked a LOEL, so could not be included. In addition, aggregation of subchronic risk was not possible since the dietary assessment did not provide MOEs for this exposure length. For chronic aggregate risk, the chronic MOEs of 100,000 and 47,619 (general US population and children 1-2 yr, respectively; Apendix IV) indicated such a minimal risk that it adding it to the relevant inhalation values would have essentially no effect.

For the reasons listed above, aggregate calculations for all exposure lengths were not carried out for this analysis.

B. CUMULATIVE EXPOSURE AND RISK

USEPA completed its "Revised N-Methyl Carbamate Cumulative Risk Assessment" (CRA) in 2007 (US EPA, 2007b). The following carbamates were included in the USEPA CRA, based on "their shared ability to inhibit acetylcholinesterase (AChE) by carbamylation of the serine hydroxyl group located in the active site of the enzyme" (p. 2): carbaryl, aldicarb, oxamyl, formetanate-HCl, methomyl, carbofuran, propoxur, methiocarb, thiodicarb and pirimicarb. Three potential exposure pathways were identified: food, drinking water and residential / non-occupational (occupational exposure was not included). The CRA was executed for acute, single day exposures using the following steps (quoted directly from the USEPA document, pages 3-4):

- Selection of an index chemical to use as the point of reference to standardize the toxic potencies of each NMC, determination of the relative toxic contribution of each NMC, and establisment of a value to estimate potential risk for the group (*i.e.*, point of departure).

- Evaluation of interspecies differences (*i.e.*, extrapolation of rat responses to human responses); intraspecies variability; and the potential sensitivity to infants and children.

- Estimation of the risks asociated with all pertinent pathways of exposure (*i.e.*, food, drinking water, residential) in a manner that is both realistic and reflective of variability due to differences in location, time, and demographic characteristics of exposed groups.

- Identification of the significant contributors to risk.

- Characterization of the confidence in the results and the uncertainties associated with the assessment.

The relative potency factor approach was used to determine cumulative risk. Oxamyl was selected as the index chemical in light of "its high quality dose response data for all routes of exposure, as well as high quality time-to-recovery data" (US EPA, 2007b; p. 4). The toxicologic endpoint was the peak level of brain AChE inhibition following gavage exposure in rats. Inhibition data were modeled using the benchmark dose approach, with the benchmark response set at 10%. USEPA stated that 10% inhibition was not associated with functional or behavioral neurotoxicity. Interspecies and FQPA safety factors were applied mathematically to the relative potency factor for each chemical when warranted by lack of specific data. The standard intraspecies factor of 10 was applied to all of the compounds, making 10 the target MOE for the overall CRA. Exposure profiles from food, drinking water and residential and other non-occupational settings were developed for each chemical, taking into account the possibilities of overlap, co-occurrence or variance between chemicals and identifying populations at potential risk of exposure.

Multipathway MOEs for children 1-2 years and 3-5 years at the 99.9th exposure percentile were 8 and 9, respectively. As the dominant exposure pathway, food was the major contributor to risk. USEPA concluded in light of recent risk mitigation efforts and assessment assumptions that minimized the possibility of risk underestimation, that there is a "reasonable certainty that no harm" will result from cumulative exposure to the NMC pesticides covered by its assessment.

C. *IN UTERO* EFFECTS

No evidence for developmental toxicity emerged from the rat or rabbit developmental toxicity studies on methomyl reviewed for this document (rat: Rogers and Culick, 1978; rabbit: Feussner, 1983). However, an epidemiologic study in California that used a hierarchical multiple-pesticide model suggested an association in offspring between neural tube defects and ambient maternal exposure, which was ascertained by linking maternal addresses with records of pesticide applications (Rull *et al*., 2006). In addition, there is growing awareness that fetal or early-life exposure to cholinesterase inhibitors may have neurodevelopmental consequences in humans. This was most clearly demonstrated for the organophosphate insecticide chlorpyrifos (*eg.*, Rauh *et al.,* 2006 and 2012). Impacts on behavior, intelligence and/or brain structure may be independent of cholinesterase inhibition and occur at doses too low to induce overt clinical signs, making them difficult to detect in standardized animal testing.

D. ENDOCRINE EFFECTS

The mechanisms by which methomyl might be associated with neural tube defects or other neurodevelopmental endpoints are unknown, though it remains possible that endocrine pathways are involved. Nonetheless, the extent of endocrine involvement, if any, in such effects should be approached with specifically designed studies.

VII. TARGET MOEs, REFERENCE DOSES (RfDs) and REFERENCE CONCENTRATIONS (RfCs)

RfDs and RfCs represent methomyl dose levels or air concentration levels below which human health impacts are unlikely according to the current toxicity database. They were obtained by dividing the critical LEDs, LECs or NOELs by uncertainty factors that reflected gaps in understanding of specific toxicity issues and/or the natural variability in human populations. For example, where appropriate, default uncertainty factors of 10 were invoked to account for possible sensitivity differences between laboratory animals and average humans (the “interspecies” factor), and between average and highly sensitive humans (the “intrahuman” factor). In addition, a child protective factor, referred to by USEPA as an “FQPA” factor, was invoked in cases of acute exposure to infants and young children when the LED, LEC or NOEL came from a study in adults. The product of the uncertainty factors for any exposure scenario—in effect, the composite uncertainty factor---is equivalent to a “target MOE”. Actual MOEs below the target MOE, or exposure doses above the RfD, were considered to constitute a human health risk.

The child protective factor was not invoked for subchronic or chronic oral toxicity. USEPA policy holds that this factor is unnecessary in the chronic case when two chronic oral studies in different species, two prenatal developmental studies in different species, and a multigeneration reproductive toxicity study in rats are available (USEPA, 2002a; p. 24), a condition that was fulfilled for methomyl.

A. Oral RfDs—acute, subchronic and chronic

Acute oral reference doses (RfDs) for adults were calculated by dividing the critical LED_{10} (0.03 mg/kg) by an uncertainty factor of 10 (*i.e.*, 10x intraspecies; a 10x interspecies factor was unnecessary because the critical study was performed in humans). For infants and children, an additional uncertainty factor of 4 was added to account for evidence that inhibition of brain cholinesterase activity in young rats (postnatal day 11) was 3.6 times more sensitive than in adults (pnd-42) (Malley, 2005). Thus,

RfD, acute for adults = (0.03 mg/kg) ÷ 10 = 0.003 mg/kg = **3 μg/kg**
RfD, acute for children = (0.03 mg/kg) ÷ 40 = 0.00075 mg/kg = **0.75 μg/kg**

Calculation of separate subchronic and chronic oral RfDs was unnecessary since those NOELs were higher than the acute LED_{10} and would have produced RfDs that were correspondingly higher than than the acute RfDs. Adherence to the acute RfC would protect from risks arising from longer-term exposures.

B. Dermal RfDs—acute, subchronic and chronic

Acute dermal reference doses for adults were calculated by dividing the critical dermal NOEL (90 mg/kg) by and uncertainty factor of 100 (10x intraspecies, 10x interspecies). As with the acute oral RfDs, an additional uncertainty factor of 4 was added to account for evidence that inhibition of brain cholinesterase activity in young rats (postnatal day 11) was 3.6 times more sensitive than in adults (pnd-42) (Malley, 2005). Thus,

RfD, acute for adults = (90 mg/kg) ÷ 100 = **0.9 mg/kg**
RfD for infants / children = (90 mg/kg) ÷ 400 = **0.2 mg/kg**

Subchronic and chronic dermal RfDs were calculated by dividing the critical NOEL (90 mg/kg/day for both scenarios) by an uncertainty factor of 100 (10x intraspecies, 10x interspecies).Separate children's oral subchronic and RfDs were not calculated.

RfD, subchronic and chronic = (90 mg/kg) ÷ 100 = **0.9 mg/kg**

C. Inhalation RfCs—acute, subchronic and chronic

Calculation of acute inhalation reference air concentrations (RfCs) required converting the critical LEC_{10} air concentration of 3.92 mg/m^3 established in rats to a human equivalent concentration (HEC), followed by imposition of uncertainty factors. Because it appeared that maximum brain cholinesterase inhibition was stable between 1 and 6 hours (Weinberg, 2014; see section IV.A.1.e.), the LEC_{10} of 3.92 mg/m^3 was considered applicable to an entire 24-hour period. Conversion to an HEC thus required only an adjustment for the purity of the test article (99.4%). The combined uncertainty factor for adults was 100 (10x intraspecies, 10x interspecies) and for children was 400 (10x intraspecies, 10x interspecies, 4x child sensitivity). Thus,

RfC for adults = (3.92 mg/m^3) x 0.994 ÷ 100 = **39 μg/m^3**
RfC for infants / children = (3.92 mg/m^3) x 0.994 ÷ 400 = **9.7 μg/m^3**

Calculation of separate subchronic and chronic inhalation RfCs was considered unnecessary because conversion of the oral NOELs used to gauge subchronic and chronic inhalation risk into corresponding air concentrations, followed by imposition of the 100x adult uncertainty factor, resulted in RfC values that were higher than the acute RfC [11]. Adherence to the acute RfC would thus protect from risks arising from longer-term exposures.

RfDs and RfCs, along with the uncertainty factors required for their calculation appear below in Table VII.1.

[11] Calculation of subchronic and chronic inhalation RfCs:
RfC subchronic = [(9 mg/kg/day) ÷ (0.96 m^3/kg/day)] ÷ 100 = 0.09 mg/m^3/day
RfC chronic = [(3 mg/kg/day) ÷ (0.96 m^3/kg/day)] ÷ 100 = 0.03 mg/m^3/day

Table VII.1 Uncertainty factors, reference doses and reference concentrations for methomyl by the oral, dermal and inhalation routes

	Interspecies factor	Intrahuman factor	Child protective factor	Total uncertainty factor (or target MOE)	NOEL or LED	RfD or RfC
Oral						RfD
acute, infant	1	10	4 [b]	40	0.03 mg/kg	0.75 µg/kg
acute, adult	1	10	1	10	0.03 mg/kg	3 µg/kg
subchronic [a]					n/a	n/a
chronic [a]					n/a	n/a
Dermal						RfD
acute, infant	10	10	4 [b]	400	90 mg/kg	0.2 mg/kg
acute, adult	10	10	1	100	90 mg/kg	0.9 mg/kg
subchronic	10	10	1	100	90 mg/kg/day	0.9 mg/kg/day
chronic	10	10	1	100	90 mg/kg/day	0.9 mg/kg/day
Inhalation						RfC
acute, infant	10	10	4 [b]	400	3.92 mg/m^3	9.7 $\mu g/m^3$
acute, adult	10	10	1	100	3.92 mg/m^3	39 $\mu g/m^3$
subchronic [a]					n/a	n/a
chronic [a]					n/a	n/a

[a] Calculation of RfDs and RfCs for subchronic and chronic exposures was obviated by the fact that the respective NOELs and LEC_{10}s were higher than the corresponding acute values (see text).

[b] USEPA recommended a child protective factor of 2 in their dietary risk assessment on methomyl (USEPA, 2007a). Both child protective factors—USEPA's 2 and DPR's 4—were based on the study of Malley (2005) and the follow-up analysis of Setzer (2006a) in which LED_{10} values for RBC and brain ChE inhibition by methomyl were compared in pnd 11 and adult rats. For RBC ChE, BMD_{10}s were 0.06 and 0.2 mg/kg for pnd11 and adult animals, respectively—a 3.3-fold difference. For brain ChE, BMD_{10}s were 0.1 and 0.36 mg/kg—a 3.6-fold difference. In light of these data, USEPA made the following statement in their dietary assessment (p. 5):

> In pnd11 pups, the RBC compartment was slightly more sensitive than the AChE activity of the brain. For adult rats, the RBC compartment was also more sensitive than brain AChE activity. Therefore, a ratio of the adult RBC BMD to pnd11 RBC BMD resulted in a 2x FQPA factor. The 2x FQPA is appropriate for scenarios for infants / childrens's subpopulations when relying on adult data.

However, we advocate using a child protective factor of 4 since it appears more appropriate to base the calculation on the comparative brain ChE inhibition data (rounding the 3.6-fold adult-to-child difference to 4) than the RBC data [12]. It is also relevant to note that USEPA proposed a FQPA factor of 3.05 in their cumulative carbamate assessment document (USEPA, 2007b; p. 53) based on an adult brain BMD_{10} of 0.317 mg/kg and pnd11 BMD_{10} of 0.104.

[12] USEPA's use of a 2x FQPA factor based on comparative RBC ChE inhibition data from Malley (2005) is questionable for two reasons: (1) the ratio of rat RBC adult-to-pnd11 BMDs was actually 3.3, not 2; and (2) the ratio of the more relevant rat brain adult-to-pnd11 BMDs was 3.6. Rounded to a factor of 4 and combined with the intrahuman uncertainty factor of 10, the total acute oral uncertainty factor would be 40x.

VIII. CONCLUSIONS

Health risks to humans from exposure to methomyl were assessed by combining toxicity analyses from studies conducted both in humans and in laboratory animals with exposure projections for humans under occupational, bystander and dietary scenios. Since DPR predicted short-term, seasonal, annual and lifetime exposures in its exposure analysis, corresponding MOE values for each of these scenarios were developed. Oncogenic risk was not calculated since the available chronic studies provided no evidence for methomyl-induced cancers.

Risk calculations

The potential for non-oncogenic health effects resulting from exposure to methomyl was expressed as the Margin of Exposure (MOE) ratio, which is the critical NOEL or LED divided by the estimated exposure. A MOE of >10 is generally considered to be protective of human adult health when the relevant adverse effects were observed in adult humans under controlled conditions. A MOE of >100 is considered to be protective of human adult health when the relevant adverse effects were observed in animal studies. An additional uncertainty factor of 4, based on the ~4-fold greater sensitivity of the newborn rat brain cholinesterase to inhibition by methomyl compared to the adult brain enzyme, was included when assessing risks to children. The product of uncertainty factors for any combination of population cohort and exposure scenario is the “target MOE”. Actual MOEs below the target MOE indicate that the scenario poses a potential risk to human populations.

Exposure estimation. The exposure estimates for methomyl from non-dietary sources were developed in an accompanying document by the Worker Health and Safety Branch (WH&S) of DPR. Assumptions regarding application rates, acres treated/day, dermal and inhalation absorption, and default body weight are detailed in that document. The estimates were derived from four sources: (1) surrogate data in the Pesticide Handlers Exposure Database (PHED), which predicts both dermal and inhalation exposure to handlers, (2) reentry scenarios involving dermal exposure to fieldworkers through contact with dislodgeable foliar residues, (3) air monitoring studies designed to estimate bystander and ambient exposures by the inhalation route, and (4) residue studies on food items. MOEs are summarized in Conclusion Table 1 and described as follows:

Occupational handler and resident bystander risks. Acute inhalation MOEs at or below the target MOE of 100 were noted for all handler categories (though some specific tasks within categories were above 100). There was only one acute dermal exposure category registering a MOE less than the target of 100 (pilots, 52). There were no annual exposure scenarios, either by the dermal or inhalation routes, with MOEs of less than 100.

Risks to landscape workers during turf re-entry tasks. Risks to landscape workers posed by dermal exposure to methomyl during turf re-entry tasks did not produce MOEs less than 1737 for acute, seasonal or annual scenarios.

Occupational re-entry risks. Evaluation of risk in these cases assumed exposure only by the dermal route. There was no MOE below 292 (target MOE = 100), which was recorded for acute exposure occurring during hand harvesting of sweet corn.

Risks incurred upon re-entry in “U-Pick” operations (non-occupational). Of the four “U-Pick” operations examined (sweet corn, blueberries, nectarines and peaches), sweet corn was found to generate the highest potential acute exposures (dermal, in this case). Because of this, U-Pick operations in sweet corn also posed the highest calculated risk. Seasonal and annual exposures were not considered likely. The MOE for adults was 600 for this acute scenario (target MOE = 100), while for children it was 1306 (target MOE = 400).

Risk to bystanders from exposure near application sites. Bystanders at application sites may be exposed to methomyl by the inhalation route. Using the calculated absorbed doses and the critical inhalation NOEL of 0.16 mg/kg/day, bystander acute infant MOEs, 1- and 24-hr, were 213 and 139 (target MOE = 400), while adult bystander MOEs were 1231 and 291 (target MOE = 100). Worker bystander MOEs, 1-hr and 8-hr, were 1143 and 552 (target MOE = 100). Seasonal or annual exposure scenarios were not expected.

Dietary exposure and risk. Using a probabilistic distributional approach at the 99.9th percentile of exposure, the food-plus-water dietary risk for children aged 1-2 years and 3-5 years exceeded the threshold of concern, registering 159% and 160% of the acute population adjusted dose (MOEs of 25 in both cases; target MOE = 40). Inclusion of grapes resulted in even higher percent acute population adjusted doses (note: grape uses were canceled in 2010 with the exception of some uses which will remain until December 2016).

MOEs calculated for tolerances on the following commodities were below the target MOEs, which indicated a potential health concern: apple, avocado, broccoli, cantaloupe, grape, lettuce, nectarine, orange, peach, peanut, spinach, watermelon, and wheat. Thus the highest legal methomyl residues for these commodities resulted in MOEs below the target. DPR has measured methomyl residues at or near the tolerance for some of these commodities. USEPA.should be informed of this finding. (Note: Acute exposure was calculated on a "per-user-day" basis, which includes in the distribution of exposures only those consumers who eat at least one of the assessed commodities in the consumption survey utilized by DEEM. In contrast, USEPA calculates acute exposure on a per capita consumption basis, which factors in all members of a particular sub-population regardless of their commodity consumption. Per-user-day is, consequently, inherently more health conservative because it restricts the analysis to those who actually consume the commodities in question.)

The results indicate that chronic dietary risk for food plus drinking water is below the threshold of concern for the general U.S. population and all population subgroups. The most highly exposed population subgroups, children 1-2 years and children 3-5 years, utilized 0.2% of the chronic population adjusted dose.

Conclusion. Several handler scenarios, in addition to infant resident bystanders (1- and 24-hr) exhibited acute inhalation MOEs that were less than the relevant target MOEs. This was also the case for one handler acute dermal MOE (pilots for aerial applications). Mitigation measures should be considered for these scenarios, as they present potential health risks to the involved populations. None of the seasonal or annual scenarios evaluated for this document exhibited sub-target MOEs.

Conclusion Table 1. Target MOEs, actual MOEs and exposure / population scenarios exhibiting MOEs lower than the target MOE; dermal and inhalation exposure to methomyl

Exposure scenario	Dermal: Target MOE	Dermal: MOE range	Dermal: Scenarios *below* target MOE (actual MOE)	Inhalation: Target MOE	Inhalation: MOE range	Inhalation: Scenarios *below* target MOE (actual MOE)
Handlers **Aerial applications**						
▪ acute	100	52-2647	pilot (52)	100	5-533	M/L water sol. powder (10), M/L liquid (24), pilot (5)
▪ annual	100	145-7377	none	100	256-30,000	none
Airblast applications						
▪ acute	100	243-6383	none	100	18-800	Applicator (18)
▪ annual	100	677-17,647	none	100	909-30,000	none
Groundboom applications						
▪ acute	100	894-1277	none	100	15-145	M/L water sol. powder (59), applicator (15)
▪ annual	100	2479-3557	none	100	789-7500	none
Chemigation						
▪ acute	100	696-730	none	100	34-80	M/L water sol. powder (34), M/L liquid (80)
▪ annual	100	1944-2032	none	100	1765-4286	none

Hand spreader—bait w/gloves						
■ acute	100	165	none	100	40	Hand spreader—bait w/gloves (40)
■ annual	100	459	none	100	2143	none
Sod transplantation						
■ acute	100	1737	none			
■ seasonal	100	56,250	none			
■ annual	100	56,250	none			
<u>Occupational reentry</u> [a]						
■ acute	100	292-391,304	none			
■ seasonal	100	9358-12,676,056	none			
■ annual	100	18,716-12,676,056	none			
<u>"U-pick" reentry</u> [b]						
■ acute	400 (child) 100 (adult)	1306-4945 (child) 600-2273 (adult)	none none			
<u>Resident bystander</u>						
■ acute				400 (child)	139-213	Infant resident—1-hr (213) Infant resident—24-hr (139)
				100 (adult)	291-1231	none

Dietary	Acute[c]			Chronic[c]		
■ General US popln.	10	23	above target	100	100,000	above target
■ All infants <1 yr	40	53	above target	100	115,385	above target
■ Children 1-2 yr	40	25	*below target*	100	47,619	above target
■ Children 3-5 yr	40	25	*below target*	100	51,724	above target
■ Children 6-12 yr	40	43	above target	100	76,923	above target
■ Youth 13-19 yr	10	41	above target	100	120,000	above target
■ Adults 20-49 yr	10	20	above target	100	115,385	above target
■ Adults 50+ yr	10	18	above target	100	115,385	above target
■ Females 13-49 yr	10	21	above target	100	120,000	above target

Abbreviations: M/L, mixer / loader

[a] Twenty-one separate scenarios were evaluated for occupational reentry operations.
[b] Four separate scenarios were evaluated for U-pick reentry operations.
[c] For acute: food + water, except grapes; for chronic: food + water.

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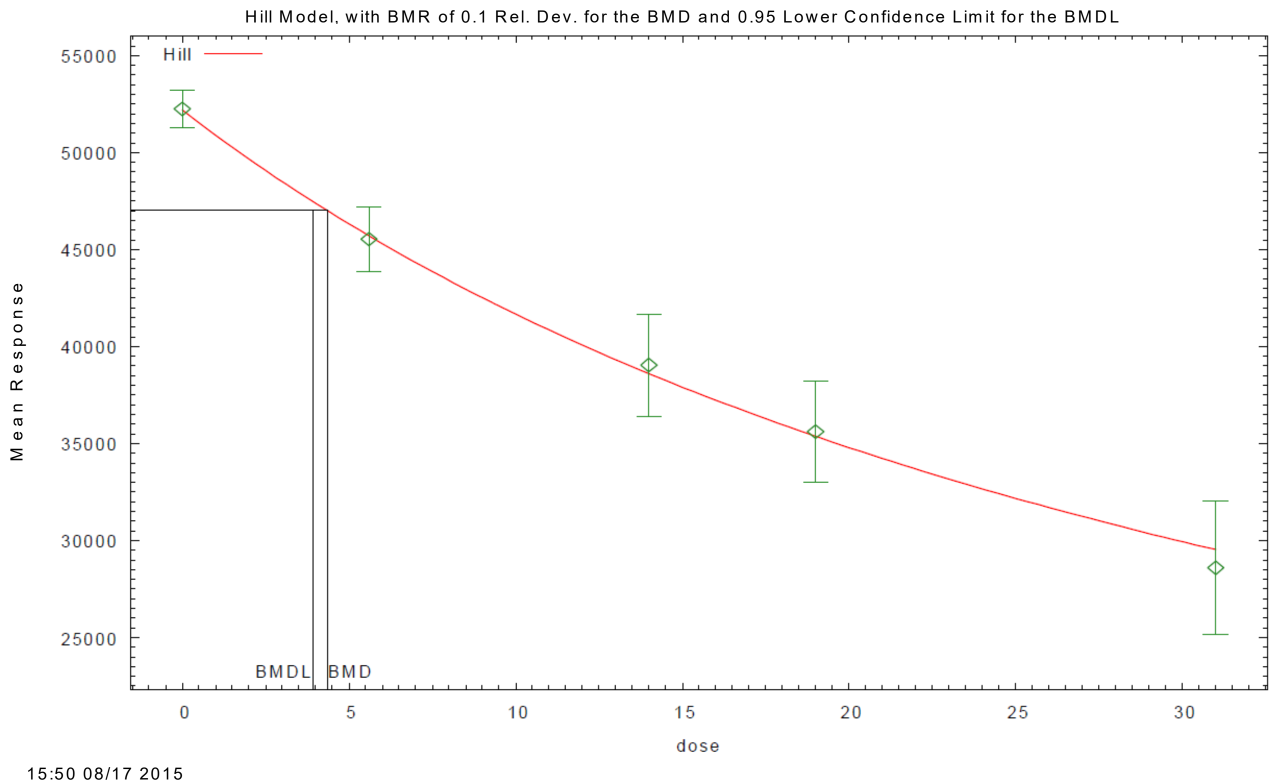
APPENDIX I. Benchmark dose analysis of brain cholinesterase inhibition in male rats exposed to methomyl by inhalation (Weinberg, 2014)




```
 ====================================================================
        Hill Model. (Version: 2.17;  Date: 01/28/2013)
        Input Data File: C:/USEPA/BMDS260/Data/methomyl IIIB - Hill.(d)
        Gnuplot Plotting File:  C:/USEPA/BMDS260/Data/methomyl IIIB - Hill.plt
                                               Mon Aug 17 15:50:52 2015
 ====================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = Mean_ChE
   Independent variable = Concentration
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho * ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008
```

```
                Default Initial Parameter Values
                       lalpha =      16.2635
                          rho =            0
                    intercept =        52257
                            v =       -23659
                            n =      1.61932
                            k =      12.2168


          Asymptotic Correlation Matrix of Parameter Estimates

          ( *** The model parameter(s)  -n
                have been estimated at a boundary point, or have been specified by the user,
                and do not appear in the correlation matrix )

                lalpha          rho    intercept            v            k

   lalpha            1           -1        0.016         0.45        -0.41

      rho           -1            1       -0.016        -0.45          0.4

intercept        0.016       -0.016            1         0.25        -0.36

        v         0.45        -0.45         0.25            1        -0.98

        k        -0.41          0.4        -0.36        -0.98            1



                                 Parameter Estimates

                                                         95.0% Wald Confidence Interval
       Variable         Estimate        Std. Err.     Lower Conf. Limit   Upper Conf. Limit
         lalpha          63.8064          13.7138            36.9278              90.685
            rho         -4.53046          1.29363           -7.06593              -1.995
      intercept          52238.1          459.757            51336.9             53139.2
              v           -50348          13536.8           -76879.6            -23816.4
              n                1               NA
              k          37.7692          15.3222            7.73822             67.8001

NA - Indicates that this parameter has hit a bound
     implied by some inequality constraint and thus
     has no standard error.
```

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	5.23e+004	5.22e+004	1.34e+003	1.47e+003	0.0407
5.6	9	4.55e+004	4.57e+004	2.18e+003	1.99e+003	-0.298
14	10	3.91e+004	3.86e+004	3.69e+003	2.92e+003	0.463
19	10	3.56e+004	3.54e+004	3.67e+003	3.56e+003	0.203
31	10	2.86e+004	2.95e+004	4.84e+003	5.36e+003	-0.557

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1         -420.318023           6     852.636045
             A2         -412.095977          10     844.191955
             A3         -413.099124           7     840.198248
         fitted         -413.225836           5     836.451671
              R         -469.500872           2     943.001744


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value

   Test 1              114.81          8          <.0001
   Test 2             16.4441          4        0.002478
   Test 3             2.00629          3          0.5711
   Test 4            0.253423          2           0.881

The p-value for Test 1 is less than .05.  There appears to be a
difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1.  A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1.  The modeled variance appears
 to be appropriate here

The p-value for Test 4 is greater than .1.  The model chosen seems
to adequately describe the data


        Benchmark Dose Computation

Specified effect =           0.1

Risk Type        =     Relative deviation

Confidence level =           0.95

             BMD =       4.37235
            BMDL =      3.91883
```

APPENDIX I (continued). Benchmark dose model comparisons using the Weinberg (2014) brain cholinesterase inhibition data

Continuous								
Model Name	**Data File Name**	**Specified Effect**	**Risk Type**	**BMD**	**BMDL**	**p-value for fit: Does the model for the**	**AIC**	**Scaled residual for dose group**
Exponential2	methomyl IIIB (	0.1	Relative deviat	5.18402	4.71956	0.4092	837.0865	-1.165
Exponential3	methomyl IIIB (	0.1	Relative deviat	5.18402	4.71956	0.4092	837.0865	-1.165
Exponential4	methomyl IIIB (	0.1	Relative deviat	4.48106	3.76428	0.7878	836.6753	-0.4361
Exponential5	methomyl IIIB (	0.1	Relative deviat	4.48106	3.76428	0.7878	836.6753	-0.4361
Hill	methomyl IIIB (	0.1	Relative deviat	4.37235	3.91883	0.881	836.451671	-0.298
Linear	methomyl IIIB (	0.1	Relative deviat	6.21635	5.65945	0.016	844.522436	-1.62
Polynomial	methomyl IIIB (	0.1	Relative deviat	4.20973	3.35842	0.8566	838.230889	-0.0502
Power	methomyl IIIB (	0.1	Relative deviat	6.21635	5.65945	0.016	844.522436	-1.62

APPENDIX II. Letter from A.L. Rubin to M.A. Shalaby requesting methodologic clarifications in his reproductive toxicity study in male rats (Food and Chemical Toxicology (48:3221-3226 (2010))

August 24, 2012

To: Dr. M.A. Shalaby
Pharmacology Department
Faculty of Veterinary Medicine
Cairo University, Giza, Egypt

Dear Dr. Shalaby,

My name is Andy Rubin. I am a toxicologist working on a methomyl risk assessment for the California Department of Pesticide Regulation. I recently reviewed your paper in Food and Chemical Toxicology (48:3221-3226 (2010)), which reports adverse impacts of two doses of methomyl on fertility index, weight of sexual organs, semen picture, serum testosterone and testicular histopathology in rats. These results may be of interest to our risk evaluation.

At this point, however, I do not completely understand your experimental design as expressed in the Materials and Methods section of the paper, particularly in regard to the "serial mating technique" described there. According to your description on page 3222, each of 60 male rats was subjected to four 5-day mating periods separated by 10 days (days 15, 30, 45 and 55 of the experimental period), with each mating period including 2 females. That procedure seems to differ from the actual data in Table 1, which show only nine females which have been mated, presumably, to nine males that had been pre-exposed to methomyl for one entire 65-day spermatogenic cycle. Can you clarify my understanding of your experimental design?

Specific questions include the following:

(1) Where are the fertility data for days 15, 30, 45 and 55 (described in section 2.5)? If they are not reported in the Results section, what is the significance of reporting these four mating periods in the Materials and Methods?

(2) If 60 males were used in the exposure and only 30 were evaluated for reproductive efficiency (section 2.6, p. 3222), why are 54 pregnant females (*i.e.*, 6 experimental groups x 9 mated females) accounted for in Table 1? It seems from your description in the Materials and Methods that there should be for 240 females (30 males x 2 females/mating x 4 matings). I cannot locate those data, but I may be overlooking something.

(3) You indicate in Table 2 that the effect of 1.1 mg/kg/day folic acid alone on testis, seminal vesicle and prostate gland weights, is statistically significantly different from controls to at least the 0.05 level. However, my examination of the mean values (testis: 2.69±0.01 for controls *vs.* 2.67±0.07** g for folic acid treated animals; seminal vesicle: 1.82±0.03 g *vs.* 1.85±0.03** g; prostate: 0.562±0.02 *vs.* 0.563±0.02* g; *, **p<0.05, 0.01, as reported in the paper) does not agree with this, as there is little difference between the controls and the folic acid treated animals.

(4) You state the following at the bottom of page 3222: "Coadministration of folic acid at acceptable daily intake (1.1 $mg \cdot kg^{-1}$ b.wt.) with methomyl (1.0 and 0.5 $mg \cdot kg^{-1}$ b.wt./day) significantly increased the weight of testes, seminal vesicles and prostate gland, *as compared to the normal control group*" [my italics]. I could not confirm this from your data. For example, for testes, the normal control weight was 2.69±0.01 g, while the weight in the presence of folic acid was 2.57±0.02 g, which was *less* than the control. Perhaps you meant to say that the weight of methomyl-treated reproductive tissues increased in the presence of folic acid compared to the weight of methomyl-treated reproductive tissues not exposed to folic acid?

I would appreciate any help you could give that would clarify these issues or correct my interpretations.

Sincerely,

Andrew L. Rubin, Ph.D., D.A.B.T.
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Medical Toxicology Branch, Dept. of Pesticide Regulation
California Environmental Protection Agency
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APPENDIX III. Toxicology summaries, Medical Toxicology Branch, DPR

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
METHOMYL

Chemical Code # 000383, **Tolerance #** 00253
SB 950 # 169

August 8, 1986
Revised 11/6/87, 6/15/88, 7/21/89, 1/10/90, 9/15/97, 5/2/98, 1/12/99, 9/28/07, 8/28/12

I. DATA GAP STATUS

Chronic, rat:	No data gap, possible adverse effect
Chronic, dog:	No data gap, possible adverse effect
Oncogenicity, rat:	No data gap, no adverse effect
Oncogenicity, mouse:	No data gap, possible adverse effect (not oncogenicity)
Reproduction, rat:	No data gap, no adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosomal aberration:	No data gap, no adverse effect
DNA damage/repair:	No data gap, no adverse effect
Neurotoxicity:	No data gap, possible adverse effect*

* An acute neurotoxicity study in the rat identified a possible adverse effect (tremors). A subchronic rat neurotoxicity study did not indicate adverse effects. Both of these studies were acceptable. One unacceptable hen neurotoxicity study is on file.

Note, Toxicology one-liners are attached
** indicates acceptable study
Bold face indicates possible adverse effect

Reviews by C. Aldous, A. Apostolou, J. Carlisle, F. Martz, J. Remsen (Gee), M. Silva, and T. Moore

All relevant DPR records on file as of Jan. 4, 1999 have been evaluated (including record numbers through 265393, Document No. 253-0303). Several older record numbers evaluated are of the series 900,000+.

II. TOXICOLOGY ONE-LINERS AND DISCUSSION

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED RAT

****253-164, 253-165 037842, 037843** (with rebuttal and supplemental data in -176, 052178): Kaplan, A. M., "Long-Term Feeding Study in Rats with S-Methyl N-[(Methylcarbamoyl)Oxy] Thioacetimidate, (Methomyl; INX-1179), Final Report". (Haskell Laboratory, E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware, # 235-81, 5/1/81). Methomyl technical 99+%, Lot # INX-1179-255; fed in the diet to 80/sex/group at 0, 50, 100 and 400 ppm (of these, 70/sex/group were designated for the 2 year study, and 10/sex/group were used for a 1-yr interim sacrifice). NOEL = 100 ppm (body weight decrements in both sexes: possible mild anemia). At 400 ppm there were some reductions in RBC parameters (RBC count, Hb concentration, HCT) in high dose females. There was some bone marrow hyperplasia at this dose in males, and slightly elevated extramedullary hematopoiesis in liver, spleen, or adrenals; typically marginal in scope and generally observed in only one sex. CDFA/DPR review history: study was first reviewed by J. Gee, 4/18/86, who classified study as unacceptable and upgradeable (needing individual clinical observation data and historical control hematology data). Re-reviewed by J. Carlisle and F. Martz, 10/9/87. Above requested data were provided, but study was still not acceptable for chronic data requirements for lack of eye exams. Study was considered acceptable as an oncogenicity study. With submission of additional data on eye histopathology for the 2-year dog study (CDFA # 072204), the lack of ophthalmology in the rat study was no longer considered as an issue, and the study was upgraded to **acceptable** as a combined study. Gee, 7/21/89. Re-evaluation and consolidation of older reviews into one document by Green and Aldous, Jan. 12, 1999.
EPA one-liner: Oncogenic NOEL => 400 ppm (HDT). Systemic NOEL = 100 ppm. ChE NOEL **>** 400 ppm (HDT) (Ellman method). Minimum.

CHRONIC RAT

-025, 024197 (With rebuttal and full report in -176, 051310): "22-Month Dietary Feeding - Rats, Lannate Methomyl Insecticide, (S-Methyl-N-[(Methyl-carbamoyl)Oxy]Thioacetimidate), Final Report". (Hazleton Laboratories, Inc., Falls Church, VA., # 201-164, 7/26/68). Lannate methomyl insecticide, 90-100% purity; 35/sex/group was fed at 0, 0, 50, 100, 200, & 400 ppm. Decreased growth at 200 and 400 ppm; dosage-related decrease in hemoglobin in females, accompanied by extramedullary hematopoiesis in the 200 and 400 ppm groups. Renal tubular dilation, hypertrophy, vacuolation at 200 and 400 ppm. Overall NOEL = 100 ppm. Unacceptable, but useful supplementary information. Reviewed by J. Gee, 5/22/86. Additional information (Document No. 253-176) led to no change in status. J. Carlisle, 7/16/87. [See acceptable combined study, above].
EPA one-liner: One year report, systemic NOEL = 100 ppm and ChE NOEL = 400 ppm (HDT).

-008, 042606; -025, 024024; -090, 963995; and 407-003, 024988-89 are summaries of 051310.

CHRONIC DOG

****253-167 037845, 037846** "Two-year dietary administration - dogs: Lannate methomyl insecticide (S-Methyl N-[(Methylcarbamoyl)Oxy] Thioacetimidate)", (William M. Busey, Hazleton Laboratories, Inc., Falls Church, VA., Report number MRO-888-1, Project number 201-165, 25 June 1968). Three beagle dogs per sex per group received methomyl (90% purity) in the diet at 0, 50, 100, 400, and 1000 ppm for 2 years. An interim sacrifice group of one additional dog per sex per group was terminated at 1 year. Two females died at 1000 ppm. NOEL = 100 ppm (presence and/or increased degree of pigmentation of kidney proximal tubular epithelial cells, often with swelling/irregularity of the cells, and pigmentation of spleen in 400 ppm males). Common high dose findings, typically in both sexes, included the above observations, plus hematology changes (reduced HCT, Hb, RBC counts), extramedullary hematopoiesis in spleen, and increased hematopoiesis in marrow. Findings are considered to indicate “possible adverse effects”. The findings which defined the LOEL were typically either uncommon findings which were “slight” in degree, or were findings commonly seen in dogs, but somewhat increased in degree over the norm. For this reason, these results do not suggest pivotal findings for toxicity evaluation. One high dose male had sustained hematology changes, plus marked changes consistent with severe anemia (greatly enlarged spleen and liver, and severe extramedullary hematopoiesis in these organs). A summary of the CDFA/DPR evaluations of this study is included in the background section of this review. This review provides tabular data supporting previous conclusions regarding methomyl toxicity. Green and Aldous, 12/22/98.

Data review history of Record No. 037845, above: The 1985 “reviews” by Apostolou and Aldous on this study were simply references to brief summary data in Document/Record Nos. 253-025:024203 and 407-003:033910. These submissions were by Shell and Union Carbide, respectively. The “final report” was later submitted as Document/ Record Nos. 253-167:037845, submitted by du Pont in October, 1985. E. I. du Pont de Nemours and Company has been the primary or exclusive source of data since then, and has retained the Tolerance No. of 253. The 1986 CDFA review by de Vlaming and Gee highlighted study results and identified study deficiencies, including a lack of ophthalmology data. A rebuttal response to Document No. 253-176 (no record number) shows all data requirements except for ophthalmology to be satisfied (J. Carlisle and F. Martz, 11/6/87). A meeting of E. I. du Pont de Nemours and Company representatives and CDFA (including CDFA reviewers J. Carlisle and F. Martz) was held on 6/14/88, in which it was agreed that du Pont should submit histopathology data based on multiple sections of eyes to address the primary remaining deficiency of the dog chronic study. Following submission of the dog eye histopathology data (Document/Record No. 253-186:072204), the study was upgraded to acceptable status (J. Gee, 7/18/89). There were no treatment-related ocular effects. The Dec. 1998 examination of the original report provides data tables which can be used for risk assessment evaluation. Aldous, 12/22/98.

EPA one-liner: Systemic NOEL = 100 ppm. Enlargement of prostate gland. Increase kidney pigmentation and swelling of the proximal convoluted tubules. Minimum.

-008, -025, -090, 024203, 042607, 035859; and 407-003, 033910 are summaries of 037845-46.

-186 072204 Supplement to 037845. Results of additional sections of the eyes made as a result of the meeting held April 21, 1988, between the registrant and CDFA.

ONCOGENICITY MOUSE

253-166 037844, “104-week Chronic Toxicity and Carcinogenicity Study in Mice”, (David G. Serota, Hazleton Laboratories America, Inc, Report # HLO-253-81, Project # 201-510, 12 February 1981). 80 CD®-1 mice per sex per group received methomyl in the diet at 0, 50, 100 (reduced to 75 ppm at week 39), and 800 ppm (reduced to 400 ppm at week 28, and further reduced to 200 ppm at week 39) for 104 weeks. Chronic NOEL = 75 ppm (modest RBC parameter reductions: Hb levels, HCT: increased mortality). **No adverse effects. **Acceptable** with diet analyses and clarifications on pathology data provided in Document No. 253-176 (no record No.) (V. de Vlaming and J. Gee, 4/22/86; acceptability upgrade by J. Carlisle, 7/16/87; worksheet updated by Green and Aldous, 12/16/98).

EPA one-liner: Oncogenic NOEL => 200 ppm (HDT). Systemic NOEL = 50 ppm. Decreased hematocrit and hemoglobin. Increased adrenal weight at 200 ppm. Histologic NOEL = 200 ppm. Minimum.

REPRODUCTION RAT

**253-177 051313 Lu, C. C., “Nudrin® two-generation reproduction study in rats”, WIL Research Laboratories, Inc., 12/13/82. Laboratory Study # WRC RIR-275. CD® rats were tested in a 2-generation study with one littering period per generation at dietary levels of 0, 75, 600, or 1200 ppm NUDRIN® (SD-14999 Technical =

methomyl). Groups sizes were 13 males and 26 females for F0 parents, and 20 males and 40 females for F1 parents. A conservative NOEL for reproductive and non-reproductive effects is 3.5 mg/kg/day (typical intake of 75 ppm rats which were not rapidly growing, prior to mating). Substantially higher intake on an animal weight basis for 75 ppm rats, such as occurred during maternal lactation and rapid growth of young pups, led to marginally reduced pre-weaning pup body weights and reduction in weights of young post-weanling rats. These findings corresponded to intakes on the order of at least 14 mg/kg/day for maternal rats and 18 mg/kg/day for rapidly growing offspring. Levels of 600 to 1200 ppm reduced food consumption and body weights in both parental rats and pre-weanling pups. The highest dose reduced pup survival during the first few days of life. There was a marginally reduced live litter size for the 600 ppm parental F1 group, which may have been treatment-related. There were marginal reductions in RBC parameters, in females only, at 600 to 1200 ppm (reduced HCT, Hb, and RBC count). There was a general increase in spleen weights in weanling 1200 ppm pups, without associated histopathology. The latter findings are consistent with those of several other studies. The highest dose elicited clinical signs of “increased activity, pilo erection, depressed righting reflex and myoclonic body tics”. These signs were primarily limited to the first three weeks of treatment. Study remains **acceptable** with **no adverse effects**. Re-examination by Aldous, Jan. 12, 1999.

CDFA/DPR review history: An abbreviated version of the present report (Document No. 253-113, Record Nos. 035815 and 035816) was evaluated by de Vlaming and Martz on 1/13/86. They determined that the available data appeared to reflect a viable study, but they did not have the information to do an analysis of the findings. These reviewers requested individual data to upgrade the study. The complete report was later submitted (Document No. 253-177, Record No. 051313). This was examined by Martz and Carlisle (11/6/87). They upgraded the study to acceptable status, but provided only a summary paragraph of the findings. The 1998 worksheet provides tabular presentations and re-analyses of the study results.

EPA One-liner: None in Branch library.

253-255 140400 Hurtt, M. E. (author of supplement). "Nudrin, Two-generation Reproduction Study in the Rat" (Supplement No. 1). Information was sent in response to U.S. EPA request for additional data. CDFA had accepted the study as presented in 1987. Most complete report is Document No. 253-177, Record No. 051313. Final Report Date: 12/13/82. Laboratory Study #: 61531. Mean daily mg/kg/day intakes during premating periods for 75, 600, and 1200 ppm groups were 5, 37, and 74 for F0 males; 5, 39, and 76 for F0 females; 7, 56, and 117 for F1 males; and 7, 59, and 128 mg/kg/day for F1 females. Test article stability was proven over the period of the study, and stability was shown at RT for at least 3 weeks. This supplement included summary data for gross observations, and summary and individual data for clinical observations. These data did not change the NOEL’s nor did they indicate adverse effects. Study remains acceptable. Aldous, Jan. 11, 1999.
-176, 051311 (With partial versions in -008, 964001): "Three-Generation Reproduction Study, Lannate Methomyl Insecticide, Final Report" (Hazleton Laboratories, Inc., # 201-166, 7/18/68). Lannate methomyl insecticide, no purity stated, administered in the diet at 0, 50, or 100 ppm to 10 males and 20 females per group with 2 litters/generation for 3 generations (an additional post-weaning growing phase was conducted with F_{3C} females). **No adverse reproductive effects**. Unacceptable, not upgradeable (only 10 males/group, no individual data, no MTD). (Schreider, Apostolou 5/28/85; de Vlaming, Remsen 4/4/86; Green, Carlisle 8/12/87; Martz, 11/5/87).

EPA one-liner: Reproductive NOEL > 100 ppm (HDT). Fetotoxic NOEL = 100 ppm. Minimum.

-008, 964001, and -168, 37847 are partial duplicates of #51311.

-008, 024201, -025, 042601, and 407-003, 024990 are summaries of # 051311.

TERATOLOGY RAT

**253-176 051312 (Full report: -008, 96500 and -170, 037854 are partial versions) "Oral Teratogenic Study in Rats with Lannate (INX-1179)", (E. I du Pont de Nemours & Co., Haskell Laboratory, # 498-78, 9/5/78).

Lannate (methomyl), 99% purity; was fed in the diet to 25 females per group at 0, 50, 100, or 400 ppm on days 6 through 15 of gestation. NOEL: maternal = 100 ppm (body weight and food consumption); developmental ≥ 400 ppm (no effects). Original review by J. Gee, 4-18-86: unacceptable with insufficient information for evaluation. Re-reviewed by F. Martz, 9-11-87: additional information (complete report including diet analysis) did not result in change of status because there was no MTD. On April 21, 1988, a meeting was held with the registrant, and the dose selection was discussed with respect to the oral gavage LD50. As a result, the dose selection was considered as justified and the study was upgraded to acceptable status (Gee, 6/15/88). A worksheet was produced by Aldous on 12/29/98, with no change in study status.
EPA one-liner: NOEL (maternal toxicity) = 100 ppm. Minimum.

-008, 964000, and -170, 37854 are partial reports of #51312.

-025, 24200, and 407-003, 33909 are summaries of #51312.

TERATOLOGY RABBIT

253-170 037855, "Embryo-Fetal Toxicity and Teratogenicity Study of Methomyl in the Rabbit", Elizabeth L. Feussner (Study Director), Argus Research Laboratories, Inc., Horsham, PA., Report # HLO-331-83, 9/18/83). Twenty artificially-inseminated New Zealand White (DLI:NZW) female rabbits per group received methomyl by gavage at 0, 2, 6, and 16 mg/kg/day on gestation days 7 through 19. Maternal NOEL = 6 mg/kg/day (7 high-dose females died: common signs in this group included tremors, hyperactivity, body jerks, excessive salivation, convulsions, and ataxia). Developmental NOEL = 16 mg/kg/day (no adverse effects**). Initially classified as unacceptable (dosing solution analyses required). Dosing solution analysis, reported in Document No. 253-176, prompted an upgrade to **acceptable** status (see rebuttal response of 11/9/87). CDFA reviews were by de Vlaming and Remsen (Gee), 4/18/86; and Carlisle (in 11/9/87 rebuttal). An updated worksheet (with additional tables) was produced by Green and Aldous on 12/09/98. This re-evaluation did not result in any change of study status.
EPA one-liner: NOEL (teratogenicity and fetotoxicity) > 16 mg/kg/day. Maternal NOEL = 2 mg/kg/day. Minimum.

-008, 963999: "Teratology Study - Rabbits, Lannate Methomyl Insecticide, Final Report" (Hazleton, 7/28/67). Lannate methomyl insecticide 90-100% purity, lot no. H-4429 and H-5116; fed in the diet in two non-concurrent trials at 0, 50, and 100 or 0, 45, and 90 mg/kg/day to 12 pregnant females/group from days 8 through 16 of gestation. No teratogenic effect reported. Unacceptable and not upgradeable (two non-concurrent studies combined, unclear protocol, only two dosage levels with no justification, all results are missing). A. Apostolou, 5/28/85.
EPA one-liner: None in Branch library.

-008,- 025, 042605, 035858, 024199, and 407-003, 024986 are summaries of 963999.

GENE MUTATION

** -169, 037852 "CHO/HGPRT Assay for Gene Mutation". (Haskell Laboratory, 1/13/84) Methomyl ~ 99%; CHO cells were exposed to 0, 10, 20, 40, 50, or 55 mM (-S9 aroclor-induced rat liver fraction) with EMS as positive control, or 0, 100, 150, 200, 250, or 350 mM (+S9 aroclor-induced rat liver fraction) with DMBA as positive control and selected for resistance to 6-TG; **No increased mutation frequency.** Survival decreased at higher concentration. Complete, acceptable. J. Gee, 4/4/86.
EPA one-liner: Negative. Acceptable.

-169, 037848 "Evaluation of Selected Pesticides as Chemical Mutagens *In vitro* and *In vivo* Studies." (SRI, May 1977). Lannate 99% purity, lot no. 6602-82; *Salmonella typhimurium* strains TA1535, TA1537, TA1538, and TA100 tested at 0, 1, 10, 50, 100, 500, or 1000 µg/plate, with/without S9 (not described). **No increased**

reversion rate. Unacceptable (lacks adequate positive controls, no justification of 1000 µg/plate as highest concentration no indication of cytotoxicity), no individual plate counts, no TA98, source of S9 not stated). J. Gee, 4/4/86.
EPA one-liner: None in Branch library.

-025, 142 964002 Reference material, insufficient information for review.

-025, 024205 Reference material, no methomyl data.

CHROMOSOMAL ABERRATION

-169, 037851 "In Vivo Bone Marrow Chromosome Study in Rats, H# 15,000, Final Report." (Hazleton (VA), 12/18/84). Methomyl ~ 99% purity; in water @ 0, 2, 6, & 20 mg/kg, 5/sex/group, by single gavage; Sacrificed @ 6, 24, & 48 hr. **No increase in chromosomal aberrations. Complete, acceptable. J. Gee, 4/1/86.
EPA one-liner: Negative. Acceptable.

** 253-0303; 265392; "Mouse Bone Marrow Micronucleus Assay of DPX-X1179-394"; (K.S. Bentley; Report No. 413-95; 10/19/95); Fifteen Crl:CD-1(ICR) BR mice/sex/group were dosed orally by gavage with 0 (vehicle: sterile water), 3.0 or 6.0 mg/kg of Methomyl Technical (batch no. DPX-X1179-394; purity: 98.35%) and 5 animals/sex/time point were euthanized at 24, 48 and 72 hours post-dose. Another 18 animals/sex were dosed with 12.0 mg/kg of the test material and 6 animals/sex/time point were euthanized at the same time intervals. A positive control group of 5 animals/sex were treated orally by gavage with 40 mg/kg of cyclophosphamide and euthanized at 24 hours post-dose. Bone marrow samples from the femur were examined and the mean number of polychromatic erythrocytes (PCE) with a micronucleus per 2000 PCEs/animal, the mean number of micronucleated normochromatic erythrocytes (NCE) per 2000 PCEs and the mean number of PCEs per 1000 erythrocytes were determined. Hyperactivity and/or lethargy were the only clinical signs which were noted. There was no treatment-related increase in the number of micronucleated PCE's. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 6/27/12)

DNA DAMAGE

-169, 037853 "Assessment of Methomyl (INX-1179-255) in the In Vitro Unscheduled DNA Synthesis Assay in Primary Rat Hepatocytes." (Haskell Laboratory, 8/2/85). Methomyl, 99% purity; primary rat hepatocytes were exposed to 0, 1, 10, 100, 1000, 5000, & 75,000 µM for 18 hr. **No increase in net grain counts, 4 slides/each concentration, 2 trials. Complete, Acceptable. J. Gee, 4/4/86.
EPA one-liner: None in Branch library.

-169, 037850 "Evaluation of Selected Pesticides as Chemical Mutagens In vitro and In vivo Studies." (SRI, May 1977). Methomyl 99% purity, Saccharomyces cerevisiae were tested in mitotic recombinant assay; Two trials @ 2.0 and 3.0 % (w/v); Table of data only no protocol. Incomplete, unacceptable, with adverse effect (increased mitotic recombinants) indicated. J. Gee, 4/4/86.
EPA one-liner: None in Branch library.

-003, 024991: Insufficient information for review.

Comment: There are conflicting results in the two studies in this test area. They, however, measure different endpoints and are not directly comparable. In accordance with most thinking, the acceptable study in mammalian cells, which was negative for UDS, would be given more weight than the study in yeast, especially in view of the deficiencies in the report. Because of the negative findings in other acceptable studies in the area of genotoxicity, the biological significance of the result in yeast is questionable. J. Gee, 11/6/87.

NEUROTOXICITY

HEN

253-171 037856 (with rebuttal in 253-176): "Oral LD_{50} and Delayed Paralysis Tests (Hens)." (Haskell Laboratory, 9/25/67). Methomyl technical, no purity given; was administered in acetone/water mixture at 28 mg/kg to 10 hens (cross of Barred Rock and Rhode Island Red varieties) without atropine; TOCP positive control. Evidently 4/10 died. Four additional hens were dosed with atropine pre-treatment at methomyl doses of 60, 90, 120, or 200 mg/kg (all survived). Salivation, lacrimation, and some convulsions, but no paralysis, were observed in the survivors. No microscopic lesions in sciatic nerve (which was evidently the only histopathologic feature assessed). No paralysis or sciatic nerve lesions arose in hens given 60, 90, 120, or 200 mg/kg with atropine. Original review by J. Gee, 4/12/86, Unacceptable, not upgradeable (no repeat dosing, inadequate protocol and data presentation). Rebuttal containing no additional data did not upgrade study; no change in status. J. Carlisle, 7/22/87. One-liner updated by Green and Aldous, 12/8/98.

EPA one-liner: Negative. Minimum.

-008,-025, 042608, 024202, and 407-003, 024987 are summaries of 037856.

Comment: Delayed neurotoxicity testing is not a current data requirement for this class of compounds. F. Martz, 10/20/87.

RAT

** **253-272 160438** "Methomyl Technical (DPX-X1179-512): Acute Oral Neurotoxicity Study in Rats"; (K. A. Mikles; E.I. du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Project ID: HL-1998-01080; 2/2/98); Fifty two rats/sex/group were dosed orally by gavage with 0, 0.25, 0.50, 0.75 or 2.0 mg/kg of Methomyl technical (purity: 98.6%). Twelve rats/sex/group were included in the neurobehavioral study in which they were examined in the functional observational battery (FOB) and motor activity assessments prior to dosing, 30 minutes after dosing (day 1) and on study days 8 and 15. Six animals/sex/group of this cohort were randomly chosen for histological examination of the nervous system and muscle. Erythrocyte and plasma blood cholinesterase activities were measured in 10 animals/sex/group of the clinical pathology subgroup on the day prior to dosing, at 30 minutes post-dose (Day 1) and one day after treatment (Day 2). At the latter two time points, brain cholinesterase activities were determined as well. No test material-related mortality resulted from the treatment. Among the animals in the clinical pathology group, males (5/40) and females (5/40) in the 2 mg/kg group exhibited tremors 30 minutes after dosing. The incidence of other possible treatment-related signs were not significant from that of the control group. By 24 hours after dosing, no clinical signs were evident. The mean body weight gain for females in the 2 mg/kg group was significantly less ($p<0.05$) than that of the control between days 2 and 8. In the FOB, treatment-related tremors were noted in 4/12 males in the 2 mg/kg group 30 minutes after dosing. Lacrimation was observed for 1/12 males in this group at this time point. No signs of toxicity were noted 24 hours after dosing. No treatment-related effect was evident for the forelimb and hindlimb grip strength or foot splay measurements. No significant alteration in motor activity was noted. Significant cholinesterase inhibition ($p<0.05$) was evident in the plasma for both the males and females in the 0.75 and 2 mg/kg groups ((M) 77 and 58% of control, (F) 60 and 64% of control, respectively) at 30 minutes post-dose. Erythrocyte cholinesterase was significantly inhibited ($p<0.05$) 30 minutes post-dose for the males in the 2.0 mg/kg group (54% of control) and the females in the 0.5, 0.75 and 2.0 mg/kg (75, 62, and 43% of control, respectively). Brain cholinesterase activity was significantly inhibited ($p<0.05$) 30 minutes after dosing for the males and females in the 0.5, 0.75, and 2.0 mg/kg groups ((M) 81, 75, and 53% of control, (F) 80, 70, and 49% of control, respectively). All of the cholinesterase activity parameters for the treated animals were comparable to those of the control animals by 24 hours after dosing. No gross lesions nor treatment-related neuropathology were evident. **Adverse effect indicated**:: tremors occurred in conjunction with significant brain cholinesterase inhibition. **NOEL:** (M/F) 0.25 mg/kg (based upon inhibition of brain cholinesterase activity in the 0.5 mg/kg group). **Study acceptable**. (Moore, 4/28/98)

253-271; 159979; "Reversibility Study with Carbamate Insecticides in Rats"; (L.A. Malley; E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Study No. HL-1997-00641; 11/10/97); Forty rats/sex/group were orally gavaged with 0 or 1 mg/kg of oxamyl technical (purity: 98.3%) or 0 or 3 mg/kg of methomyl technical (purity: 98.6%). Plasma, RBC, and brain cholinesterase (ChE) activities were measured for 10 animals/sex/group at 30 minutes and 2, 3 and 4 hours post-dose. Tremors were noted at 30 minutes post-dose in animals treated with both of the test materials. This sign was not evident at 2 hours after dosing. For the oxamyl treated animals, at 30 minutes after dosing, plasma, RBC and brain ChE activities were significantly inhibited (plasma: (M) 43%, (F) 50% of control; RBC: (M) 42%, (F) 39% of control; brain: (M) 55%, (F) 52%). By two hours, ChE activity had returned to control levels. Likewise, for the methomyl treated animals, at 30 minutes post-dose, plasma, RBC and brain ChE activities were significantly inhibited (plasma: (M) 73% of control; RBC: (M) 44%, (F) 59% of control; brain: (M) 54%, (F) 61% of control). By 2 hours, the ChE activities had returned to control levels. Study data indicate that significant ChE inhibition is largely reversible by 2 hours after dosing for both of the test materials. **Possible adverse effect indicated:** tremors and significant brain cholinesterase inhibition evident. **NOEL:** (oxamyl) < 1 mg/kg, (methomyl) < 3 mg/kg; **Study supplemental.** (Moore, 3/26/98)

253-273 164573 Mikles, K. A., "Methomyl Technical (DPX-X1179-512): Subchronic oral neurotoxicity study in rats", Haskell Laboratory Project ID# DuPont HL-1998-01639, 9/25/98. Forty-two Crl:CD®BR rats/sex/group were dosed with 0, 20, 50, 150, or 1500 ppm methomyl (98.6% purity) in diet for up to 91 days. Three sets of 10/sex/dose were used in cholinesterase studies. These were sacrificed at weeks 4, 8, and 13, respectively for assays of RBC, plasma, and brain cholinesterase. The other 12/sex/dose underwent neurobehavioral testing (FOB and motor activity) at pre-test and at weeks 4, 8, and 13. Of these, six/sex/dose were perfused *in situ*. Neuropathology was performed on control and high dose central and peripheral nervous system preparations. NOEL = 150 ppm. Body weights and food consumption were markedly reduced at 1500 ppm in both sexes throughout the study. The most prominent of the clinical observations were tremors in most 1500 ppm males and females during the first 4 weeks, and occasionally thereafter. Common FOB observations included increased resistance to handling and removal from the cage, ptosis, and absent pupillary response in both sexes. In addition, females tended to have increased urination during open field observations, and decreased urination during motor activity assessment. None of these findings were progressive over time. Histopathology was negative. Brain cholinesterase was marginally inhibited at 1500 ppm (significant for each sex at one of three assay times). Plasma and RBC cholinesterase activities were unaffected. Since findings were consistent with expected acute responses to a cholinesterase inhibitor, no "adverse effects" are indicated. **Acceptable. Aldous, 1/4/99.

253-275 169902 Exact duplicate of 253-273, 164573.

253-0287; 220034; "Methomyl (DPX-X1179) Technical: Comparison of Cholinesterase Activity in Adult and Preweanling Rats"; (L.A. Malley; E.I. du Pont de Nemours and Company, Haskell Laboratory for Health and Environmental Sciences, Newark, DE; Project ID. DuPont-15433; 9/12/05); Three studies were performed. In the first study, approximately 35 Crl:CD®(SD)IGS BR 11-day old pups/sex were dosed orally by gavage with 0.3 mg/kg of Methomyl (DPX-X1179) Technical (sample no. 22577; purity: 98.08%). Five animals/sex/time point were euthanized at 30, 60, 90, 120, 180, 240, and 360 minutes post-dose and red blood cell (RBC) and brain cholinesterase (ChE) activities were assayed. A control group of 15 animals/sex were dosed orally by gavage with distilled water and 5 animals/sex/time point were euthanized at 60, 120 and 240 minutes post-dose. RBC and brain ChE activities were assayed for these animals. In the second study, 10 11-day old pups/sex/group were dosed orally by gavage with 0, 0.1, 0.2, 0.3 or 0.4 mg/kg of the test material and euthanized at 30 minutes post-dose. The RBC and brain ChE activities were assayed for these animals. In the third study, twenty 42-day old rats/sex/group were dosed with 0, 0.3, 0.5 or 0.75 mg/kg of the test material and 10 animals/sex/group were euthanized at 30 and 240 minutes post-dose. RBC and brain ChE activities were assayed for these animals. In the first study, maximal inhibition of both enzymes was noted at 30 minutes post-dose. Therefore, ChE activity in both the RBC and brain were assayed at 30 minutes post-dose in both the 2nd

and 3rd studies. A dose-response of ChE inhibition was noted in both the RBC and brain of the pups and young adults. A maximal inhibition of RBC ChE of 49% was observed at a dose of 0.4 mg/kg in the pups. The % inhibition noted in the brain of the pups at this dose was 41 to 42%. In the RBC of the adult rats, ChE was inhibited 41 and 25% for the male and females, respectively, at 30 minutes post-dose at the highest dose level of 0.75 mg/kg. At that dose level, brain ChE was inhibited 19 and 29% in the males and females, respectively, at 30 minutes post-dose. These data indicate that the percentage of cholinesterase inhibition in the RBC and brains of the11-day old rats was greater at comparable dose levels in comparison to the young adult animals. **Possible adverse effect:** significant brain cholinesterase inhibition demonstrated in both pups and adult rats. **Study supplemental** (non-guideline study). (Moore, 9/18/07)

383-0296; 264057; "Reversibility Study with Carbamate Insecticides in Rats"; (L.A.. Malley; E.I. du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Project ID. HL-1997-00641; 11/10/97); Two cohorts of Crl:CD BR rats of both sexes were treated with either 0 (vehicle: deionized water) or 3 mg/kg of methomyl technical (batch no. DPX-X1179-512, purity: 98.6%) or 0 (vehicle: deionized water) or 1 mg/kg of oxamyl technical (batch no. DPX-D1410-196, purity: 98.3%) by oral gavage. Ten animals/sex/time point were euthanized at 30 minutes and 2, 3, and 4 hours post-dose and cholinesterase (ChE) activity in the brain, red blood cells and plasma was assayed (note: no effort was made to differentiate between acetylcholinesterase and butylcholinesterase activities). The dose levels were selected from dose range finding studies in which the time to peak effect and the appropriate treatment level which resulted in approximately 50% inhibition of ChE activity was achieved. In the methomyl cohort, ChE activity in the red blood cells and brain of both sexes was reduced by 40 to 55% of the control values at 30 minutes post-dose. ChE activity in the plasma was not as severely affected by the treatment. The effect on the rbc and brain ChE activities had largely been reversed by 3 and 2 hours post-dose for the males and females, respectively. For the oxamyl cohort, ChE activity at all 3 sites ranged from 39 to 55% of the control values for both sexes at 30 minutes post-dose. Recovery to control levels was observed at 2 to 3 hours post-dose for both sexes. **Possible adverse effect:** significant inhibition of brain ChE. **Supplemental Study** (non-guideline protocol employed). (Moore, 4/2/12)

METABOLISM

253-0296; 264058; "The Metabolism of [1-^{14}C]Methomyl in Male Cynomolgus Monkeys"; (D.R. Hawkins, B.C. Mayo, A.D. Pollard, L.M. Haynes; Department of Chemical Metabolism and Radiosynthesis and Department of Non-Rodent Toxicology, Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, PE18 6ES, England; Report No. DPT 258/920494; 6/16/92); Four male cynomolgous monkeys were dosed orally by gavage with 5 mg/kg of [1-^{14}C]Methomyl (lot no. 2729-122, purity: 99.9%, radiochemical purity: >97%, specific activity: 44.8 uCi/mg). The final specific activity was adjusted to 15.1 uCi/mg with [1-^{13}C]Methomyl (lot no. 2565-151, chemical purity: 99.9%) and unlabeled methomyl (lot no. DPX-X1179-379, purity: 98.9%). Urine and feces were collected up to 168 hours post-dose. The most important route of excretion was via exhalation with 39% of the administered dose excreted within the first 48 hours. Another 32% was recovered in the urine (urine and cage wash). Only 3% of the label was recovered from the feces. At 168 hours post-dose, 4.76% of the label was still retained in the tissues. Only 79% of the administered dose was recovered. The reason for this low percentage of recovery was likely due to the fact that excretion via exhalation persisted beyond 48 hours post-dose when the collection of air samples was discontinued and the carcasses, in which additional radiolabel could have been recovered, were not analyzed. A significant fraction of radiolabel was ^{14}carbon dioxide which was not only exhaled but also incorporated into other chemicals through catabolic metabolism. This incorporation was evident in the high percentage of the administered dose which was recovered in the tissue after 168 hours and the relatively equal distribution of the radiolabel throughout the body. Due to the myriad of radiolabeled compounds recovered in the urine, identification of specific moieties was limited. Tentatively identified compounds included the mercapturic acid derivative of methomyl (0.8%), methomyl oxime sulfate (1.5%), acetonitrile (1.7%), acetate (0.4%) and acetamide (0.4%). **Study supplemental** (non-guideline study). (Moore, 4/3/12)

253-0296; 264059; "The Metabolism of [1-^{14}C]Methomyl in Rats"; (D.R. Hawkins, B.C. Mayo, A.D. Pollard, L. Haynes; Department of Chemical Metabolism and Radiosynthesis, Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, PE18 6ES, England, E.I. du Pont de Nemours & Co., Du Pont Agricultural Products, Research and Development Division, Experimental Station, Wilmington, DE; Report No. DPT 210/91311; 9/6/91); Five Sprague Dawley rats/sex were dosed orally by gavage with 5 mg/kg of [1-^{13}C/^{14}C]Methomyl ([1-^{14}C]Methomyl: lot no. 2449-040, radiochemical purity: >97%, specific activity: 66.9 uCi/mg; [1-^{13}C]Methomyl: lot no. 2565-151, chemical purity: 99.9%). Urine and feces were collected up to 168 hours post-dose. Expired air was recovered up to 120 hours post-dose. Approximately 53% of the administered dose was recovered in the urine. An important route of excretion was via exhalation with 34% to 36% of the administered dose being excreted by 120 hours post-dose. Only 2 to 3% of the label was recovered from the feces. At 168 hours post-dose, 8 to 9% of the administered label was still retained in the tissues. Predominant sites of the recovery were red blood cells and skin (1.5 to 1.9% and 2.4 to 2.5%, respectively). A significant fraction of radiolabel was ^{14}carbon dioxide and other low molecular compounds which were not only exhaled but also incorporated into other chemicals through catabolic metabolism. This incorporation was evident in the high percentage of the administered dose which was recovered in the tissue after 168 hours and the relatively equal distribution of the radiolabel throughout the body (excluding the high levels in the red blood cells and skin). Due to the myriad of radiolabeled compounds recovered in the urine, identification of specific moieties was limited. Identified compounds included the mercapturic acid derivative of methomyl (17 to 18%), methomyl oxime sulfate and acetic acid (5.0 to 5.4%), acetonitrile (6%), acetate (1.4 to 2.0%) and acetamide (0.2 to 0.4%). **Study supplemental** (non-guideline study). (Moore, 4/4/12)

SUBCHRONIC TOXICITY

Rat Subchronic Dietary Toxicity Study

253-0303; 265391; "Three-Month Dietary Administration - Rats, Insecticide 1179"; (T. Kundzin, O. Paynter; Hazleton Laboratories, Falls Church, VA; Project No. 201-151 (MRO-848); 1/4/66); Ten (strain unidentified) rats/sex/group received 0, 10, 50 or 250 ppm of Insecticide 1179 (methomyl technical) (lot no. H 4217; purity: 100%) in the diet for 3 months. Another group of 10 animals/sex received 125 ppm of the test material for 9 weeks, followed by 500 ppm for another 4 weeks. Approximate compound intakes were as follows: (**M**) 0, (10) 0.5 to 1.4, (50) 2.4 to 6.8, (125) 9.5 to 19, (250) 14 to 30, (500) 23 to 33 mg/kg/day; (**F**) 0, (10) 0.6 to 1.4, (50) 3.0 to 6.8, (125) 11 to 17, (250) 16 to 30, (500) 31 to 32 mg/kg/day. No deaths resulted from the treatment. The mean body weights of both sexes in the 125 ppm groups and above were less than the control values. The hematology and urinalysis did not indicate any treatment-related effects. There was no apparent treatment-related effect upon rbc or plasma cholinesterase acitvity in the 125 ppm group after 2 months of treatment or in the 250 (3 months of treatment) and 500 (one month of treatment) ppm groups at the termination of the study. Although the absolute and/or relative weights for the pituitary, lungs and liver among the treated groups were greater or less than the control values in certain instances, a treatment-related effect was not discernable. There were no treatment-related lesions evident in the histopathological examination. **No adverse effect.** A No-Effect Level was not assigned due to the limited assessment which was undertaken in the study (no clinical chemistry or analysis of the dietary preparations were performed); **Study supplemental** (study predated FIFRA guideline protocol). (Moore, 6/26/12)

Dog Subchronic Dietary Toxicity Study

253-0303; 265390; "Three-Month Feeding Study on Dogs with S-Methyl N-[(Methylcarbamoyl) Oxy] Thioacetimidate [Lannate Methomyl Insecticide; INX-1179]"; (H. Sherman; E.I. du Pont de Nemours & Co., Haskell Laboratories, Newark, DE; Report No. 168-67; 9/28/67); Four beagle dogs/sex/group received 0, 50, 100 or 400 ppm of Lannate Methomyl Insecticide (INX - 11791) ((Technical INX-1179: 97.5%, Hi Sil 233: 2.5%); batch no. INX-1179-68; a.i.: 90%) in the diet for 3 months ((M) 0, 1.44, 3.18, 14.7 mg/kg/day, (F) 0, 1.45, 3.01, 12.5 mg/kg/day). No deaths resulted from the treatment. There was no apparent treatment-related effect on the mean body weights or food consumption. The hematology, clinical chemistry and urinalysis parameters were not affected by the treatment. There was no apparent treatment-related effect on organ weights. No treatment-related lesions were noted in the histopathological examination. **No adverse effect indicated. Dog**

3-Month Dietary Toxicity NOEL: (M/F) > 400 ppm ((M) 14.7 mg/kg/day, (F) 12.5 mg/kg/day) (based upon the lack of a treatment-related effect on the 400 ppm treatment group); **Study supplemental** (study does not conform with present-day guideline protocols). (Moore, 6/22/12)

Rabbit 3-Week Repeated Dosing Dermal Toxicity Study

253-0303; 265393; "Methomyl Technical: 21-Day Repeated Dose Dermal Toxicity Study in Rabbits"; (C.Finlay; E.I. du Pont de Nemours & Co., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Project ID No. HL-1997-00913; 11/14/97); The skin of 6 New Zealand White rabbits/sex/group was treated with 0 (deionized water), 15, 30, 45, or 90 mg/kg/day of Methomyl technical (batch no. DPX-X1179-512; purity: 98.6%) 6 hours/day for 21 days. No deaths resulted from the treatment. No treatment-related clinical signs were evident

There was no treatment-related effect upon body weights or food consumption. No treatment-related lesions were evident in the necropsy examination. Although the cholinesterase activities in the plasma, red blood cells and/or brain of the treated animals was less than that of the controls, there was no apparent dose-related effect. **No adverse effect indicated. Rabbit 21-day repeated dosing dermal toxicity NOEL:** 90 mg/kg/day (based upon the lack of treatment-related effect on the 90 mg/kg treatment group); **Study supplemental** (clinical chemistry, hematology, ophthalmology and histopathology were not performed); (Moore, 7/2/12)

253-191; 85837;"Repeated dose dermal toxicity: 21 day with DPX-X1179-394 (Methomyl) in Rabbits"; E.I. duPont de Nemours & Co., Haskell Lab. for Toxico-logy and Industrial Medicine, Newark, DE, Report No. 387-89, 8/29/89; 822; Methomyl (98.4% purity) in deionized water, 6hr daily dermal exposure for 21 consecutive days; 0, 5, 50, 500 mg/kg to 5 rabbits/sex/dose; two additional recovery groups lasting 14 days at 0 and 500 mg/kg; decreases ($p<0.05$) in

plasma cholinesterase (ChE) activity on day 21 in males and females (36 and 55% of control, respectively) at the 500 mg/kg dose level; similar decreases ($p<0.05$) in brain ChE activity were evident in males and females (48 and 68% of control, respectively); at mid-dose level, male plasma ChE activity was 77% of control ($p<0.05$); full restoration of normal ChE activities in plasma and brain after recovery period; no adverse clinical signs consistent with ChE inhibition were observed; no compound-related effects were observed during gross and microscopic examination; NOEL > 5 mg/kg (males; decrease plasma and brain ChE), NOEL > 50 mg/kg (females; decrease plasma and brain ChE); Study **acceptable**; (Leung, 2/1/90).

APPENDIX IV. Dietary risk evaluation for methomyl

(see following pages)

Methomyl

Acute (Probabilistic) and Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments

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Executive Summary

Acute and chronic dietary (food and drinking water) exposure and risk assessments were conducted for methomyl using the Dietary Exposure Evaluation Model DEEM-FCID™, Version 3.18 which uses food consumption data from the NHANES 2003-2008. This dietary exposure assessment was initiated in conjunction with the aggregate risk characterization that is underway in the Medical Toxicology Branch.

<u>Acute Dietary (Food Only and Food Plus Drinking Water) Exposure Results and Characterization</u>

A refined acute probabilistic exposure assessment was conducted for the general U.S. population and various population subgroups using primarily U. S. Department of Agriculture (USDA) Pesticide Data Program (PDP) monitoring data for 2000 through 2011 combined with percent crop treated (PCT) estimates provided in U.S. EPA's 2009 screening level usage analysis for methomyl. For a few commodities or food forms, tolerances or anticipated residues calculated by U.S. EPA were used as residue estimates. Exposures were aggregated by eating occasion rather than over 24 hours due to the specific mechanism of action of methomyl.

Exposure was calculated with and without drinking water (included as a point estimate at the limit of detection (LOD), 5.3 ppt, and with and without grape. (Methomyl use on grape was cancelled in December 2010 with some use allowed until December 2016.)

The results indicate that at the 99.9%-tile of exposure, food-only dietary risk for children aged 1-2 years and 3-5 years exceeds the threshold of concern even when grape is excluded from the assessment. Exposure without grape was 163% of the acute population adjusted dose (aPAD) for children 1-2 years and 157% of the aPAD for children 3-5 years.

When drinking water exposure is included in the assessment as a point estimate of 5.3 ppt, a concentration that appears to be quite low compared to the results of surface water monitoring and drinking water modeling studies, food-plus-water (excluding grape) dietary risk exceeds the threshold of concern for children aged 1-2 years and 3-5 years. Exposure was 159% of the aPAD for children 1-2 years and 160% of the aPAD for children 3-5 years.

The commodities that contribute the most to exposure for children age 1-5 years are grape, apple juice, cantaloupe, peanut, and lettuce.

An examination of whether methomyl tolerances for 15 frequently consumed commodities were health protective found that MOEs were inadequate for 13/15 tolerances when exposure was evaluated at the 95%-tile of consumption for users only (consumers only).

Chronic Dietary (Food and Drinking Water) Exposure Results and Characterization

A refined chronic dietary exposure assessment was conducted for the general U.S. population and various population subgroups using the same data sources described for the acute exposure assessment. Drinking water was included in the assessment as a point estimate at the limit of detection (LOD), 5.3 ppt.

The results indicate that dietary risk for food plus drinking water is below the threshold of concern for the general U.S. population and all population subgroups. The most highly exposed population subgroups, children 1-2 years and children 3-5 years, utilized 0.2% of the chronic population adjusted dose (cPAD).

I. Introduction

This dietary exposure assessment is conducted in conjunction with an overall risk characterization for methomyl currently underway in the Medical Toxicology Branch. Comprehensive dietary exposure assessments for methomyl were completed by U.S. EPA in 1998 as part of their Reregistration Eligibility Decision (U.S. EPA, 1998) and in 2007 in conjunction with the N-methyl carbamate cumulative risk assessment (U.S. EPA, 2007). Some of the data and references used in this exposure assessment were taken from those documents. In addition, most of the procedures, descriptions, document formatting, and the dietary exposure modeling software used in this analysis were provided by U.S. EPA or based on U.S. EPA standards.

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose. This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to point of departure (POD, NOAEL, LOAEL, e.g.) divided by the required uncertainty or safety factors. For acute and non-cancer chronic exposures, 100% of the PAD is used as a threshold of concern.

II. Residue Information

Methomyl is an N-methyl carbamate insecticide that is used on a wide variety of food crops, livestock feeds, cotton, ornamentals, and turf. It is also used in fly baits around food handling and distribution facilities, livestock facilities, and refuse sites. Except for the fly bait formulations, pesticides that contain methomyl are classified as restricted-use based on their high acute toxicity to humans. No products are registered for use in residential areas.

Methomyl use in California ranged between 219,634 to 309,000 lbs/year between 2007 and 2011 (DPR, 2013). The top ten agricultural uses in the state were lettuce, corn, onion, grape, alfalfa, tomato, strawberry, nectarine/peach, pomegranate , and sugar beet (Table 1). Methomyl use on strawberry and grape were cancelled in 2010. For grape, use of existing stocks was allowed through June 2013, and subsequently use was extended through December 2016 (Federal Register, 2012).

Use of methomyl on grapes has been declining in California since at least 2007. The most recent data show that only 4,399 lbs. were used in 2011, compared to an average of 15,744 lbs/year over the previous four years. Since the tolerance for grape has not yet been revoked, grape was included in this exposure assessment.

Table 1. Ten Highest Uses of Methomyl in California (lbs.), 2007-2011.								
SITE/CROP		2007	2008	2009	2010	2011	Average, 2007-2011
1.	LETTUCE	78,713	71,203	62,370	68,526	57,385	70,762
	Leaf Lettuce	*32,184*	*32,020*	*29,664*	*35,039*	*28,395*	*31,290*
	Head Lettuce	*46,529*	*39,183*	*32,705*	*33,487*	*28,990*	*39,472*
2.	CORN	52,322	36,680	47,645	51,998	58,726	45,549
	Human Cons.	*47,731*	*31,614*	*44,417*	*49,325*	*57,420*	*41,254*
	Forage-Fodder	*4,590*	*5,066*	*3,228*	*2,673*	*1,306*	*4,295*
3.	ONION	20,705	17,956	19,487	21,062	19,665	19,383
4.	GRAPES	23,661	15,908	13,789	9,617	4,399	17,786
	Other Grapes	*21,157*	*12,598*	*8,574*	*5,953*	*3,630*	*14,109*
	Wine Grapes	*2,504*	*3,310*	*5,216*	*3,664*	*770*	*3,677*
5.	ALFALFA	22,496	21,178	8,488	9,757	13,646	17,387
6.	TOMATO	15,539	12,288	6,620	6,298	9,526	11,482
	Other Tomatoes	*4,430*	*5,056*	*2,289*	*3,234*	*2,623*	*3,925*
	Processing	*11,109*	*7,232*	*4,331*	*3,064*	*6,903*	*7,557*
7.	STRAWBERRY	16,088	10,848	6,104	3,216	26	11,013
8.	NECTARINE, PEACH	5,489	7,764	5,566	4,104	4,411	6,273
9.	POMEGRANATE	6,717	3,760	7,393	5,204	6,329	5,957
10.	SUGAR BEET	9,694	2,395	3,260	4,891	3,978	5,116
TOTAL USE FOR ALL SITES/CROPS		**309,000**	**251,382**	**221,248**	**231,459**	**219,634**	**260,543**

There are 75 individual tolerances and five crop group tolerances for methomyl, ranging from 0.1 to 40 ppm (e-CFR 40 §180.253, updated July 31, 2013; Table 2). All tolerances are permanent except grape.

Table 2. Methomyl tolerances (e-CFR 40 §180.253, updated July 31, 2013).

Commodity	Tolerance (ppm)
Alfalfa, forage	10
Alfalfa, hay	10
Apple	1
Asparagus	2
Avocado	2
Barley, grain	1
Barley, hay	10
Barley, straw	10
Bean, dry, seed	0.1
Bean, forage	10
Bean, succulent	2
Beet, garden, tops	6
Bermudagrass, forage	10
Bermudagrass, hay	40
Blueberry	6
Broccoli	3
Brussels sprouts	2
Cabbage	5
Cabbage, Chinese, bok choy	5
Cabbage, Chinese, napa	5
Cauliflower	2
Celery	3
Collards	6
Corn, field, forage	10
Corn, field, grain	0.1
Corn, field, stover	10
Corn, pop, grain	0.1
Corn, pop, stover	10
Corn, sweet, forage	10
Corn, sweet, kernel plus cob with husks removed (30)	0.1
Corn, sweet, stover	10
Cotton, undelinted seed	0.1
Dandelion, leaves	6

Table 2. Methomyl tolerances (e-CFR 40 §180.253, updated July 31, 2013).

Commodity	Tolerance (ppm)
Endive	5
Grape [1]	5
Grapefruit	2
Hop, dried cones [2]	12
Kale	6
Lemon	2
Lentil, seed	0.1
Lettuce	5
Mustard greens	6
Nectarine	5
Oat, forage	10
Oat, grain	1
Oat, hay	10
Oat, straw	10
Onion, green	3
Orange	2
Parsley, leaves	6
Pea	5
Pea, field, vines	10
Peach	5
Peanut	0.1
Pecan	0.1
Pepper	2
Peppermint, tops	2
Pomegranate	0.2
Rye, forage	10
Rye, grain	1
Rye, straw	10
Sorghum, forage	1
Sorghum, grain	0.2
Soybean	0.2
Soybean, forage	10
Spearmint, tops	2
Spinach	6
Swiss chard	6
Tangerine	2
Tomato	1
Turnip, greens	6

Table 2. Methomyl tolerances (e-CFR 40 §180.253, updated July 31, 2013).	
Commodity	**Tolerance (ppm)**
Vegetable, brassica, leafy, group 5	6.0
Vegetable, cucurbit, group 9	0.2
Vegetable, fruiting, group 8	0.2
Vegetables, leafy [exc. beet (tops), broccoli, Brussels sprouts, cabbage, cabbage, Chinese, cauliflower, celery, collards, dandelions, endive (escarole), kale, lettuce, mustard greens, parsley, spinach, Swiss chard, turnip, greens (tops), and watercress]	0.2
Vegetable, root and tuber, group 1	0.2
Wheat, forage	10
Wheat, grain	1
Wheat, hay	10
Wheat, straw	10
[1]Expires December 31, 2016. [2]There are no U.S. registrations for use of methomyl on hop, dried cone, as of February 14, 1990. N = negligible.	

The residue of concern in both plants and animals is methomyl. Metabolism studies in poultry and ruminants showed that methomyl residues in animal products are unlikely, therefore no tolerances for these commodities are required (U.S. EPA, 1998).

<u>Residue Data used for Acute and Chronic Assessments:</u>

The primary source of residue data for this assessment was the USDA Pesticide Data Program, 2000 through 2011. In general, the most recent three years of data for each commodity or food form was used to create a residue data file (RDF) in DEEM-FCID. Data were adjusted for percent crop treated according to data provided in U.S. EPA's 2009 screening level usage analysis (U.S. EPA, 2009a) by substituting zeroes for the appropriate number of non-detects in the data set. For acute exposure analysis, the entire data set was used in a probabilistic Monte-Carlo analysis. For chronic exposure analysis, and for blended commodities in the acute exposure analysis, the mean residue value was used (U.S. EPA, 1999). Table 3 is a summary of primary PDP data used in the assessment and Attachment 1, Table 1a is a summary of primary PDP data used in RDF file construction. The data showed that bell pepper had the highest percentage of samples with detectible residues (12.4%) while spinach had the highest single detected residue (2.3 ppm).

TABLE 3: Summary of Primary PDP Data

CROP GROUP	PDP PRIMARY COMMODITY	TOLERANCE	PCT AVG	PCT MAX	PDP, YEARS	TOTAL SAMPLES	# DETECTS	% DETECTS	HIGHEST DETECTED RESIDUE	AVG LOD OF NON-DETECTS
CROP GROUP 00										
0	Asparagus	2	5	10	2008-2010	1488	52	3.49%	1.8	0.0106
	Asparagus, canned				2003	354	0	0.00%	n/a	0.0106
0	Peanut butter	0.1	5	10	2000, 2006	1390	0	0.00%	n/a	0.0100
0	Raisin	5	2.5	5	2006, 2007	744	0	0.00%	n/a	0.0083
CROP GROUP 01										
1AB	Beets, canned	0.2	n/c	40	2011	756	0	0.00%	n/a	0.0125
1AB	Carrot	0.2	15	35	2002, 2006, 2007	2020	1	0.05%	0.023	0.0083
1C	Potato	0.2	2.5	5	2002, 2008, 2009	1858	0	0.00%	n/a	0.0103
	Potato, frozen				2006, 2007	1544	0	0.00%	n/a	0.0049
1CD	Sweet potato	0.2	n/c	15	2004, 2008, 2009	1662	0	0.00%	n/a	0.0083
CROP GROUP 03										
3A	Onion	3	35	55	2011	93	0	0.00%	n/a	0.0120
3B	Onion, green	3	35	55	2008, 2009	744	64	8.60%	0.26	0.0024
CROP GROUP 04										
4B	Celery	3	35	60	2002, 2007, 2008	2217	147	6.63%	0.62	0.0059
4A	Lettuce	5	35	45	2005, 2009, 2011	1874	129	6.88%	2.2	0.0505
4A	Spinach	6	10	25	2009, 2008, 2006	1999	87	4.35%	2.3	0.0099
	Spinach, canned				2004, 2011	569	0	0.00%	n/a	0.0113
	Spinach, frozen				2011	198	1	0.51%	0.014	0.0100
CROP GROUP 05										
5A	Broccoli	3	10	20	2006-2008	1475	18	1.22%	0.14	0.0033
5A	Cabbage	5	10	15	2010, 2011	1485	23	1.55%	0.03	0.0036
5A	Cauliflower	2	10	15	2005, 2006, 2011	1485	19	1.28%	0.13	0.0014
5B	Collard greens	6	n/a		2006-2008	679	10	1.47%	1	0.0113
5B	Kale	6	n/a		2006-2008	799	5	0.63%	0.025	0.0111
CROP GROUP 06										
6C	Bean, black, canned	0.1	10	25	2010	367	0	0.00%	n/a	0.0100
6C	Bean, garbanzo, canned	0.1	10	25	2009	186	0	0.00%	n/a	0.0105
6C	Bean, kidney, canned	0.1	10	25	2008, 2009	372	0	0.00%	n/a	0.0109
6C	Bean, pinto, canned	0.1	10	25	2009	372	0	0.00%	n/a	0.0106
6A	Green bean	2	10	20	2005, 2007, 2008	920	22	2.39%	0.34	0.0117
	Green bean, canned				2003, 2004	928	0	0.00%	n/a	0.0141
	Green bean, frozen				2005	555	8	1.44%	0.2	0.0147
	Green bean, baby food				2011	584	0	0.00%	n/a	0.0125

TABLE 3: Summary of Primary PDP Data

CROP GROUP	PDP PRIMARY COMMODITY	TOLERANCE	PCT		PDP, YEARS	TOTAL SAMPLES	# DETECTS	% DETECTS	HIGHEST DETECTED RESIDUE	AVG LOD OF NON-DETECTS
			AVG	MAX						
6A	Pea, snap	5	1	2.5	2011	744	14	1.88%	0.18	0.0072
6B	Pea, sweet, canned	5	1	2.5	2002, 2003, 2006	1278	0	0.00%	n/a	0.0188
6C	Soybean, grain	0.2	1	2.5	2004, 2005, 2011	1574	0	0.00%	n/a	0.0030
CROP GROUP 08										
8BC	Eggplant	0.2	5	5	2005, 2006	1476	31	2.10%	0.22	0.0120
8B	Pepper, bell	2	20	35	2003, 2004, 2011	2040	253	12.40%	1.3	0.0054
8B	Pepper, hot	2	20	35	2011	553	16	2.89%	0.3	0.0260
8A	Tomato	1	10	20	2007, 2008, 2011	2219	1	0.05%	0.013	0.0037
	Tomato, canned				2000	369	0	0.00%	n/a	0.0098
	Tomato, paste				2001, 2009	1111	0	0.00%	n/a	0.0233
CROP GROUP 09										
9A	Cantaloupe	0.2	15	30	2005, 2010, 2011	1668	152	9.11%	0.17	0.0108
9B	Cucumber	0.2	10	20	2004, 2009, 2010	2045	51	2.49%	0.11	0.0077
9B	Squash, summer	0.2	5	15	2006-2008	1482	23	1.55%	0.56	0.0083
9B	Squash, winter	0.2	5	15	2005, 2006, 2011	1286	2	0.16%	0.023	0.0125
9A	Watermelon	0.2	5	10	2005, 2006	732	36	4.92%	0.14	0.0094
CROP GROUP 10										
10C	Grapefruit	2	n/a		2005, 2006	1463	0	0.00%	n/a	0.0140
10A	Orange	2	1	2.5	2004, 2005, 2009	2227	0	0.00%	n/a	0.0130
	Orange, juice				2005, 2006, 2011	1886	0	0.00%	n/a	0.0098
10A	Tangerine	2	n/a		2011	717	0	0.00%	n/a	0.0100
CROP GROUP 11										
11	Apple	1	5	10	2005, 2009, 2010	2231	7	0.31%	0.028	0.0044
	Apple, juice				2007, 2008	740	1	0.14%	0.023	0.0183
	Apple, sauce				2002, 2006	1102	0	0.00%	n/a	0.0092
CROP GROUP 12										
12B	Nectarine	5	5	10	2001, 2007, 2008	1594	38	2.38%	0.22	0.0051
12B	Peach	5	5	10	2006-2008	1261	37	2.93%	0.49	0.0067
	Peach, single serving				2000	534	15	2.81%	0.43	0.0080
	Peach, canned				2003, 2004	1485	0	0.00%	n/a	0.0120
CROP GROUP 13										
13B	Blueberry	6	25	35	2007, 2008	1437	50	3.48%	0.77	0.0079
	Blueberry, frozen				2007, 2008	40	3	7.50%	0.031	0.0072
13D	Grape	5	2.5	5	2005, 2009, 2010	2119	92	4.34%	1.77	0.0121
	Grape, juice				2008	722	0	0.00%	n/a	0.0224

TABLE 3: Summary of Primary PDP Data

CROP GROUP	PDP PRIMARY COMMODITY	TOLERANCE	PCT		PDP, YEARS	TOTAL SAMPLES	# DETECTS	% DETECTS	HIGHEST DETECTED RESIDUE	AVG LOD OF NON-DETECTS
			AVG	MAX						
CROP GROUP 15										
15	Barley	1	n/a		2002, 2003	1177	0	0.00%	n/a	0.0090
15	Corn, grain	0.1	1	2.5	2007, 2008	1291	0	0.00%	n/a	0.0030
15	Corn, sweet	0.1	25	65	2008-2010	181	0	0.00%	n/a	0.0104
	Corn, sweet on cob				2008-2010	1300	1	0.08%	0.011	0.0109
CROP GROUP 99										
86A	Water, unfinished	n/a	n/a		2008, 2009, 2011	733	0	0.00%	n/a	0.0053
86A	Water, finished	n/a	n/a		2008, 2009, 2011	733	0	0.00%	n/a	0.0053

For foods or commodities that were not monitored by PDP, data from similar crops, usually in the same crop group, were substituted. Adjustments were made to the translated data to correct for percent crop treated if necessary. Attachment 1, Table 1b is a summary of the translated PDP data used in RDF file construction.

For some foods or commodities, neither primary or translated PDP data were available or appropriate for use. Anticipated residues reported in USEPA's 2007 dietary exposure assessment were used directly for the following commodities: peanut (0.05 ppm), pomegranate (0.1 ppm), dried tomato (0.000004 ppm), dried apple (0.00039), dried peach (0.0054 ppm), and cottonseed oil (0.05 ppm). Unadjusted tolerance values were used for the following commodities: peppermint and peppermint oil (2.0 ppm), spearmint and spearmint oil (2.0 ppm), garden beet tops (6.0 ppm), and soybean (vegetable) (0.2 ppm).

The following commodities were monitored by PDP but showed no detectible residues: peanut butter, raisin, canned beets, potato, frozen potatoes, sweet potato, onion, canned spinach, canned dry beans, canned green beans, canned peas, soybean (grain), canned tomato, tomato paste, grapefruit, orange, orange juice, tangerines, apple sauce, canned peaches, grape juice, barley, corn grain, and sweet corn.

Illegal residue values for any commodity were excluded from the analysis. Tolerance violations reported by the department's Pesticide Residue Monitoring Program and by PDP are shown in Table 4. The most recent 10 years of data showed 16 violations reported by DPR and eight reported by PDP. Illegal residues were most frequently detected on strawberry, with eight violations. The highest detected illegal residue was 9.75 ppm on winter purslane. It should be noted that the goal of DPR's program is regulatory compliance, so samples are prepared according to the tolerance definition (usually "in or on"), while the PDP program is designed for dietary risk assessment so standard consumer practices such as rinsing are followed and only the edible portion of samples is analyzed for pesticide residues.

TABLE 4: Presumptive Tolerance Violations for Methomyl, Most Recent 10 Years of Data

USDA PESTICIDE DATA PROGRAM, 2002 - 2011					
YEAR	STATE	COMMOD	PEST_NAME	CONCEN (PPM)	COUNTRY_NAME
2002	NONE =====>				
2003	NONE =====>				
2004	CA	Cantaloupe	Methomyl	0.5	Guatemala
2004	TX	Cantaloupe	Methomyl	0.39	Guatemala
2004	CA	Cantaloupe	Methomyl	0.32	
2004	MD	Strawberry	Methomyl	4.1	
2004	MD	Strawberry	Methomyl	3.7	
2005	NONE =====>				
2006	NONE =====>				
2007	WI	Summer Squash	Methomyl	0.56	
2008	NONE =====>				
2009	NONE =====>				
2010	TX	Cilantro	Methomyl	8.4	
2010	OH	Cilantro	Methomyl	0.79	Mexico
2011	NONE =====>				

CALIFORNIA PESTICIDE RESIDE MONITORING PROGRAM, 2003 - 2013				
DATE	COMMOD	CHEMNAME	RESIDUE_AMT	ORIGIN_CD
4/21/04	CUCUMBER	METHOMYL	0.21	Mexico
8/9/05	EGGPLANT	METHOMYL	0.48	California
9/5/06	PAPAYA	METHOMYL	0.09	Mexico
9/19/06	STRAWBERRY	METHOMYL	2.6	California
2/19/09	BASIL	METHOMYL	0.11	California
2/23/09	BASIL	METHOMYL	0.94	Mexico
5/17/10	BASIL	METHOMYL	0.6	Hawaii
12/13/10	BEANS	METHOMYL	2.5	Mexico
6/15/11	STRAWBERRY	METHOMYL	1.57	California
4/23/12	STRAWBERRY	METHOMYL	0.526	Mexico
9/11/12	STRAWBERRY	METHOMYL	1.332	California
10/17/12	SPINACH, NEW ZEALAND	METHOMYL	1.27	California
11/28/12	STRAWBERRY	METHOMYL	0.09	California
4/22/13	PURSLANE, WINTER	METHOMYL	9.75	Mexico
4/29/13	PURSLANE, GARDEN	METHOMYL	4.06	Mexico
4/30/13	STRAWBERRY	METHOMYL	1.44	California

Thiodicarb Residues:

Thiodicarb is an N-methyl carbamate insecticide that is closely related to methomyl. The chemical structure is essentially two methomyl molecules joined through their amino nitrogen by sulfur, and it rapidly degrades to methomyl in the environment. All commodities that have a tolerance for thiodicarb, except soybean hulls, also have a tolerance for methomyl (Table 5). The tolerance expression for thiodicarb includes the parent compound plus methomyl.

Table 5: Thiodicarb Tolerances (e-CFR 40 §180.407, updated July 31, 2013) and Corresponding Methomyl Tolerances.

COMMODITY	TOLERANCE	
	THIODICARB	METHOMYL
Broccoli	7.0	3.0
Cabbage	7.0	5.0
Cauliflower	7.0	2.0
Corn, sweet, kernel plus cob with husks removed	2.0	0.1
Cotton, undelinted seed	0.4	0.1
Soybean, hulls	0.8	n/a
Soybean	0.2	0.2
Vegetable, leafy, except brassica, group 4:		
Amaranth	35.0	0.2
Arugula	35.0	0.2
Cardoon	35.0	0.2
Celery	35.0	3.0
Celery, Chinese	35.0	0.2
Celtuce	35.0	0.2
Chervil	35.0	0.2
Chrysanthemum, edible-leaved	35.0	0.2
Chrysanthemum, garland	35.0	0.2
Corn salad	35.0	0.2
Cress, garden	35.0	0.2
Cress, upland	35.0	0.2
Dandelion	35.0	6.0
Dock	35.0	0.2
Endive (escarole)	35.0	5.0
Fennel, Florence (finochio)	35.0	0.2
Lettuce, head and leaf	35.0	5.0

Table 5: Thiodicarb Tolerances (e-CFR 40 §180.407, updated July 31, 2013) and Corresponding Methomyl Tolerances.

COMMODITY	TOLERANCE	
	THIODICARB	METHOMYL
Orach	35.0	0.2
Parsley	35.0	6.0
Purslane, garden	35.0	0.2
Purslane, winter	35.0	0.2
Radicchio (red chicory)	35.0	0.2
Rhubarb	35.0	0.2
Spinach	35.0	6.0
Spinach, New Zealand	35.0	0.2
Spinach, vine	35.0	0.2
Swiss chard	35.0	6.0
Vegetable, leafy, brassica, group 5:		
Broccoli	7.0	3.0
Broccoli, Chinese	n/a	6.0
Broccoli raab	n/a	6.0
Brussels sprouts	n/a	2.0
Cabbage	7.0	5.0
Cabbage, Chinese (bok choy)	n/a	5.0
Cabbage, Chinese (napa)	n/a	5.0
Cabbage, Chinese mustard (gai choy)	n/a	6.0
Cauliflower	7.0	2.0
Cavalo broccolo	n/a	6.0
Collards	n/a	6.0
Kale	n/a	6.0
Kohlrabi	n/a	6.0
Mizuna	n/a	6.0
Mustard greens	n/a	6.0
Mustard spinach	n/a	6.0
Rape greens	n/a	6.0

n/a = No thiodicarb tolerance for this commodity.

Although once heavily used in California, mainly on cotton, thiodicarb use has declined steeply in the state since about 1998 when total use was 177,000 lbs. Average annual use between 2007 and 2011 was only 446 lbs. /year (Table 6). Considering that methomyl use for the same period was 260,543 lbs. /year, thiodicarb use in California was 0.2% of methomyl use by weight. In the 2009 screening level usage analyses for both pesticides, U.S. EPA listed use of 113,000 lbs. of thiodicarb and 802,500 lbs. of methomyl, indicating that thiodicarb use was approximately 14% of methomyl use nationally (U.S. EPA, 2009, 2009b). Most thiodicarb is used on sweet corn, soybeans, and cotton, with the total for those three crops approximately 100,000 lbs.

Table 6. Use of Thiodicarb in California (lbs.), 2007-2011.

	2007	2008	2009	2010	2011	Average, 2007-2011
CELERY	324	141	70	32	262	166
CORN (Human Cons.)	42	241	297	32	0	122
LETTUCE	169	24	45	66	129	87
Leaf Lettuce	*4*	*0*	*0*	*0*	*10*	*3*
Head Lettuce	*165*	*24*	*45*	*66*	*119*	*84*
COTTON	124	0	0	0	0	25
CABBAGE	11	1	78	21	0	22
CAULIFLOWER	0	0	8	0	51	12
BROCCOLI	0	0	11	0	30	8
SPINACH	17	1	0	0	0	4
N-GRNHS GRWN TRNSPLNT/PRPGTV MTRL	0	3	1	1	1	1
TOTAL USE FOR ALL SITES/CROPS	**686**	**411**	**511**	**152**	**472**	446

Thiodicarb is rarely detected in PDP monitoring studies. Between 2004 and 2011, PDP analyzed 12,974 food and drinking water samples for thiodicarb and detected residues in only two samples (Table 7). A pear sample in 2004 contained a thiodicarb residue but no methomyl, and a cabbage sample in 2011 contained residues of both thiodicarb and methomyl. These results could indicate the rapid degradation of the parent compound or the declining use of the pesticide during the sampling period.

Since thiodicarb use is relatively minor compared to methomyl, and thiodicarb itself is rarely detected in monitoring studies, it was not included in this dietary exposure assessment, except to the extent that some methomyl residues may have resulted from thiodicarb use.

Table 7: Summary of PDP Residue Data for Thiodicarb, 1994 - 2011.			
YEAR	**NUMBER OF COMMODITIES SAMPLED**	**TOTAL SAMPLES**	**NUMBER OF DETECTS (a)**
1994 -2003	no data ==>		
2004	2	163	1
2005	3 (b)	440	0
2006	no data ==>		
2007	3	131	0
2008	14	2,721	0
2009	12	2,416	0
2010	4	1,835	0
2011	14	5,268	1

(a) LOD (food) = 0.001 - 0.05 ppm; LOD (water) = 25 ppt.
(b) Water was monitored only in 2005. Results included unfinished water (111 samples), and finished water (113 samples). Remaining samples were lettuce (216 samples).

III. Drinking Water Data

Methomyl is considered to be a potential contaminant of surface water and ground water based on its physical properties (Van Scoy, 2013) but was not detected in municipal drinking water sources monitored by PDP from 2001 through 2011 (LOD = 1.8 – 20 ppt). Tables 8, 9, and 10 present the most recent 10 years of monitoring data for methomyl in California surface and ground water, as well as the national PDP data from municipal water treatment plants. Concentrations in surface water in California ranged as high as 55.3 ppb. In ground water, there was only one detected residue (15 ppb) and it was considered to be an error based on the results of retesting. PDP showed no detections in water treatment plant samples that were collected either before treatment or after treatment. The average LOD for the last three years of PDP monitoring of treated municipal drinking water was 5.3 ppt.

U.S EPA used modeled estimates of drinking water concentrations in their 2007 dietary exposure assessment for methomyl (U.S. EPA, 2007). Seventeen agricultural use patterns were included in the PRZM/EXAMS model, including five in California: lettuce, grapes, corn, onion, and tomato. One-in-10 year peak concentration estimates for these five uses ranged from 2.5 to 56 ppb. The results were characterized as conservative but not unreasonable.

Current monitoring studies are not considered representative of the range of possible methomyl exposures through drinking water because they aren't statistically balanced with respect to water sources or frequency of sampling. In addition, individual exposures could vary widely depending on methomyl use patterns, weather, soil types, depth of the water table, water treatment processes, etc.

However, modeled data specific to California were not available. For this analysis, the average LOD from the most recent three years of PDP monitoring was used as a point estimate for both acute and chronic exposure. Using a point estimate in this way may underestimate acute exposure but probably overestimates chronic exposure.

To estimate theoretical concentrations of methomyl in drinking water that may pose a health concern for sensitive populations, drinking water levels of comparison, or DWLOCs, were calculated for the general U.S. population and eight subpopulations. The 99.9%-tile food-only (except grape) exposure estimates were subtracted from the aPAD for each group and the remaining exposure was considered the maximum allowable exposure from drinking water. This value was divided by the 95%-tile acute water consumption values from DEEM-FCID (total of direct and indirect water) to estimate a methomyl drinking water concentration that would result in food plus water exposure equivalent to 100% of the aPAD (assuming no other sources of exposure except food and water). For two subpopulations, children 1-2 years and 3-5 years, food only exposure (except grape) exceeded 100% of the aPAD, so a DWLOC was not possible. For the remaining subpopulations, the DWLOCs for acute exposure to methomyl ranged from 0.9 ppb for all infants and children 6-12 years, to 49.7 ppb for youth 13-19 years (Table 11). These concentrations are within the range of acute concentrations estimated by U.S. EPA modeling for California use scenarios, and below the maximum concentration measured in California surface water since 2003, indicating that total dietary exposure to methomyl from food and drinking water could exceed 100% of the aPAD for any subpopulation in certain situations.

TABLE 8: Summary of CDPR Surface Water Monitoring for Methomyl, 2003 - 2012					
YEAR	CHEMICAL	SAMPLE COUNT	DETECTS	RANGE (PPB)	AVG. LOQ FOR NON-DETECTS (PPB)
2003	NO DATA ====>				
2004	Methomyl	8	0	NR	0.274
2005	Methomyl	61	0	NR	0.149
2006	Methomyl	249	12	0.08 - 12	0.112
2007	Methomyl	590	35	0.056 - 10.29	0.071
2008	Methomyl	688	65	0.046 - 32.8	0.066
2009	Methomyl	267	40	0.062 - 9.38	0.059
2010	Methomyl	87	21	0.052 - 55.3	0.086
2011	NO DATA ====>				
2012	NO DATA ====>				
NR = not reported					

TABLE 9: Summary of Ground Water Monitoring for Methomyl in California, 2003 - 2012

CHEMICAL	YEAR	AGENCY	SAMPLES	WELLS	DETECTION LIMITS (PPB)		RESULTS (PPB)	
					min.	max.	min.	max.
METHOMYL	2003	USGS	77	77	0.001	0.03	0	0
METHOMYL	2003	CDPH	1177	921	0.5	5	0	0
METHOMYL	2004	CDPH	800	621	0.5	5	0	0
METHOMYL	2005	CDPH	759	637	NR	2	0	0
METHOMYL	2006	CDPH	672	605	NR	2	0	15(a)
METHOMYL	2007	CDPR	1	1	0.05	0.05	0	0
METHOMYL	2007	CDPH	654	510	NR	2	0	0
METHOMYL	2008	CDPH	543	446	NR	5	0	0
METHOMYL	2009	CDPH	668	603	NR	5	0	0
METHOMYL	2010	CDPH	535	411	NR	5	0	0
METHOMYL	2011	CDPH	420	328	NR	5	0	0
METHOMYL	2012	SWRCB/USGS	727	723	0.004	0.12	0	0
METHOMYL	2012	CDPH	483	406	NR	2	0	0

(a) USGS = US Geological Survey; CDPH = California Dept. of Public Health; CDPR = California Dept. of Pesticide Regulation; SWRCG = (California) State Water Resources Control Board.

(b) Represents a single detection from a well in San Joaquin County. Six subsequent samples from the well showed no detectible residue.

NR = Not Reported

TABLE 10: Summary of PDP Analysis of Drinking Water for Methomyl, 2001-2011, Including Results of Paired Samples (Pre-Treatment and Post-Treatment) From Community Water Systems that Use Surface Water From Agricultural Areas

YEAR	PESTICIDE	COMMODITY	TOTAL SAMPLES (CALIF. SAMPLES)	DETECTS	LOD RANGE (PPT)
2001	Methomyl	Water, Finished	134 (134)	0	20 - 20
2002	Methomyl	Water, Finished	495 (267)	0	1.8 - 23
2003	Methomyl	Water, Finished	542 (261)	0	1.8 - 23
2004	Methomyl	Water, Finished	113 (0)	0	6 - 6
2004	Methomyl	Water, Untreated	114 (0)	0	6 - 6
2005	Methomyl	Water, Finished	230 (26)	0	3.6 - 25
2005	Methomyl	Water, Untreated	231 (26)	0	3.6 - 25
2006	Methomyl	Water, Finished	365 (9)	0	3.6 - 75
2006	Methomyl	Water, Untreated	367 (9)	0	3.6 - 75
2007	Methomyl	Water, Finished	368 (0)	0	3.6 - 75
2007	Methomyl	Water, Untreated	362 (0)	0	3.6 - 75
2008	Methomyl	Water, Finished	309 (0)	0	1.8 - 7.3
2008	Methomyl	Water, Untreated	308 (0)	0	1.8 - 7.3
2009	Methomyl	Water, Finished	306 (0)	0	1.8 - 7.3
2009	Methomyl	Water, Untreated	305 (0)	0	1.8 - 7.3
2010	NO DATA ====>				
2011	Methomyl	Water, Finished	118 (0)	0	3.6 - 3.6
2011	Methomyl	Water, Untreated	120 (0)	0	3.6 - 3.6

Table 11: Drinking Water Levels of Comparison for Methomyl Using 99%-tile Food-Only (Except Grape) Exposures and 95%-tile Direct + Indirect Water Consumption Values

Population Subgroup	aPAD (mg/kg/day)	Estimated exposure from food only (except grapes) (mg/kg/day) (a)	Allowable 1-day exposure from water (aPAD - food exposure) (mg/kg/day)	Acute water consumption values from DEEM-FCID (g/kg/day) (b)	Calculated DWLOC (ppb) (c)
General U.S. Population	0.003	0.001319	0.001681	54	31.1
All Infants (< 1 year old)	0.00075	0.000602	0.000148	171	0.9
Children 1-2 years old	0.00075	0.001219	-0.000469	84	0 (d)
Children 3-5 years old	0.00075	0.001177	-0.000427	68	0 (d)
Children 6-12 years old	0.00075	0.000702	0.000048	52	0.9
Youth 13-19 years old	0.003	0.000762	0.002238	45	49.7
Adults 20-49 years old	0.003	0.001451	0.001549	54	28.7
Adults 50+ years old	0.003	0.001610	0.001390	48	29.0
Females 13-49 years old	0.003	0.001450	0.001550	54	28.7

(a) 99.9%-tile per user exposure values.
(b) 95%-tile per capita consumption values for all direct and indirect water.
(c) DWLOC = Drinking Water Level of Comparison, assumes all non-food exposures result from drinking water since there are no residential exposures for methomyl.
(d) Food-only (except grape) exposure exceeds the aPAD, therefore DWLOC = 0.

IV. DEEM-FCID™ Program and Consumption Information

Methomyl acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database DEEM-FCID™, Version 3.18 which uses food consumption data from the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) from 2003-2008.

Foods "as consumed" (e.g., apple pie) are linked to U.S. EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and U.S. EPA. For chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups, but for acute exposure assessment are retained as individual consumption events. Risk is typically reported for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic dietary exposure assessment, an estimate of the residue level in each food or food-form on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD based only on users (only those who reported eating relevant commodities/food forms).

V. Toxicological Information

A summary of the toxicological doses and endpoints selected for dietary exposure assessment is provided in Table 12. These endpoints will be discussed in detail in the comprehensive risk characterization document.

Table 12: Summary of Toxicological Doses and Endpoints for Methomyl

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD	Study and Toxicological Effects
Acute Dietary (General Population, including Infants and Children)	BMDL10 = 0.03 mg/kg	UF_H= 10x FQPA SF= 4x (applies to infants/children)	Acute RfD = 0.003 mg/kg/day aPAD = 0.00075 mg/kg/day	Human RBC cholinesterase inhibition (McFarlane, 1998)
Chronic Dietary (All Populations)	NOAEL = 3 mg/kg/day	UF_A = 10x UF_H = 10x	Chronic RfD = 0.03 mg/kg/day cPAD = 0.03 mg/kg/day	Histopathologic abnormalities in the kidney and spleen in a chronic dog feeding study (Busey, 1968)
Cancer (oral, dermal, inhalation)		(Not Applicable)		

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. UF_A = extrapolation from animal to human (intraspecies). UF_H = potential variation in sensitivity among members of the human population (interspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose.

VI. Results/Discussion

Acute Dietary (Food Only and Food Plus Drinking Water) Exposure Results and Characterization

A refined acute probabilistic exposure assessment was conducted for the general U.S. population and various population subgroups using primarily U. S. Department of Agriculture (USDA) Pesticide Data Program (PDP) monitoring data for 2000 through 2011 combined with percent crop treated (PCT) estimates provided in U.S. EPA's 2009 screening level usage analysis for methomyl. For a few commodities or food forms, tolerances or anticipated residues calculated by U.S. EPA were used as residue estimates. Exposures were aggregated by eating occasion rather than over 24 hours due to the specific mechanism of action of methomyl.

Exposure was calculated with and without drinking water (included as a point estimate at the limit of detection (LOD), 5.3 ppt, and with and without grape. (Methomyl use on grape was cancelled in December 2010 with some use allowed until December 2016.)

The results indicate that at the 99.9%-tile of exposure, food-only dietary risk for children aged 1-2 years and 3-5 years exceeds the threshold of concern even when grape is excluded from the assessment Tables 13 and 14). Exposure without grape was 163% of the aPAD for children 1-2 years and 157% of the aPAD for children 3-5 years.

When drinking water exposure is included in the assessment as a point estimate of 5.3 ppt, a concentration that appears to be quite low compared to the results of surface water monitoring and drinking water modeling studies, food-plus-water (excluding grape) dietary risk exceeds the threshold of concern for children aged 1-2 years and 3-5 years (Tables 15 and 16). Exposure was 159% of the aPAD for children 1-2 years and 160% of the aPAD for children 3-5 years.

Table 13. Results of Acute Dietary (Food Only) Exposure Analysis for Methomyl Using DEEM-FCID (a)

FOOD ONLY											
Population Subgroup	POD (mg/kg)	aPAD (mg/kg/day)	95th Percentile (Users)			99th Percentile (Users)			99.9th Percentile (Users)		
			Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)
General U.S. Population	0.03	0.003	0.000067	2.2	448	0.000177	5.9	169	0.001495	49.8	20
All Infants (< 1 year old)		0.00075	0.000097	12.9	309	0.000201	26.8	149	0.000731	97.5	41
Children 1-2 years old		0.00075	0.000169	22.5	178	0.000402	53.6	75	0.002327	310.3	13
Children 3-5 years old		0.00075	0.000133	17.7	226	0.000307	40.9	98	0.001977	263.6	15
Children 6-12 years old		0.00075	0.000086	11.5	349	0.000179	23.9	168	0.001149	153.2	26
Youth 13-19 years old		0.003	0.000052	1.7	577	0.000135	4.5	222	0.000843	28.1	36
Adults 20-49 years old		0.003	0.000053	1.8	566	0.000142	4.7	211	0.001491	49.7	20
Adults 50+ years old		0.003	0.000051	1.7	588	0.000146	4.9	205	0.001685	56.2	18
Females 13-49 years old		0.003	0.000049	1.6	612	0.000141	4.7	213	0.001499	50.0	20

(a) Shaded cells indicate exposures that exceed 100% of the aPAD.
(b) Target MOE is 10 for youth and adults, 40 for infants and children.

Table 14. Results of Acute Dietary (Food Only Except Grapes) Exposure Analysis for Methomyl Using DEEM-FCID (a)

FOOD ONLY EXCEPT GRAPE										
Population Subgroup	POD (mg/kg)	aPAD (mg/kg/day)	95th Percentile (Users)			99th Percentile (Users)			99.9th Percentile (Users)	
			Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)
General U.S. Population	0.03	0.003	0.000064	2.1	469	0.000162	5.4	185	0.001319	44.0	23
All Infants (< 1 year old)		0.00075	0.000093	12.4	323	0.000185	24.7	162	0.000602	80.3	50
Children 1-2 years old		0.00075	0.000153	20.4	196	0.000317	42.3	95	0.001219	162.5	25
Children 3-5 years old		0.00075	0.000124	16.5	242	0.000276	36.8	109	0.001177	156.9	25
Children 6-12 years old		0.00075	0.000082	10.9	366	0.000159	21.2	189	0.000702	93.6	43
Youth 13-19 years old		0.003	0.000050	1.7	600	0.000125	4.2	240	0.000762	25.4	39
Adults 20-49 years old		0.003	0.000051	1.7	588	0.000134	4.5	224	0.001451	48.4	21
Adults 50+ years old		0.003	0.000049	1.6	612	0.000133	4.4	226	0.001610	53.7	19
Females 13-49 years old		0.003	0.000047	1.6	638	0.000132	4.4	227	0.001450	48.3	21

(a) Shaded cells indicate exposures that exceed 100% of the aPAD.
(b) Target MOE is 10 for youth and adults, 40 for infants and children.

Table 15. Results of Acute Dietary (Food Plus Water) Exposure Analysis for Methomyl Using DEEM-FCID (a)

FOOD PLUS WATER											
Population Subgroup	POD (mg/kg)	aPAD (mg/kg/day)	95th Percentile (Users)			99th Percentile (Users)			99.9th Percentile (Users)		
			Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)
General U.S. Population	0.03	0.003	0.000067	2.2	448	0.000177	5.9	169	0.001508	50.3	20
All Infants (< 1 year old)		0.00075	0.000098	13.1	306	0.000200	26.7	150	0.000745	99.3	40
Children 1-2 years old		0.00075	0.000169	22.5	178	0.000402	53.6	75	0.002247	299.6	13
Children 3-5 years old		0.00075	0.000134	17.9	224	0.000308	41.1	97	0.002102	280.3	14
Children 6-12 years old		0.00075	0.000086	11.5	349	0.000179	23.9	168	0.001125	150.0	27
Youth 13-19 years old		0.003	0.000052	1.7	577	0.000135	4.5	222	0.000857	28.6	35
Adults 20-49 years old		0.003	0.000053	1.8	566	0.000142	4.7	211	0.001498	49.9	20
Adults 50+ years old		0.003	0.000051	1.7	588	0.000146	4.9	205	0.001728	57.6	17
Females 13-49 years old		0.003	0.000049	1.6	612	0.000142	4.7	211	0.001519	50.6	20

(a) Shaded cells indicate exposures that exceed 100% of the aPAD.
(b) Target MOE is 10 for youth and adults, 40 for infants and children.

Table 16. Results of Acute Dietary (Food Plus Water Except Grapes) Exposure Analysis for Methomyl Using DEEM-FCID (a)

FOOD PLUS WATER EXCEPT GRAPE										
Population Subgroup	POD (mg/kg)	aPAD (mg/kg/day)	95th Percentile (Users)			99th Percentile (Users)			99.9th Percentile (Users)	
			Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)	Exposure (mg/kg/day)	% aPAD	MOE (b)
General U.S. Population	0.03	0.003	0.000065	2.2	462	0.000162	5.4	185	0.001323	44.1	23
All Infants (< 1 year old)		0.00075	0.000094	12.5	319	0.000185	24.7	162	0.000561	74.8	53
Children 1-2 years old		0.00075	0.000154	20.5	195	0.000320	42.7	94	0.001195	159.3	25
Children 3-5 years old		0.00075	0.000124	16.5	242	0.000275	36.7	109	0.001200	160.0	25
Children 6-12 years old		0.00075	0.000082	10.9	366	0.000160	21.3	188	0.000698	93.1	43
Youth 13-19 years old		0.003	0.000051	1.7	588	0.000125	4.2	240	0.000739	24.6	41
Adults 20-49 years old		0.003	0.000051	1.7	588	0.000134	4.5	224	0.001465	48.8	20
Adults 50+ years old		0.003	0.000049	1.6	612	0.000134	4.5	224	0.001659	55.3	18
Females 13-49 years old		0.003	0.000047	1.6	638	0.000132	4.4	227	0.001454	48.5	21

(a) Shaded cells indicate exposures that exceed 100% of the aPAD.
(b) Target MOE is 10 for youth and adults, 40 for infants and children.

Chronic Dietary (Food and Drinking Water) Exposure Results and Characterization

A refined chronic dietary exposure assessment was conducted for the general U.S. population and various population subgroups using the same data sources described for the acute exposure assessment. Drinking water was included in the assessment as a point estimate at the limit of detection, 5.3 ppt.

The results indicate that dietary risk for food plus drinking water is below the threshold of concern for the general U.S. population and all population subgroups (Table 17). The most highly exposed population subgroups, children 1-2 years and children 3-5 years, utilized 0.2% of the cPAD.

Table 17. Results of Chronic Dietary (Food Plus Water) Exposure Analysis for Methomyl Using DEEM-FCID

Population Subgroup	cPAD (mg/kg/day)	Chronic Dietary		
		Dietary Exposure (mg/kg/day)	% cPAD	MOE
General U.S. Population	0.03	0.000030	0.1	100,000
All Infants (< 1 year old)		0.000026	0.1	115,385
Children 1-2 years old		0.000063	0.2	47,619
Children 3-5 years old		0.000058	0.2	51,724
Children 6-12 years old		0.000039	0.1	76,923
Youth 13-19 years old		0.000025	0.1	120,000
Adults 20-49 years old		0.000026	0.1	115,385
Adults 50+ years old		0.000026	0.1	115,385
Females 13-49 years old		0.000025	0.1	120,000

VII. Sensitivity Analysis

A sensitivity analysis was performed to determine the commodities contributing to acute risks that exceed 100% of the aPAD and to determine whether residues based on analytical detection limits contributed significantly to overall exposure. Risk levels for children 1-2 years and 3-5 years exceeded 100% of the aPAD for food only and food plus water at the 99.9%-tile of exposure, even when grape was eliminated from the assessment. Grape was the highest contributor for both groups, consisting of 27% of total exposure for children 1-2 years and 25% of total exposure for children 3-5 years. The grape residue data used in the analysis was from PDP surveys conducted in 2005, 2009, and 2010 that showed 92 detections out of 2,119 samples, therefore the data were current and based on actual detected residues.

When grape is eliminated from the assessment, apple juice is the highest contributor to exposure for both groups (35% for children 1-2 years and 19% for children 3-5 years). Methomyl exposure from apple juice is based on a single detected residue of 0.023 ppm out of 740 samples analyzed during 2007 and 2008. Looking back at older PDP data, there has been only one other detected residue in apple juice out of 2,283 samples analyzed since 1996.

After apple juice, cantaloupe, head lettuce, and peanuts are the next highest contributors (Table 18). Cantaloupe and lettuce residues estimates were based on actual, detected residues in the PDP survey, however, since peanuts were not monitored by PDP, the residue was based a field trial that showed no detections in treated crops (anticipated residue was ½ LOD = 0.05 ppm).

Table 18. Ten Top Foods or Food Forms (Except Grape) That Contribute to Acute Methomyl Exposure in Children 1-2 Years and Children 3-5 Years

Children 1-2

```
Low percentile for CEC records: 99     Exposure (mg/day) =    0.000251
High percentile for CEC records: 99.9  Exposure (mg/day) =    0.001202
Number of actual records in this interval: 2511


Critical foods with foodforms for this population (as derived from these records):
  N=number of appearances in all records (including duplicates)
  %=percent of total exposure for all records (including duplicates)

Food         FF       N     Percent   Food Name
----------   ---    -----   -------   -------------
1100010000   110     1424    34.80%   Apple, juice-Uncooked; Fresh or N/S; Cook Meth N/S
0901075000   110      264    10.04%   Cantaloupe-Uncooked; Fresh or N/S; Cook Meth N/S
0401204000   110      172     5.72%   Lettuce, head-Uncooked; Fresh or N/S; Cook Meth N/S
0901399000   110      135     5.32%   Watermelon-Uncooked; Fresh or N/S; Cook Meth N/S
1100010001   240      165     4.80%   Apple, juice-babyfood-Cooked; Canned; Cook Meth N/S
9500020000   110       59     3.88%   Avocado-Uncooked; Fresh or N/S; Cook Meth N/S
9500263000   211      181     3.63%   Peanut-Cooked; Fresh or N/S; Baked
1202260000   110       68     3.16%   Peach-Uncooked; Fresh or N/S; Cook Meth N/S
1100010000   240      160     3.13%   Apple, juice-Cooked; Canned; Cook Meth N/S
0601043000   212      110     2.91%   Bean, snap, succulent-Cooked; Fresh or N/S; Boiled
```

Children 3-5

```
Low percentile for CEC records: 99     Exposure (mg/day) =    0.000239
High percentile for CEC records: 99.9  Exposure (mg/day) =    0.001173
Number of actual records in this interval: 1854


Critical foods with foodforms for this population (as derived from these records):
  N=number of appearances in all records (including duplicates)
  %=percent of total exposure for all records (including duplicates)

Food         FF       N     Percent   Food Name
----------   ---    -----   -------   -------------
1100010000   110      620    19.21%   Apple, juice-Uncooked; Fresh or N/S; Cook Meth N/S
9500263000   211      373    14.13%   Peanut-Cooked; Fresh or N/S; Baked
0401204000   110      248    11.54%   Lettuce, head-Uncooked; Fresh or N/S; Cook Meth N/S
9500289000   110       92     7.10%   Pomegranate-Uncooked; Fresh or N/S; Cook Meth N/S
0901075000   110      158     6.70%   Cantaloupe-Uncooked; Fresh or N/S; Cook Meth N/S
0901399000   110      132     6.54%   Watermelon-Uncooked; Fresh or N/S; Cook Meth N/S
0601043000   212       76     3.70%   Bean, snap, succulent-Cooked; Fresh or N/S; Boiled
9500020000   110       40     3.32%   Avocado-Uncooked; Fresh or N/S; Cook Meth N/S
1202260000   110       44     2.48%   Peach-Uncooked; Fresh or N/S; Cook Meth N/S
0802270000   210       49     1.64%   Pepper, bell-Cooked; Fresh or N/S; Cook Meth N/S
```

To determine whether residue estimates based on the LOD were having a significant effect on exposure and risk, food only exposure was recalculated after deleting residues for all commodities with no detectible residues. The results are shown in Table 19. Excluding commodities with no detectible residues had no effect on risk for the general U.S. population (49.8% of the aPAD in both cases) and it had a small effect for the two subpopulations with highest exposures: for children 1-2 years, risk decreased from 155% to 125%, and in children 3-5 years, risk increased from 132% to 177%. These results indicate that, in general, risk estimates are based on consumption of commodities with detectible residues.

Table 19. Sensitivity Analysis: Comparison of Exposure With and Without Commodities With No Detectible Residues in the PDP Survey (99.9th Percentile, Users)				
FOOD ONLY				
Population Subgroup	**ALL FOODS**		**EXCLUDING NON-DETECTS**	
	Exposure (mg/kg/day)	**% aPAD**	**Exposure (mg/kg/day)**	**% aPAD**
General U.S. Population	0.001495	49.8	0.001493	49.8
All Infants (< 1 year old)	0.000731	48.8	0.000656	43.8
Children 1-2 years old	0.002327	155.1	0.001876	125.1
Children 3-5 years old	0.001977	131.8	0.002650	176.7
Children 6-12 years old	0.001149	76.6	0.001478	98.6
Youth 13-19 years old	0.000843	28.1	0.000995	33.2
Adults 20-49 years old	0.001491	49.7	0.001448	48.3
Adults 50+ years old	0.001685	56.2	0.001649	55.0
Females 13-49 years old	0.001499	50.0	0.001452	48.4

VIII. Tolerance Assessment

Introduction

A tolerance is the legal maximum residue concentration of a pesticide that is allowed on a raw agricultural commodity or processed food. Tolerances are established at levels necessary for the maximum application rate and frequency, and not expected to produce deleterious health effects in humans from chronic dietary exposure (U.S. EPA, 1991). U.S. EPA is responsible for setting tolerances for pesticide residues in raw agricultural commodities (Section 408 of FFDCA) and processed commodities (Section 409 of FFDCA) under the Federal Food, Drug, and Cosmetic Act (FFDCA). The data requirements for tolerances include: (1) residue chemistry, (2) environmental fate, (3) toxicology, (4) product performance such as efficacy, and (5) product chemistry (Code of Federal Regulations, 1996). Field studies must reflect the proposed use with respect to the rate and mode of application, number and timing of applications and formulations proposed (U.S. EPA, 1982).

In 1996, the Food Quality Protection Act (FQPA) amended the overall regulation of pesticide residues under FIFRA and FFDCA (U.S. EPA, 1997). One major change was the removal of the Delaney Clause that prohibited residues of cancer-causing pesticides in processed foods. Tolerances must be health-based and the same standards are used to establish tolerances for both the raw agricultural commodities and their processed forms. FQPA required an explicit finding that tolerances are safe for children. U.S. EPA was required to use an extra 10-fold safety factor to take into account potential pre- and post-natal developmental toxicity and the completeness of the data unless they determined, based on reliable data, that a different margin would be safe. In addition, evaluations of the tolerance must take into account: (1) aggregate exposure from all non-occupational sources, (2) effects from cumulative exposure to the pesticide and other substances with common mechanisms of toxicity, (3) effects of in utero exposure; and (4) potential for endocrine disrupting effects. Under FQPA, U.S. EPA is also required to reassess all existing tolerances and exemptions from tolerances for both active and inert ingredients by 2006 (U.S. EPA, 1997). Previously, they reassessed tolerances as part of its reregistration and Special Review processes. In the evaluation of tolerances, U.S. EPA uses a tiered approach and the assessment includes all label-use commodities. Tolerances for methomyl were reassessed under FQPA in 1998 and then again in 2007 in conjunction with the N-methyl carbamate cumulative risk assessment.

In California, U.S. EPA established tolerances are evaluated under the mandate of Assembly Bill 2161, generally referred to as the Food Safety Act (Bronzan and Jones, 1989). The Act requires DPR to conduct an assessment of dietary risks associated with the consumption of produce and processed food treated with pesticides. When the risk is considered deleterious to human health, DPR can promulgate regulations to mitigate the exposure.

At DPR, the tolerance assessment is conducted for a single individual label-approved commodity (DPR, 2009). The commodities are selected with potential for high exposures based on commodity contribution analyses. Exposure is the sum of the 95th percentile exposure to the individual commodity with the residue level set at the tolerance and a background exposure. For each analysis, the background exposure is the chronic dietary exposure for all commodities. While this approach results in double counting of the commodity of interest, it conserves time and resources since chronic exposure analysis would have been conducted. If the MOEs for the sum of the exposures indicate potential health concern, then the total exposure is refined with the commodity of interest eliminated from the background exposure.

Acute Dietary Exposure

For methomyl, tolerances for the following commodities were evaluated: apple, avocado, bell pepper, broccoli, cantaloupe, field corn, grape, lettuce, nectarine, orange, peach, peanut, spinach, watermelon, and wheat (Table 15). These commodities were selected because of high consumption rates or high contribution to exposure in U.S. EPA's 2007 dietary exposure assessment. Since the calculated MOEs were usually far below the target MOE (10 for youths and adults, 40 for infants and children), chronic background exposure was not added to the tolerance.

Results showed that tolerances for the following commodities were health protective for all populations: bell pepper and peanut. Results showed that tolerances for the following commodities were not health protective (calculated MOE < target MOE) for one or more population groups: apple, avocado, broccoli, cantaloupe, field corn, grape, lettuce, nectarine, orange, peach, spinach, watermelon, and wheat. That is, the highest legal methomyl residue for these commodities would not have health protective MOEs, and DPR has measured methomyl residues at or near the tolerance for some of these commodities. For this reason, current tolerances should be reexamined by U.S. EPA.

Chronic Dietary Exposure

A chronic exposure assessment using residues equal to the established tolerances for individual or combinations of commodities was not conducted because it is highly improbable, that an individual would habitually consume single or multiple commodities with pesticide residues at the tolerance levels. Support for this conclusion comes from FDA and DPR pesticide monitoring programs which indicate that less than 1 percent of all sampled commodities have residue levels at or above the established tolerance.

TABLE 20: Acute Margins of Exposure for Consumption of Single Commodities With Tolerance Level Residues										
COMMODITY (includes all food forms)	TOLERANCE	MOE (95th percentile, Users) (a)								
		US pop.	All infants	1-2 years	3-5 years	6-12 years	13-19 years	20-49 years	50+ years	Females 13-49 yrs
Apple	**1**	1	0	0	0	1	3	4	6	4
Avocado	**2**	5	2	5	3	2	6	6	6	6
Bell pepper	**0.2**	204	401	118	116	160	193	189	244	197
Broccoli	**3**	2	1	1	1	1	3	3	3	3
Cantaloupe	**0.2**	21	14	6	7	13	10	34	37	36
Corn, field	**0.1**	69	20	37	40	50	67	81	139	85
Grape	**5**	0	0	0	0	0	1	1	1	1
Lettuce	**5**	2	2	1	1	2	3	2	3	2
Nectarine	**5**	1	0	0	0	0	1	1	2	1
Orange	**2**	0	0	0	0	0	0	0	1	0
Peach	**5**	2	0	0	1	2	4	4	3	5
Peanut	**0.1**	236	168	81	102	136	265	313	320	311
Spinach	**6**	2	1	1	1	1	2	2	2	2
Watermelon	**0.2**	8	4	4	2	7	9	10	16	10
Wheat flour	**1**	6	6	3	3	4	6	9	12	9
(a) Target MOE is 10 for youths and adults, 40 for infants and children. Shaded cells indicate MOEs less than the target, e.g., the tolerance is not health protective.										

IX. Conclusions

Refined chronic and acute probabilistic dietary exposure assessments for methomyl were conducted for the general U.S. population and various population subgroups. Drinking water exposure was included as a point estimate at the LOD, 5.3 ppt. Exposures were calculated with and without grape residues. Acute food-only and food plus water dietary risk exceeds the threshold of concern for children 1-2 years and 3-5 years even when grape is excluded from the analysis. Chronic food plus water dietary risks were acceptable for all subpopulations.

X. References

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Attachment 1

Summary of PDP Data Used to Construct Residue Data Files

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
ASPARAGUS	**CG0**						
	2010	372	16	10 %CT			
	2009	744	24	ZEROES	1339		
	2008	372	12	1/2LOD	97		
				DETECTS	52	***1/2LOD=***	***0.0053***
	TOTAL	***1488***	***52***		1488		
ASPARAGUS, CANNED	**CG0**						
	2003	354	0	10 %CT			
				ZEROES	319		
				1/2LOD	35		
				DETECTS	0	***1/2LOD=***	***0.0053***
	TOTAL	***354***	***0***		354		
PEANUT BUTTER	**CG0**						
	2006	674	0	10 %CT			
	2000	716	0	ZEROES	0		
				1/2LOD	1390	***1/2LOD=***	***0.0050***
				DETECTS	0		
	TOTAL	***1390***	***0***		1390		
RAISIN	**CG0**						
	2007	372	0	5 %CT			
	2006	372	0	ZEROES	707		
				1/2LOD	37	***1/2LOD=***	***0.0042***
				DETECTS	0		
	TOTAL	***744***	***0***		744		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
BEETS, CANNED	**CG01**						
	2011	756	0	40 %CT			
				ZEROES	302		
				1/2LOD	454	***1/2LOD=***	***0.0063***
				DETECTS	0		
	TOTAL	***756***	***0***		756		
CARROT	**CG01**						
	2007	722	0	35 %CT			
	2006	744	1	ZEROES	1313		
	2002	554	0	1/2LOD	706	***1/2LOD=***	***0.0041***
				DETECTS	1		
	TOTAL	***2020***	***1***		2020		
POTATO	**CG01**						
	2009	744	0	5 %CT			
	2008	744	0	ZEROES	1765		
	2002	370	0	1/2LOD	93	***1/2LOD=***	***0.0051***
				DETECTS	0		
	TOTAL	***1858***	***0***		1858		
POTATO, FZN	**CG01**						
	2007	800	0	5 %CT			
	2006	744	0	ZEROES	1467		
				1/2LOD	77	***1/2LOD=***	***0.0024***
				DETECTS	0		
	TOTAL	***1544***	***0***		1544		
SWEET POTATO	**CG01**						
	2009	739	0	15 %CT			
	2008	184	0	ZEROES	1413		
	2004	739	0	1/2LOD	249	***1/2LOD=***	***0.0041***
				DETECTS	0		
	TOTAL	***1662***	***0***		1662		

PDP Years Used		NO. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
EGGPLANT100PCT	**CG08 BC**						
	2006	740	9	100 %CT			
	2005	736	22	ZEROES	0		
				1/2LOD	1445	***1/2LOD=***	***0.0060***
				DETECTS	31		
	TOTAL	***1476***	***31***		1476		
CANTALOUPE100pct	**CG09 A**						
	2010	371	37	100 %CT			
	2005	558	88	ZEROES	0		
	2011	739	27	1/2LOD	1516	***1/2LOD=***	***0.0054***
				DETECTS	152		
	TOTAL	***1668***	***152***		1668		
CUCUMBER100PCT	**CG09 B**						
	2010	744	16	100 %CT			
	2009	744	22	ZEROES	0		
	2004	557	13	1/2LOD	1994	***1/2LOD=***	***0.0039***
				DETECTS	51		
	TOTAL	***2045***	***51***		2045		
WINTERSQ100PCT	**CG09 B**						
	2006	369	2	100 %CT			
	2005	731	0	ZEROES	0		
	2011	186	0	1/2LOD	1284	***1/2LOD=***	***0.0062***
				DETECTS	2		
	TOTAL	***1286***	***2***		1286		
WINTERSQ10PCT	**CG09 B**						
	2006	369	2	10 %CT			
	2005	731	0	ZEROES	1157		
	2011	186	0	1/2LOD	127	***1/2LOD=***	***0.0062***
				DETECTS	2		
	TOTAL	***1286***	***2***		1286		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
SPINACH	**CG04**						
	2009	744	33	25 %CT			
	2008	744	18	ZEROES	1499		
	2006	511	36	1/2LOD	413	***1/2LOD=***	***0.0049***
				DETECTS	87		
	TOTAL	***1999***	***87***		1999		
SPINACH, CANNED	**CG04**						
	2004	371	0	25 %CT			
	2011	198	0	ZEROES	427		
				1/2LOD	142	***1/2LOD=***	***0.0057***
				DETECTS	0		
	TOTAL	***569***	***0***		569		
SPINACH, FROZEN	**CG04**						
	2011	198	1	25 %CT			
				ZEROES	149		
				1/2LOD	48	***1/2LOD=***	***0.0050***
				DETECTS	1		
	TOTAL	***198***	***1***		198		
BROCCOLI	**CG05**						
	2008	554	3	20 %CT			
	2007	736	10	ZEROES	1180		
	2006	185	5	1/2LOD	277	***1/2LOD=***	***0.0017***
				DETECTS	18		
	TOTAL	***1475***	***18***		1475		
CABBAGE	**CG05**						
	2010	743	14	15 %CT			
	2011	742	9	ZEROES	1262		
				1/2LOD	200	***1/2LOD=***	***0.0018***
				DETECTS	23		
	TOTAL	***1485***	***23***		1485		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)							
PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
CAULIFLOWER	**CG05**						
	2006	558	4	15 %CT			
	2005	741	14	ZEROES	1262		
	2011	186	1	1/2LOD	204	***1/2LOD=***	***0.0007***
				DETECTS	19		
	TOTAL	***1485***	***19***		1485		
COLLARD GREENS	**CG05**						
	2008	240	4	n/a			
	2007	353	6	ZEROES	0		
	2006	86	0	1/2LOD	669	***1/2LOD=***	***0.0056***
				DETECTS	10		
	TOTAL	***679***	***10***		679		
KALE	**CG05**						
	2008	318	1	n/a			
	2007	383	3	ZEROES	0		
	2006	98	1	1/2LOD	794	***1/2LOD=***	***0.0055***
				DETECTS	5		
	TOTAL	***799***	***5***		799		
BEANS, BLACK CANNED	**CG06**						
	2010	367	0	25 %CT			
				ZEROES	0		
				1/2LOD	367	***1/2LOD=***	***0.0050***
				DETECTS	0		
	TOTAL	***367***	***0***		367		
BEANS, GARBANZO CANNED	**CG06**						
	2009	186	0	25 %CT			
				ZEROES	0		
				1/2LOD	186	***1/2LOD=***	***0.0053***
				DETECTS	0		
	TOTAL	***186***	***0***		186		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
BEANS, GREEN	**CG06**						
	2008	741	10	20 %CT			
	2007	739	15	ZEROES	726		
	2005	181	7	1/2LOD	162	***1/2LOD=***	***0.0058***
				DETECTS	32		
	TOTAL	***920***	***32***		920		
BEANS, GREEN BF	**CG06**						
	2011	584	0	20 %CT			
				ZEROES	467		
				1/2LOD	117	***1/2LOD=***	***0.0060***
				DETECTS	0		
	TOTAL	***584***	***0***		584		
BEANS, GREEN CANNED	**CG06**						
	2004	185	0	20 %CT			
	2003	743	0	ZEROES	742		
				1/2LOD	186	***1/2LOD=***	***0.0071***
				DETECTS	0		
	TOTAL	***928***	***0***		928		
BEANS, GREEN FZN	**CG06**						
	2005	555	8	20 %CT			
				ZEROES	444		
				1/2LOD	103	***1/2LOD=***	***0.0074***
				DETECTS	8		
	TOTAL	***555***	***8***		555		
BEANS, KIDNEY CANNED	**CG06**						
	2009	186	0	25 %CT			
	2008	186	0	ZEROES	0		
				1/2LOD	372	***1/2LOD=***	***0.0054***
				DETECTS	0		
	TOTAL	***372***	***0***		372		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)							
PDP Years Used		**No. of Samples**	**No. of Detects**	**RDF Calculation**		**1/2 LOD (PPM)**	
BEANS, PINTO CANNED	**CG06**						
	2009	372	0	25 %CT			
				ZEROES	279		
				1/2LOD	93	***1/2LOD=***	***0.0053***
				DETECTS	0		
	TOTAL	***372***	***0***		372		
PEA, SNAP	**CG06**						
	2011	744	14	2.5 %CT			
				ZEROES	725		
				1/2LOD	5	***1/2LOD=***	***0.0036***
				DETECTS	14		
	TOTAL	***744***	***14***		744		
PEAS, SWEET CANNED	**CG06**						
	2006	744	0	2.5 %CT			
	2003	549	0	ZEROES	1246		
	2002	729	0	1/2LOD	32	***1/2LOD=***	***0.0059***
				DETECTS	0		
	TOTAL	***1278***	***0***		1278		
SOYBEAN GRAIN	**CG06**						
	2005	663	0	2.5 %CT			
	2004	611	0	ZEROES	0		
	2011	300		1/2LOD	1574	***1/2LOD=***	***0.0015***
				DETECTS	0		
	TOTAL	***1574***	***0***		1574		
EGGPLANT	**CG08**						
	2006	740	9	5 %CT			
	2005	736	22	ZEROES	1402		
				1/2LOD	43	***1/2LOD=***	***0.0060***
				DETECTS	31		
	TOTAL	***1476***	***31***		1476		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
PEPPER, HOT	**CG08**						
	2011	553	16	35 %CT			
				ZEROES	359		
				1/2LOD	178	***1/2LOD=***	***0.0130***
				DETECTS	16		
	TOTAL	***553***	***16***		553		
PEPPER, SWEET BELL	**CG08**						
	2004	558	74	35 %CT			
	2003	741	116	ZEROES	1326		
	2011	741	63	1/2LOD	461	***1/2LOD=***	***0.0027***
				DETECTS	253		
	TOTAL	***2040***	***253***		2040		
TOMATO	**CG08**						
	2008	740	0	20 %CT			
	2007	741	0	ZEROES	1775		
	2011	738	1	1/2LOD	443	***1/2LOD=***	***0.0018***
				DETECTS	1		
	TOTAL	***2219***	***1***		2219		
TOMATO CANNED	**CG08**						
	2000	369	0	20 %CT			
				ZEROES	295		
				1/2LOD	74	***1/2LOD=***	***0.0049***
				DETECTS	0		
	TOTAL	***369***	***0***		369		
TOMATO PASTE	**CG08**						
	2009	742	0	20 %CT			
	2001	369	0	ZEROES	889		
				1/2LOD	222	***1/2LOD=***	***0.0116***
				DETECTS	0		
	TOTAL	***1111***	***0***		1111		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
CANTALOUPE	**CG09**						
	2011	739	27	30 %CT			
	2010	371	37	ZEROES	1168		
	2005	558	88	1/2LOD	348	***1/2LOD=***	***0.0054***
				DETECTS	152		
	TOTAL	***1668***	***152***		1668		
CUCUMBER	**CG09**						
	2010	744	16	20 %CT			
	2009	744	22	ZEROES	1636		
	2004	557	13	1/2LOD	358	***1/2LOD=***	***0.0039***
				DETECTS	51		
	TOTAL	***2045***	***51***		2045		
SQUASH SUMMER	**CG09**						
	2008	554	10	15 %CT			
	2007	742	9	ZEROES	1260		
	2006	186	4	1/2LOD	199	***1/2LOD=***	***0.0042***
				DETECTS	23		
	TOTAL	***1482***	***23***		1482		
SQUASH WINTER	**CG09**						
	2006	369	2	15 %CT			
	2005	731	0	ZEROES	1093		
	2011	186	0	1/2LOD	191	***1/2LOD=***	***0.0062***
				DETECTS	2		
	TOTAL	***1286***	***2***		1286		
WATERMELON	**CG09**						
	2006	550	20	10 %CT			
	2005	182	16	ZEROES	659		
				1/2LOD	37	***1/2LOD=***	***0.0047***
				DETECTS	36		
	TOTAL	***732***	***36***		732		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
GRAPEFRUIT	**CG10**						
	2006	743	0	n/a			
	2005	720	0	ZEROES			
				1/2LOD		***1/2LOD=***	***0.0070***
				DETECTS	0		
	TOTAL	***1463***	***0***		0		
ORANGE	**CG10**						
	2009	744	0	2.5 %CT			
	2005	741	0	ZEROES	2171		
	2004	742	0	1/2LOD	56	***1/2LOD=***	***0.0065***
				DETECTS	0		
	TOTAL	***2227***	***0***		2227		
ORANGE JUICE	**CG10**						
	2006	557	0	2.5 %CT			
	2005	744	0	ZEROES	1839		
	2011	585	0	1/2LOD	47	***1/2LOD=***	***0.0049***
				DETECTS	0		
	TOTAL	***1886***	***0***		1886		
TANGERINE	**CG10**						
	2011	717	0	100 %CT			
				ZEROES	0		
				1/2LOD	717	***1/2LOD=***	***0.0050***
				DETECTS	0		
	TOTAL	***717***	***0***		717		
APPLE	**CG11**						
	2010	744	0	10 %CT			
	2009	744	3	ZEROES	2008		
	2005	743	4	1/2LOD	216	***1/2LOD=***	***0.0022***
				DETECTS	7		
	TOTAL	***2231***	***7***		2231		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
APPLE JUICE	**CG11**						
	2008	372	1	10 %CT			
	2007	368	0	ZEROES	666		
				1/2LOD	73	***1/2LOD=***	***0.0091***
				DETECTS	1		
	TOTAL	***740***	***1***		740		
APPLE SAUCE	**CG11**						
	2006	744	0	10 %CT			
	2002	358	0	ZEROES	992		
				1/2LOD	110	***1/2LOD=***	***0.0046***
				DETECTS	0		
	TOTAL	***1102***	***0***		1102		
NECTARINES	**CG12**						
	2008	672	11	10 %CT			
	2007	563	6	ZEROES	1435		
	2001	359	21	1/2LOD	121	***1/2LOD=***	***0.0026***
				DETECTS	38		
	TOTAL	***1594***	***38***		1594		
PEACH	**CG12**						
	2008	616	9	10 %CT			
	2007	555	17	ZEROES	1135		
	2006	90	11	1/2LOD	89	***1/2LOD=***	***0.0034***
				DETECTS	37		
	TOTAL	***1261***	***37***		1261		
PEACH CANNED	**CG12**						
	2004	743	0	10 %CT			
	2003	742	0	ZEROES	1337		
				1/2LOD	148	***1/2LOD=***	***0.0060***
				DETECTS	0		
	TOTAL	***1485***	***0***		1485		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
PEACH, SINGLE SERVINGS	**CG12**						
	2000	534	15	10 %CT			
				ZEROES	481		
				1/2LOD	38	***1/2LOD=***	***0.0040***
				DETECTS	15		
	TOTAL	***534***	***15***		534		
BLUEBERRY	**CG13**						
	2008	726	21	35 %CT			
	2007	711	29	ZEROES	934		
				1/2LOD	453	***1/2LOD=***	***0.0039***
				DETECTS	50		
	TOTAL	***1437***	***50***		1437		
BLUEBERRY, FZN	**CG13**						
	2008	18	1	35 %CT			
	2007	22	2	ZEROES	26		
				1/2LOD	11	***1/2LOD=***	***0.0036***
				DETECTS	3		
	TOTAL	***40***	***3***		40		
GRAPE	**CG13**						
	2010	636	19	5 %CT			
	2009	744	30	ZEROES	2013		
	2005	739	43	1/2LOD	14	***1/2LOD=***	***0.0061***
				DETECTS	92		
	TOTAL	***2119***	***92***		2119		
GRAPE, JUICE	**CG13**						
	2008	722	0	5 %CT			
				ZEROES	686		
				1/2LOD	36	***1/2LOD=***	***0.0112***
				DETECTS	0		
	TOTAL	***722***	***0***		722		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)

PDP Years Used		No. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
BARLEY	**CG15**						
	2003	452	0	n/a			
	2002	725	0	ZEROES	0		
				1/2LOD	1177	***1/2LOD=***	***0.0045***
				DETECTS	0		
	TOTAL	***1177***	***0***		1177		
CORN GRAIN	**CG15**						
	2008	631	0	2.5 %CT			
	2007	660	0	ZEROES	1259		
				1/2LOD	32	***1/2LOD=***	***0.0015***
				DETECTS	0		
	TOTAL	***1291***	***0***		1291		
CORN, SWEET	**CG15**						
	2010	73	0	65 %CT			
	2009	75	0	ZEROES	63		
	2008	33	0	1/2LOD	118	***1/2LOD=***	***0.0052***
				DETECTS	0		
	TOTAL	***181***	***0***		181		
CORN, SWEET ON COB	**CG15**						
	2010	480	0	65 %CT			
	2009	668	1	ZEROES	455		
	2008	152	0	1/2LOD	844	***1/2LOD=***	***0.0054***
				DETECTS	1		
	TOTAL	***1300***	***1***		1300		
WATER, FIN	**CG99**						
	2008	309	0				
	2009	306	0	ZEROES	0		
	2011	118	0	LOD	733	***LOD=***	***0.0053***
				DETECTS	0		***PPB***
	TOTAL	***733***	***0***		733		

TABLE 1a: PRIMARY PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)							
PDP Years Used		**No. of Samples**	**No. of Detects**	**RDF Calculation**		**1/2 LOD (PPM)**	
WATER, UNF	**CG99**						
	2008	308	0				
	2009	305	0	ZEROES	0		
	2011	120	0	LOD	733	***LOD=***	***0.0053***
				DETECTS	0		***PPB***
	TOTAL	***733***	***0***		733		

TABLE 1b: TRANSLATED PDP DATA USED IN RISK ASSESSMENT (CROP GROUP ORDER)							
PDP Years Used		**NO. of Samples**	**No. of Detects**	**RDF Calculation**		**1/2 LOD (PPM)**	
CARROT100PCT	**CG01 AB**						
	2007	722	0	100 %CT			
	2006	744	1	ZEROES	0		
	2002	554	0	1/2LOD	2019	***1/2LOD=***	***0.0041***
				DETECTS	1		
	TOTAL	***2020***	***1***		2020		
CARROT40PCT	**CG01 AB**						
	2007	722	0	40 %CT			
	2006	744	1	ZEROES	1212		
	2002	554	0	1/2LOD	807	***1/2LOD=***	***0.0041***
				DETECTS	1		
	TOTAL	***2020***	***1***		2020		
GRNONION100PCT	**CG03**						
	2009	558	55	100 %CT			
	2008	186	9	ZEROES	0		
				1/2LOD	680	***1/2LOD=***	***0.0012***
				DETECTS	64		
	TOTAL	***744***	***64***		744		
SPINACH100PCT	**CG04 A**						
	2009	744	33	100 %CT			
	2008	744	18	ZEROES	0		
	2006	511	36	1/2LOD	1912	***1/2LOD=***	***0.0049***
				DETECTS	87		
	TOTAL	***1999***	***87***		1999		
SPINACH1PCT	**CG04 A**						
	2009	744	33	1 %CT			
	2008	744	18	ZEROES	1979		
	2006	511	36	1/2LOD	0	***1/2LOD=***	***0.0049***
				DETECTS	20		
	TOTAL	***1999***	***(20)***		1999		

PDP Years Used		NO. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
SPINCANNED1PCT	**CG04**						
	2004	371	0	1 %CT			
	2011	198	0	ZEROES	563		
				1/2LOD	6	***1/2LOD=***	***0.0057***
				DETECTS	0		
	TOTAL	***569***	***0***		569		
CELERY100PCT	**CG04**						
	2008	741	27	100 %CT			
	2007	739	37	ZEROES	0		
	2002	737	83	1/2LOD	2070	***1/2LOD=***	***0.0030***
				DETECTS	147		
	TOTAL	***2217***	***147***		2217		
BROCCABB100PCT	**CG05 A**						
	2008	554	3	100 %CT			
	2007	736	10	ZEROES	0		
	2006	185	5	1/2LOD	2186	***1/2LOD=***	***0.0017***
	2010	743	14	DETECTS	32		
	2011	742	9				
	TOTAL	***2218***	***32***		2218		
COLLKALE100PCT	**CG05 B**						
	2006	240	4	100 %CT			
	2005	353	6	ZEROES	0		
	2004	86	0	1/2LOD	1463	***1/2LOD=***	***0.0056***
	2008	318	1	DETECTS	15		
	2007	383	3				
	2006	98	1				
	TOTAL	***1478***	***15***		1478		
GRNBEANS100PCT	**CG06**						
	2008	741	10	100 %CT			
	2007	739	15	ZEROES	0		
	2005	181	7	1/2LOD	888	***1/2LOD=***	***0.0058***
				DETECTS	32		
	TOTAL	***920***	***32***		920		

PDP Years Used		NO. of Samples	No. of Detects	RDF Calculation		1/2 LOD (PPM)	
EGGPLANT100PCT	**CG08 BC**						
	2006	740	9	100 %CT			
	2005	736	22	ZEROES	0		
				1/2LOD	1445	***1/2LOD=***	***0.0060***
				DETECTS	31		
	TOTAL	***1476***	***31***		1476		
CANTALOUPE100pct	**CG09 A**						
	2010	371	37	100 %CT			
	2005	558	88	ZEROES	0		
	2011	739	27	1/2LOD	1516	***1/2LOD=***	***0.0054***
				DETECTS	152		
	TOTAL	***1668***	***152***		1668		
CUCUMBER100PCT	**CG09 B**						
	2010	744	16	100 %CT			
	2009	744	22	ZEROES	0		
	2004	557	13	1/2LOD	1994	***1/2LOD=***	***0.0039***
				DETECTS	51		
	TOTAL	***2045***	***51***		2045		
WINTERSQ100PCT	**CG09 B**						
	2006	369	2	100 %CT			
	2005	731	0	ZEROES	0		
	2011	186	0	1/2LOD	1284	***1/2LOD=***	***0.0062***
				DETECTS	2		
	TOTAL	***1286***	***2***		1286		
WINTERSQ10PCT	**CG09 B**						
	2006	369	2	10 %CT			
	2005	731	0	ZEROES	1157		
	2011	186	0	1/2LOD	127	***1/2LOD=***	***0.0062***
				DETECTS	2		
	TOTAL	***1286***	***2***		1286		

Attachment 2

Acute Food Plus Water Residue File

ACUTE FOOD PLUS WATER RESIDUE FILE

```
California Dept of Pesticide Regulation                    Ver. 3.18, 03-08-d
DEEM-FCID Acute analysis for METHOMYL
Residue file name: H:\MyFiles\HAS docs\dietary exposure\DPR projects\methomyl 2012\DEEM runs\v4
deem runs\methomylacutefoodpluswater.R08
Analysis Date 08-16-2013             Residue file dated: 08-16-2013/10:57:09
Reference dose (aRfD) = 0.003 mg/kg bw/day
---------------------------------------------------------------------------------
RDL indices and parameters for Monte Carlo Analysis:
Index Dist Parameter #1           Param #2    Param #3    Comment
  #   Code
----- ---- ------------           ----------- ----------- ----------
  1    6   H:\RDF files\apple juice.rdf
  2    6   H:\RDF files\apple sauce.rdf
  3    6   H:\RDF files\apple.rdf
  4    6   H:\RDF files\asparagus canned.rdf
  5    6   H:\RDF files\asparagus.rdf
  6    6   H:\RDF files\avocadotol5pct.rdf
  7    6   H:\RDF files\beans green bf.rdf
  8    6   H:\RDF files\beans green canned.rdf
  9    6   H:\RDF files\beans green fzn.rdf
  10   6   H:\RDF files\beans green.rdf
  11   6   H:\RDF files\beets canned..rdf
  12   6   H:\RDF files\blueberry fzn.rdf
  13   6   H:\RDF files\blueberry.rdf
  14   6   H:\RDF files\broccabb100pct.rdf
  15   6   H:\RDF files\broccoli.rdf
  16   6   H:\RDF files\cabbage.rdf
  17   6   H:\RDF files\cantaloupe.rdf
  18   6   H:\RDF files\cantaloupe100pct.rdf
  19   6   H:\RDF files\carrot.rdf
  20   6   H:\RDF files\carrot40pct.rdf
  21   6   H:\RDF files\carrot100pct.rdf
  22   6   H:\RDF files\cauliflower.rdf
  23   6   H:\RDF files\celery.rdf
  24   6   H:\RDF files\celery100pct.rdf
  25   6   H:\RDF files\collard greens.rdf
  26   6   H:\RDF files\collkale100pct.rdf
  27   6   H:\RDF files\corn sweet on cob.rdf
  28   6   H:\RDF files\corn sweet.rdf
  29   6   H:\RDF files\cucumber.rdf
  30   6   H:\RDF files\cucumber100pct.rdf
  31   6   H:\RDF files\eggplant.rdf
  32   6   H:\RDF files\eggplant100pct.rdf
  33   6   H:\RDF files\grape juice.rdf
  34   6   H:\RDF files\grape.rdf
  35   6   H:\RDF files\grapefruit.rdf
  36   6   H:\RDF files\green onion.rdf
  37   6   H:\RDF files\grnbeans100pct.rdf
  38   6   H:\RDF files\grnonion100pct.rdf
  39   6   H:\RDF files\kale.rdf
  40   6   H:\RDF files\lettuce.rdf
  41   6   H:\RDF files\nectarine.rdf
  42   6   H:\RDF files\nutstol2.5pct.rdf
  43   6   H:\RDF files\onion.rdf
  44   6   H:\RDF files\onion65pct.rdf
  45   6   H:\RDF files\orange juice.rdf
  46   6   H:\RDF files\orange.rdf
  47   6   H:\RDF files\pea snap.rdf
  48   6   H:\RDF files\peach canned.rdf
  49   6   H:\RDF files\peach.rdf
  50   6   H:\RDF files\peas sweet canned.rdf
  51   6   H:\RDF files\pepper hot.rdf
  52   6   H:\RDF files\pepper sweet bell.rdf
  53   6   H:\RDF files\potato fzn.rdf
  54   6   H:\RDF files\raisin.rdf
  55   6   H:\RDF files\soybean grain.rdf
  56   6   H:\RDF files\spinach canned.rdf
  57   6   H:\RDF files\spinach fzn.rdf
  58   6   H:\RDF files\spinach.rdf
  59   6   H:\RDF files\spinach1pct.rdf
  60   6   H:\RDF files\spincanned1pct.rdf
  61   6   H:\RDF files\spinlett100pct.rdf
  62   6   H:\RDF files\squash summer.rdf
  63   6   H:\RDF files\squash winter.rdf
  64   6   H:\RDF files\sweet potato bf.rdf
  65   6   H:\RDF files\sweet potato.rdf
  66   6   H:\RDF files\tomato canned.rdf
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  67   6   H:\RDF files\tomato paste.rdf
  68   6   H:\RDF files\tomato.rdf
  69   6   H:\RDF files\watermelon.rdf
  70   6   H:\RDF files\wintersq10pct.rdf
  71   6   H:\RDF files\wintersq100pct.rdf
  72   6   H:\RDF files\potato.rdf

  EPA       Crop Food Name                         Def Res     Adj.Factors  RDL  Comment
  Code       Grp                                    (ppm)       #1     #2   Pntr
---------- ---- ------------------------------  ----------  ------ ------ ---  -------
0401005000 4A   Amaranth, leafy                   1.000000   1.000  1.000  61
1100007000 11   Apple, fruit with peel            1.000000   1.000  1.000   3
1100008000 11   Apple, peeled fruit               1.000000   1.000  1.000   3
1100008001 11   Apple, peeled fruit-babyfood      1.000000   1.000  1.000   3
1100009000 11   Apple, dried                      0.000390   1.000  1.000       2007 U
    Full comment: 2007 USEPA DEA
1100009001 11   Apple, dried-babyfood             0.000390   1.000  1.000       2007 U
    Full comment: 2007 USEPA DEA
1100010000 11   Apple, juice                      1.000000   1.000  1.000   1
1100010001 11   Apple, juice-babyfood             1.000000   1.000  1.000   1
1100011000 11   Apple, sauce                      1.000000   1.000  1.000   2
1100011001 11   Apple, sauce-babyfood             1.000000   1.000  1.000   2
0103015000 1CD  Arrowroot, flour                  0.005100   1.000  1.000
0103015001 1CD  Arrowroot, flour-babyfood         0.005100   1.000  1.000
0103017000 1CD  Artichoke, Jerusalem              0.005100   1.000  1.000
0401018000 4A   Arugula                           1.000000   1.000  1.000  61
9500019000 O    Asparagus
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000   5
                   212-Cooked; Fresh or N/S; Boiled
                                                  1.000000   1.000  1.000   5
                   213-Cooked; Fresh or N/S; Fried
                                                  1.000000   1.000  1.000   5
                   222-Cooked; Frozen; Boiled     1.000000   1.000  1.000   5
                   242-Cooked; Canned; Boiled     1.000000   1.000  1.000   4
9500020000 O    Avocado                           1.000000   1.000  1.000   6
0902021000 9B   Balsam pear                       1.000000   1.000  1.000  30
1500025000 15   Barley, pearled barley            0.004500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for barley PDP
1500025001 15   Barley, pearled barley-babyfood   0.004500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for barley PDP
1500026000 15   Barley, flour                     0.004500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for barley PDP
1500026001 15   Barley, flour-babyfood            0.004500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for barley PDP
1500027000 15   Barley, bran                      0.004500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for barley PDP
0603030000 6C   Bean, black, seed                 0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602031000 6B   Bean, broad, succulent            1.000000   1.000  1.000  37
0603032000 6C   Bean, broad, seed                 0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602033000 6B   Bean, cowpea, succulent           1.000000   1.000  1.000  37
0603034000 6C   Bean, cowpea, seed                0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603035000 6C   Bean,  great northern, seed       0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603036000 6C   Bean, kidney, seed                0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602037000 6B   Bean, lima, succulent             1.000000   1.000  1.000  37
0603038000 6C   Bean, lima, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603039000 6C   Bean, mung, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603040000 6C   Bean, navy, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603041000 6C   Bean, pink, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603042000 6C   Bean, pinto, seed                 0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0601043000 6A   Bean, snap, succulent
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000  10
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000  10
                   211-Cooked; Fresh or N/S; Baked
                                                  1.000000   1.000  1.000  10
                   212-Cooked; Fresh or N/S; Boiled
                                                  1.000000   1.000  1.000  10
                   213-Cooked; Fresh or N/S; Fried
                                                  1.000000   1.000  1.000  10
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		215-Cooked; Fresh or N/S; Boiled/baked	1.000000	1.000	1.000	10	
		220-Cooked; Frozen; Cook Meth N/S	1.000000	1.000	1.000	9	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	9	
		222-Cooked; Frozen; Boiled	1.000000	1.000	1.000	9	
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	10	
		240-Cooked; Canned; Cook Meth N/S	1.000000	1.000	1.000	8	
		242-Cooked; Canned; Boiled	1.000000	1.000	1.000	8	
0601043001	6A	Bean, snap, succulent-babyfood	1.000000	1.000	1.000	7	
0101050000	1AB	Beet, garden, roots					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	20	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	20	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	20	
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	20	
		240-Cooked; Canned; Cook Meth N/S	1.000000	1.000	1.000	11	
		242-Cooked; Canned; Boiled	1.000000	1.000	1.000	11	
		250-Cooked; Cured etc; Cook Meth N/S	1.000000	1.000	1.000	20	
0101050001	1AB	Beet, garden, roots-babyfood	1.000000	1.000	1.000	11	
0200051000	2	Beet, garden, tops	6.000000	1.000	1.000		
0101052000	1A	Beet, sugar	0.004100	1.000	1.000		
0101052001	1A	Beet, sugar-babyfood	0.004100	1.000	1.000		
0101053000	1A	Beet, sugar, molasses	0.004100	1.000	1.000		
0101053001	1A	Beet, sugar, molasses-babyfood	0.004100	1.000	1.000		
9500054000	O	Belgium endive	1.000000	1.000	1.000	61	
1302057000	13B	Blueberry					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	13	
		120-Uncooked; Frozen; Cook Meth N/S	1.000000	1.000	1.000	12	
		130-Uncooked; Dried; Cook Meth N/S	1.000000	1.000	1.000	13	
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	13	
		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	13	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	13	
		214-Cooked; Fresh or N/S; Fried/baked	1.000000	1.000	1.000	13	
		223-Cooked; Frozen; Fried	1.000000	1.000	1.000	13	
		230-Cooked; Dried; Cook Meth N/S	1.000000	1.000	1.000	13	
		240-Cooked; Canned; Cook Meth N/S	1.000000	1.000	1.000	13	
1302057001	13B	Blueberry-babyfood	1.000000	1.000	1.000	13	
0501061000	5A	Broccoli	1.000000	1.000	1.000	15	
0501061001	5A	Broccoli-babyfood	1.000000	1.000	1.000	15	
0501062000	5A	Broccoli, Chinese	1.000000	1.000	1.000	14	
0502063000	5B	Broccoli raab	1.000000	1.000	1.000	26	
0501064000	5A	Brussels sprouts	1.000000	1.000	1.000	14	
0101067000	1AB	Burdock	1.000000	1.000	1.000	21	
0501069000	5A	Cabbage	1.000000	1.000	1.000	16	
0502070000	5B	Cabbage, Chinese, bok choy	1.000000	1.000	1.000	14	
0501071000	5A	Cabbage, Chinese, napa	1.000000	1.000	1.000	14	
0501072000	5A	Cabbage, Chinese, mustard	1.000000	1.000	1.000	14	
0901075000	9A	Cantaloupe	1.000000	1.000	1.000	17	
0402076000	4B	Cardoon	1.000000	1.000	1.000	24	
0101078000	1AB	Carrot	1.000000	1.000	1.000	19	
0101078001	1AB	Carrot-babyfood	1.000000	1.000	1.000	19	
0101079000	1AB	Carrot, juice	1.000000	1.000	1.000	19	
0103082000	1CD	Cassava	0.005100	1.000	1.000		
0103082001	1CD	Cassava-babyfood	0.005100	1.000	1.000		
0501083000	5A	Cauliflower	1.000000	1.000	1.000	22	
0101084000	1AB	Celeriac	1.000000	1.000	1.000	21	
0402085000	4B	Celery	1.000000	1.000	1.000	23	
0402085001	4B	Celery-babyfood	1.000000	1.000	1.000	23	
0402086000	4B	Celery, juice	1.000000	1.000	1.000	23	
0402087000	4B	Celtuce	1.000000	1.000	1.000	61	
0902088000	9B	Chayote, fruit	1.000000	1.000	1.000	71	
0603098000	6C	Chickpea, seed	0.005200	1.000	1.000		1/2LOD
Full comment: 1/2LOD for canned beans PDP							
0603098001	6C	Chickpea, seed-babyfood	0.005200	1.000	1.000		1/2LOD
Full comment: 1/2LOD for canned beans PDP							
0603099000	6C	Chickpea, flour	0.005200	1.000	1.000		1/2LOD
Full comment: 1/2LOD for canned beans PDP							

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0101100000 1AB  Chicory, roots                    1.000000   1.000  1.000  21
0902102000 9B   Chinese waxgourd                  1.000000   1.000  1.000  30
0401104000 4A   Chrysanthemum, garland            1.000000   1.000  1.000  61
1001106000 10A  Citron                            0.006500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for orange PDP
1001107000 10A  Citrus hybrids                    0.006500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for orange PDP
1001108000 10A  Citrus, oil                       0.006500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for orange PDP
0502117000 5B   Collards                          1.000000   1.000  1.000  25
1500120000 15   Corn, field, flour                0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500120001 15   Corn, field, flour-babyfood       0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500121000 15   Corn, field, meal                 0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500121001 15   Corn, field, meal-babyfood        0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500122000 15   Corn, field, bran                 0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500123000 15   Corn, field, starch               0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500123001 15   Corn, field, starch-babyfood      0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500124000 15   Corn, field, syrup                0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500124001 15   Corn, field, syrup-babyfood       0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500125000 15   Corn, field, oil                  0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500125001 15   Corn, field, oil-babyfood         0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500126000 15   Corn, pop                         0.001500   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500127000 15   Corn, sweet
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000  27
                   140-Uncooked; Canned; Cook Meth N/S
                                                  1.000000   1.000  1.000  28
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000  27
                   211-Cooked; Fresh or N/S; Baked
                                                  1.000000   1.000  1.000  27
                   212-Cooked; Fresh or N/S; Boiled
                                                  1.000000   1.000  1.000  27
                   213-Cooked; Fresh or N/S; Fried
                                                  1.000000   1.000  1.000  27
                   220-Cooked; Frozen; Cook Meth N/S
                                                  1.000000   1.000  1.000  28
                   221-Cooked; Frozen; Baked      1.000000   1.000  1.000  28
                   222-Cooked; Frozen; Boiled     1.000000   1.000  1.000  28
                   232-Cooked; Dried; Boiled      1.000000   1.000  1.000  28
                   240-Cooked; Canned; Cook Meth N/S
                                                  1.000000   1.000  1.000  28
                   242-Cooked; Canned; Boiled     1.000000   1.000  1.000  28
                   243-Cooked; Canned; Fried      1.000000   1.000  1.000  28
1500127001 15   Corn, sweet-babyfood              1.000000   1.000  1.000  28
0401133000 4A   Cress, garden                     1.000000   1.000  1.000  61
0401134000 4A   Cress, upland                     1.000000   1.000  1.000  61
0902135000 9B   Cucumber                          1.000000   1.000  1.000  29
0401138000 4A   Dandelion, leaves                 1.000000   1.000  1.000  61
0103139000 1CD  Dasheen, corm                     0.005100   1.000  1.000
0802148000 8BC  Eggplant                          1.000000   1.000  1.000  31
0401150000 4A   Endive                            1.000000   1.000  1.000  61
0402152000 4B   Fennel, Florence                  1.000000   1.000  1.000  24
0301165000 3A   Garlic, bulb                      1.000000   1.000  1.000  44
0301165001 3A   Garlic, bulb-babyfood             1.000000   1.000  1.000  44
0103166000 1CD  Ginger                            0.005100   1.000  1.000
0103166001 1CD  Ginger-babyfood                   0.005100   1.000  1.000
0103167000 1CD  Ginger, dried                     0.005100   1.000  1.000
0101168000 1AB  Ginseng, dried                    0.005100   1.000  1.000
1304175000 13D  Grape                             1.000000   1.000  1.000  34
1304176000 13D  Grape, juice                      1.000000   1.000  1.000  33
1304176001 13D  Grape, juice-babyfood             1.000000   1.000  1.000  33
9500177000 O    Grape, leaves                     1.000000   1.000  1.000  34
9500178000 O    Grape, raisin                     1.000000   1.000  1.000  54
1304179000 13D  Grape, wine and sherry            1.000000   1.000  1.000  33
1003180000 10C  Grapefruit                        1.000000   1.000  1.000  35
1003181000 10C  Grapefruit, juice                 1.000000   1.000  1.000  35
0603182000 6C   Guar, seed                        0.005200   1.000  1.000        1/2LOD
    Full comment: 1/2LOD for canned beans PDP
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0603182001	6C	Guar, seed-babyfood	0.005200	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for canned beans PDP					
0901187000	9A	Honeydew melon	1.000000	1.000	1.000	18	
9500188000	O	Hop	0.040000	1.000	1.000		LOD
0101190000	1AB	Horseradish	1.000000	1.000	1.000	21	
0502194000	5B	Kale	1.000000	1.000	1.000	39	
0501196000	5A	Kohlrabi	1.000000	1.000	1.000	14	
1002197000	10B	Kumquat	0.006500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for orange PDP					
0302198000	3B	Leek	1.000000	1.000	1.000	38	
1002199000	10B	Lemon	1.000000	1.000	1.000	46	
1002200000	10B	Lemon, juice	1.000000	1.000	1.000	45	
1002200001	10B	Lemon, juice-babyfood	1.000000	1.000	1.000	45	
1002201000	10B	Lemon, peel	1.000000	1.000	1.000	46	
0603203000	6C	Lentil, seed	0.005200	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for canned beans PDP					
0401204000	4A	Lettuce, head	1.000000	1.000	1.000	40	
0401205000	4A	Lettuce, leaf	1.000000	1.000	1.000	40	
1002206000	10B	Lime	0.006500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for orange PDP					
1002207000	10B	Lime, juice	0.005000	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for oj PDP					
1002207001	10B	Lime, juice-babyfood	0.005000	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for oj PDP					
0502229000	5B	Mustard greens	1.000000	1.000	1.000	26	
1202230000	12B	Nectarine	1.000000	1.000	1.000	41	
1500231000	15	Oat, bran	0.004500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for barley PDP					
1500232000	15	Oat, flour	0.004500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for barley PDP					
1500232001	15	Oat, flour-babyfood	0.004500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for barley PDP					
1500233000	15	Oat, groats/rolled oats	0.004500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for barley PDP					
1500233001	15	Oat, groats/rolled oats-babyfood	0.004500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for barley PDP					
0802234000	8BC	Okra	1.000000	1.000	1.000	32	
0301237000	3A	Onion, bulb	1.000000	1.000	1.000	43	
0301237001	3A	Onion, bulb-babyfood	1.000000	1.000	1.000	43	
0301238000	3A	Onion, bulb, dried	0.006000	1.000	1.000		
0301238001	3A	Onion, bulb, dried-babyfood	0.006000	1.000	1.000		
0302239000	3B	Onion, green	1.000000	1.000	1.000	36	
1001240000	10A	Orange	1.000000	1.000	1.000	46	
1001241000	10A	Orange, juice	1.000000	1.000	1.000	45	
1001241001	10A	Orange, juice-babyfood	1.000000	1.000	1.000	45	
1001242000	10A	Orange, peel	1.000000	1.000	1.000	46	
0401248000	4A	Parsley, leaves					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	59	
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	59	
		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	59	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	59	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	59	
		215-Cooked; Fresh or N/S; Boiled/baked	1.000000	1.000	1.000	59	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	59	
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	59	
		240-Cooked; Canned; Cook Meth N/S	1.000000	1.000	1.000	60	
		242-Cooked; Canned; Boiled	1.000000	1.000	1.000	60	
1901249000	19A	Parsley, dried leaves	0.005700	1.000	1.000		
1901249001	19A	Parsley, dried leaves-babyfood	0.005700	1.000	1.000		
0101250000	1AB	Parsley, turnip rooted	1.000000	1.000	1.000	21	
0101251000	1AB	Parsnip	1.000000	1.000	1.000	21	
0101251001	1AB	Parsnip-babyfood	1.000000	1.000	1.000	21	
0602255000	6B	Pea, succulent					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	47	
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	47	
		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	47	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	47	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	47	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	47	

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                   222-Cooked; Frozen; Boiled      1.000000   1.000  1.000  47
                   232-Cooked; Dried; Boiled       1.000000   1.000  1.000  47
                   240-Cooked; Canned; Cook Meth N/S
                                                   1.000000   1.000  1.000  50
                   242-Cooked; Canned; Boiled      1.000000   1.000  1.000  50
0602255001 6B   Pea, succulent-babyfood            1.000000   1.000  1.000  50
0603256000 6C   Pea, dry                           0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603256001 6C   Pea, dry-babyfood                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0601257000 6A   Pea, edible podded, succulent      1.000000   1.000  1.000  47
0603258000 6C   Pea, pigeon, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602259000 6B   Pea, pigeon, succulent
                   212-Cooked; Fresh or N/S; Boiled
                                                   1.000000   1.000  1.000  47
                   242-Cooked; Canned; Boiled      1.000000   1.000  1.000  50
1202260000 12B  Peach
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  49
                   120-Uncooked; Frozen; Cook Meth N/S
                                                   1.000000   1.000  1.000  49
                   130-Uncooked; Dried; Cook Meth N/S
                                                   1.000000   1.000  1.000  49
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  49
                   211-Cooked; Fresh or N/S; Baked
                                                   1.000000   1.000  1.000  49
                   213-Cooked; Fresh or N/S; Fried
                                                   1.000000   1.000  1.000  49
                   223-Cooked; Frozen; Fried       1.000000   1.000  1.000  49
                   230-Cooked; Dried; Cook Meth N/S
                                                   1.000000   1.000  1.000  49
                   240-Cooked; Canned; Cook Meth N/S
                                                   1.000000   1.000  1.000  48
1202260001 12B  Peach-babyfood                     1.000000   1.000  1.000  48
1202261000 12B  Peach, dried                       0.005400   1.000  1.000       2007 U
    Full comment: 2007 USEPA DEA
1202261001 12B  Peach, dried-babyfood              0.005400   1.000  1.000       2007 U
    Full comment: 2007 USEPA DEA
1202262000 12B  Peach, juice                       1.000000   1.000  1.000  49
1202262001 12B  Peach, juice-babyfood              1.000000   1.000  1.000  49
9500263000 O    Peanut                             0.050000   1.000  1.000
9500264000 O    Peanut, butter                     0.005000   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for peanut butter PDP
9500265000 O    Peanut, oil                        0.005000   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for peanut butter PDP
1400269000 14   Pecan                              1.000000   1.000  1.000  42
0802270000 8B   Pepper, bell                       1.000000   1.000  1.000  52
0802270001 8B   Pepper, bell-babyfood              1.000000   1.000  1.000  52
0802271000 8B   Pepper, bell, dried                1.000000   1.000  1.000  52
0802271001 8B   Pepper, bell, dried-babyfood       1.000000   1.000  1.000  52
0802272000 8BC  Pepper, nonbell                    1.000000   1.000  1.000  51
0802272001 8BC  Pepper, nonbell-babyfood           1.000000   1.000  1.000  51
0802273000 8BC  Pepper, nonbell, dried             1.000000   1.000  1.000  51
9500275000 O    Peppermint                         2.000000   1.000  1.000       tolera
    Full comment: tolerance
9500276000 O    Peppermint, oil                    2.000000   1.000  1.000       tolera
    Full comment: tolerance
9500289000 O    Pomegranate                        0.100000   1.000  1.000       2007 U
    Full comment: 2007 USEPA DEA
0103296000 1C   Potato, chips                      1.000000   1.000  1.000  72
0103297000 1C   Potato, dry (granules/ flakes)     0.005100   1.000  1.000
0103297001 1C   Potato, dry (granules/ flakes)-b   0.005100   1.000  1.000
0103298000 1C   Potato, flour                      0.005100   1.000  1.000
0103298001 1C   Potato, flour-babyfood             0.005100   1.000  1.000
0103299000 1C   Potato, tuber, w/peel              1.000000   1.000  1.000  72
0103299001 1C   Potato, tuber, w/peel-babyfood     1.000000   1.000  1.000  72
0103300000 1C   Potato, tuber, w/o peel
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  72
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  72
                   211-Cooked; Fresh or N/S; Baked
                                                   1.000000   1.000  1.000  72
                   212-Cooked; Fresh or N/S; Boiled
                                                   1.000000   1.000  1.000  72
                   213-Cooked; Fresh or N/S; Fried
                                                   1.000000   1.000  1.000  72
                   221-Cooked; Frozen; Baked       1.000000   1.000  1.000  53
                   223-Cooked; Frozen; Fried       1.000000   1.000  1.000  53
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                   232-Cooked; Dried; Boiled       1.000000   1.000  1.000  72
                   233-Cooked; Dried; Fried        1.000000   1.000  1.000  72
                   240-Cooked; Canned; Cook Meth N/S
                                                   1.000000   1.000  1.000  72
                   242-Cooked; Canned; Boiled      1.000000   1.000  1.000  72
                   252-Cooked; Cured etc; Boiled   1.000000   1.000  1.000  72
0103300001 1C   Potato, tuber, w/o peel-babyfood   1.000000   1.000  1.000  72
1003307000 10C  Pummelo                            0.006500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for orange PDP
0902308000 9B   Pumpkin                            1.000000   1.000  1.000  70
0902309000 9B   Pumpkin, seed                      1.000000   1.000  1.000  70
0401313000 4A   Radicchio                          1.000000   1.000  1.000  61
0101314000 1AB  Radish, roots                      1.000000   1.000  1.000  21
0101316000 1AB  Radish, Oriental, roots            1.000000   1.000  1.000  21
0502318000 5B   Rape greens                        1.000000   1.000  1.000  26
0402322000 4B   Rhubarb                            1.000000   1.000  1.000  24
0101327000 1AB  Rutabaga                           1.000000   1.000  1.000  21
1500328000 15   Rye, grain                         0.004500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for barley PDP
1500329000 15   Rye, flour                         0.004500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for barley PDP
0101331000 1AB  Salsify, roots                     1.000000   1.000  1.000  21
0302338500 3B   Shallot, fresh leaves              1.000000   1.000  1.000  38
1500344000 15   Sorghum, grain                     0.001500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for corn grain PDP
1500345000 15   Sorghum, syrup                     0.001500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for corn grain PDP
0600347000 6    Soybean, seed                      1.000000   1.000  1.000  55
0603348000 6C   Soybean, flour                     1.000000   1.000  1.000  55
0603348001 6C   Soybean, flour-babyfood            1.000000   1.000  1.000  55
0600349000 6    Soybean, soy milk                  1.000000   1.000  1.000  55
0600349001 6    Soybean, soy milk-babyfood or in   1.000000   1.000  1.000  55
0600350000 6    Soybean, oil                       1.000000   1.000  1.000  55
0600350001 6    Soybean, oil-babyfood              1.000000   1.000  1.000  55
9500352000 O    Spearmint                          2.000000   1.000  1.000       tolera
    Full comment: tolerance
9500353000 O    Spearmint, oil                     2.000000   1.000  1.000       tolera
    Full comment: tolerance
0401355000 4A   Spinach
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  58
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  58
                   211-Cooked; Fresh or N/S; Baked
                                                   1.000000   1.000  1.000  58
                   212-Cooked; Fresh or N/S; Boiled
                                                   1.000000   1.000  1.000  58
                   213-Cooked; Fresh or N/S; Fried
                                                   1.000000   1.000  1.000  58
                   215-Cooked; Fresh or N/S; Boiled/baked
                                                   1.000000   1.000  1.000  58
                   220-Cooked; Frozen; Cook Meth N/S
                                                   1.000000   1.000  1.000  57
                   221-Cooked; Frozen; Baked       1.000000   1.000  1.000  57
                   222-Cooked; Frozen; Boiled      1.000000   1.000  1.000  57
                   232-Cooked; Dried; Boiled       1.000000   1.000  1.000  58
                   240-Cooked; Canned; Cook Meth N/S
                                                   1.000000   1.000  1.000  56
                   242-Cooked; Canned; Boiled      1.000000   1.000  1.000  56
0401355001 4A   Spinach-babyfood                   1.000000   1.000  1.000  56
0902356000 9B   Squash, summer                     1.000000   1.000  1.000  62
0902356001 9B   Squash, summer-babyfood            1.000000   1.000  1.000  62
0902357000 9B   Squash, winter                     1.000000   1.000  1.000  63
0902357001 9B   Squash, winter-babyfood            1.000000   1.000  1.000  63
0103366000 1CD  Sweet potato                       1.000000   1.000  1.000  65
0103366001 1CD  Sweet potato-babyfood              1.000000   1.000  1.000  64
0402367000 4B   Swiss chard                        1.000000   1.000  1.000  24
1001369000 10A  Tangerine                          0.005000   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for tangerine PDP
1001370000 10A  Tangerine, juice                   0.005000   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for tangerine PDP
0103371000 1CD  Tanier, corm                       0.005100   1.000  1.000
0801374000 8A   Tomatillo                          0.002500   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for tomato PDP
0801375000 8A   Tomato
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  68
                   150-Uncooked; Cured etc; Cook Meth N/S
                                                   1.000000   1.000  1.000  68
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                   1.000000   1.000  1.000  68
```

		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	68	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	68	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	68	
		214-Cooked; Fresh or N/S; Fried/baked	1.000000	1.000	1.000	68	
		215-Cooked; Fresh or N/S; Boiled/baked	1.000000	1.000	1.000	68	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	68	
		222-Cooked; Frozen; Boiled	1.000000	1.000	1.000	68	
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	68	
		240-Cooked; Canned; Cook Meth N/S	1.000000	1.000	1.000	66	
		242-Cooked; Canned; Boiled	1.000000	1.000	1.000	66	
		252-Cooked; Cured etc; Boiled	1.000000	1.000	1.000	68	
0801375001	8A	Tomato-babyfood	1.000000	1.000	1.000	66	
0801376000	8A	Tomato, paste	1.000000	1.000	1.000	67	
0801376001	8A	Tomato, paste-babyfood	1.000000	1.000	1.000	67	
0801377000	8A	Tomato, puree	1.000000	1.000	1.000	67	
0801377001	8A	Tomato, puree-babyfood	1.000000	1.000	1.000	67	
0801378000	8A	Tomato, dried	0.000004	1.000	1.000		2007 U
Full comment: 2007 USEPA DEA							
0801378001	8A	Tomato, dried-babyfood	0.000004	1.000	1.000		2007 U
Full comment: 2007 USEPA DEA							
0801379000	8A	Tomato, juice	1.000000	1.000	1.000	68	
1500381000	15	Triticale, flour	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
1500381001	15	Triticale, flour-babyfood	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
0103387000	1CD	Turmeric	0.005100	1.000	1.000		
0101388000	1AB	Turnip, roots	1.000000	1.000	1.000	21	
0502389000	5B	Turnip, greens	1.000000	1.000	1.000	26	
1400391000	14	Walnut	1.000000	1.000	1.000	42	
8601000000	86A	Water, direct, all sources	0.000005	1.000	1.000		
8602000000	86B	Water, indirect, all sources	0.000005	1.000	1.000		
0901399000	9A	Watermelon	1.000000	1.000	1.000	69	
0901400000	9A	Watermelon, juice	1.000000	1.000	1.000	69	
1500401000	15	Wheat, grain	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
1500401001	15	Wheat, grain-babyfood	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
1500402000	15	Wheat, flour	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
1500402001	15	Wheat, flour-babyfood	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
1500403000	15	Wheat, germ	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
1500404000	15	Wheat, bran	0.004500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for barley PDP							
0103406000	1CD	Yam, true	0.005100	1.000	1.000		
0103407000	1CD	Yam bean	0.005100	1.000	1.000		
0301338000	3A	Shallot, bulb	0.006000	1.000	1.000		
0601349500	6AB	Soybean, vegetable	0.200000	1.000	1.000		

Summary of Residue Distribution Files (RDF) listed in H:\MyFiles\HAS docs\dietary exposure\DPR projects\methomyl 2012\DEEM runs\v4 deem runs\methomylacutefoodpluswater.R08

RDF #	File Name	N residues w freq's	N residues w/o freq's	N LODs	LOD Value	N Zeros
1	apple juice.rdf	0	1	73	0.0091	666
2	apple sauce.rdf	0	0	110	0.0046	992
3	apple.rdf	0	7	216	0.0022	2008
4	asparagus canned.rdf	0	0	35	0.0053	319
5	asparagus.rdf	0	52	97	0.0053	1339
6	avocadotol5pct.rdf	0	1	0	0	19
7	beans green bf.rdf	0	0	117	0.006	467
8	beans green canned.rdf	0	0	186	0.0071	742
9	beans green fzn.rdf	0	8	103	0.0074	444
10	beans green.rdf	0	32	152	0.0058	736
11	beets canned..rdf	0	0	454	0.0063	302
12	blueberry fzn.rdf	0	3	11	0.0036	26
13	blueberry.rdf	0	50	453	0.0039	934
14	broccabb100pct.rdf	0	41	2919	0.0017	0
15	broccoli.rdf	0	18	277	0.0017	1180
16	cabbage.rdf	0	23	200	0.0018	1262
17	cantaloupe.rdf	0	152	348	0.0054	1168
18	cantaloupe100pct.rdf	0	152	1516	0.0054	0
19	carrot.rdf	0	1	706	0.0041	1313
20	carrot40pct.rdf	0	1	807	0.0041	1212
21	carrot100pct.rdf	0	1	2019	0.0041	0
22	cauliflower.rdf	0	19	204	0.0007	1262
23	celery.rdf	0	147	1183	0.003	887
24	celery100pct.rdf	0	147	2070	0.003	0
25	collard greens.rdf	0	10	669	0.0056	0
26	collkale100pct.rdf	0	15	1463	0.0056	0
27	corn sweet on cob.rdf	0	1	844	0.0054	455
28	corn sweet.rdf	0	0	118	0.0052	63
29	cucumber.rdf	0	51	358	0.0039	1636
30	cucumber100pct.rdf	0	51	1994	0.0039	0
31	eggplant.rdf	0	31	43	0.006	1402
32	eggplant100pct.rdf	0	31	1445	0.006	0
33	grape juice.rdf	0	0	36	0.0112	686
34	grape.rdf	0	91	14	0.0061	2013
35	grapefruit.rdf	0	0	1463	0.007	0
36	green onion.rdf	0	64	345	0.0012	335
37	grnbeans100pct.rdf	0	32	888	0.0058	0
38	grnonion100pct.rdf	0	64	680	0.0012	0
39	kale.rdf	0	5	794	0.0055	0
40	lettuce.rdf	0	129	714	0.00253	1031
41	nectarine.rdf	0	38	121	0.0026	1435
42	nutstol2.5pct.rdf	0	1	0	0	39
43	onion.rdf	0	0	51	0.006	42
44	onion65pct.rdf	0	0	60	0.006	33
45	orange juice.rdf	0	0	47	0.0049	1839
46	orange.rdf	0	0	56	0.0065	2171
47	pea snap.rdf	0	14	5	0.0036	725
48	peach canned.rdf	0	0	148	0.006	1337
49	peach.rdf	0	37	89	0.0034	1135
50	peas sweet canned.rdf	0	0	32	0.0059	1246
51	pepper hot.rdf	0	16	178	0.013	359
52	pepper sweet bell.rdf	0	253	461	0.0027	1326
53	potato fzn.rdf	0	0	77	0.0024	1467
54	raisin.rdf	0	0	37	0.0042	707
55	soybean grain.rdf	0	0	1574	0.0015	0
56	spinach canned.rdf	0	0	142	0.0057	427
57	spinach fzn.rdf	0	1	48	0.005	149

58	spinach.rdf	0	87	413	0.0049	1499
59	spinach1pct.rdf	0	21	0	0.0049	1979
60	spincanned1pct.rdf	0	0	6	0.0057	563
61	spinlett100pct.rdf	0	216	3657	0.0146	0
62	squash summer.rdf	0	23	199	0.0042	1260
63	squash winter.rdf	0	2	191	0.0062	1093
64	sweet potato bf.rdf	0	0	88	0.006	497
65	sweet potato.rdf	0	0	249	0.0041	1412
66	tomato canned.rdf	0	0	74	0.0049	295
67	tomato paste.rdf	0	0	222	0.0116	889
68	tomato.rdf	0	1	443	0.0018	1775
69	watermelon.rdf	0	36	37	0.0047	659
70	wintersq10pct.rdf	0	2	127	0.0062	1157
71	wintersq100pct.rdf	0	2	1284	0.0062	0
72	potato.rdf	0	0	93	0.0051	1765

Attachment 3

Acute Analysis Reports (a)

(a) Note that some DEEM-FCID acute results indicate an FQPA safety factor of 2. All final calculations were made with an FQPA safety factor of 4.

ACUTE FOOD ONLY RESULTS

```
California Dept of Pesticide Regulation                    Ver. 3.18, 03-08-d
DEEM-FCID ACUTE Analysis for METHOMYL                   NHANES 2003-2008 2-Day
Residue file: methomylacutefoodonly.r08          Adjustment factor #2 NOT used.
Analysis Date: 08-16-2013/13:07:54    Residue file dated: 08-16-2013/11:16:20
Acute Pop Adjusted Dose (aPAD) varies with population; see individual reports
RAC/FF intake reported by eating occasion
MC iterations = 1000; MC list in residue file; MC seed = 10; RNG = MS VB
Run Comment: ""
===============================================================================
```

Summary calculations--users:

	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	% aPAD	Exposure	% aPAD	Exposure	% aPAD
Total US Population:	0.000067	2.23	0.000177	5.90	0.001495	49.83
All Infants:	0.000097	6.49	0.000201	13.38	0.000731	48.75
Children 1-2:	0.000169	11.24	0.000402	26.80	0.002327	155.12
Children 3-5:	0.000133	8.89	0.000307	20.44	0.001977	131.77
Children 6-12:	0.000086	5.71	0.000179	11.96	0.001149	76.58
Youth 13-19:	0.000052	1.73	0.000135	4.49	0.000843	28.11
Adults 20-49:	0.000053	1.75	0.000142	4.73	0.001491	49.70
Adults 50-99:	0.000051	1.70	0.000146	4.86	0.001685	56.17
Female 13-49:	0.000049	1.63	0.000141	4.72	0.001499	49.97

ACUTE FOOD PLUS WATER RESULTS

```
California Dept of Pesticide Regulation                    Ver. 3.18, 03-08-d
DEEM-FCID ACUTE Analysis for METHOMYL                    NHANES 2003-2008 2-Day
Residue file: methomylacutefoodpluswater.R08      Adjustment factor #2 NOT used.
Analysis Date: 08-16-2013/11:36:40    Residue file dated: 08-16-2013/10:57:09
Acute Pop Adjusted Dose (aPAD) varies with population; see individual reports
RAC/FF intake reported by eating occasion
MC iterations = 1000; MC list in residue file; MC seed = 10; RNG = MS VB
Run Comment: ""
===============================================================================
```

Summary calculations--users:

	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	% aPAD	Exposure	% aPAD	Exposure	% aPAD
Total US Population:	0.000067	2.24	0.000177	5.91	0.001508	50.27
All Infants:	0.000098	6.51	0.000200	13.32	0.000745	49.66
Children 1-2:	0.000169	11.25	0.000402	26.82	0.002247	149.79
Children 3-5:	0.000134	8.95	0.000308	20.52	0.002102	140.13
Children 6-12:	0.000086	5.71	0.000179	11.97	0.001125	74.97
Youth 13-19:	0.000052	1.73	0.000135	4.51	0.000857	28.57
Adults 20-49:	0.000053	1.76	0.000142	4.74	0.001498	49.94
Adults 50-99:	0.000051	1.71	0.000146	4.87	0.001728	57.59
Female 13-49:	0.000049	1.63	0.000142	4.74	0.001519	50.64

ACUTE FOOD ONLY X GRAPES RESULTS

```
California Dept of Pesticide Regulation                    Ver. 3.18, 03-08-d
DEEM-FCID ACUTE Analysis for METHOMYL                   NHANES 2003-2008 2-Day
Residue file: methomylacutefoodonlyxgrape.r08     Adjustment factor #2 NOT used.
Analysis Date: 08-16-2013/13:20:09    Residue file dated: 08-16-2013/13:05:37
Acute Pop Adjusted Dose (aPAD) varies with population; see individual reports
RAC/FF intake reported by eating occasion
MC iterations = 1000; MC list in residue file; MC seed = 10; RNG = MS VB
Run Comment: ""
===============================================================================
```

Summary calculations--users:

	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	% aPAD	Exposure	% aPAD	Exposure	% aPAD
Total US Population:	0.000064	2.15	0.000162	5.40	0.001319	43.97
All Infants:	0.000093	6.22	0.000185	12.34	0.000602	40.14
Children 1-2:	0.000153	10.22	0.000317	21.12	0.001219	81.27
Children 3-5:	0.000124	8.26	0.000276	18.38	0.001177	78.47
Children 6-12:	0.000082	5.44	0.000159	10.61	0.000702	46.81
Youth 13-19:	0.000050	1.68	0.000125	4.17	0.000762	25.41
Adults 20-49:	0.000051	1.70	0.000134	4.47	0.001451	48.36
Adults 50-99:	0.000049	1.63	0.000133	4.42	0.001610	53.68
Female 13-49:	0.000047	1.57	0.000132	4.40	0.001450	48.33

ACUTE FOOD PLUS WATER X GRAPES RESULTS

```
California Dept of Pesticide Regulation                    Ver. 3.18, 03-08-d
DEEM-FCID ACUTE Analysis for METHOMYL                    NHANES 2003-2008 2-Day
Residue file: methomylacutefoodpluswaterxgrape.R08
Adjustment factor #2 NOT used.
Analysis Date: 08-16-2013/13:30:44    Residue file dated: 08-16-2013/13:06:57
Acute Pop Adjusted Dose (aPAD) varies with population; see individual reports
RAC/FF intake reported by eating occasion
MC iterations = 1000; MC list in residue file; MC seed = 10; RNG = MS VB
Run Comment: ""
===============================================================================
```

Summary calculations--users:

	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	% aPAD	Exposure	% aPAD	Exposure	% aPAD
Total US Population:	0.000065	2.15	0.000162	5.40	0.001323	44.09
All Infants:	0.000094	6.26	0.000185	12.30	0.000561	37.37
Children 1-2:	0.000154	10.25	0.000320	21.31	0.001195	79.69
Children 3-5:	0.000124	8.24	0.000275	18.31	0.001200	80.02
Children 6-12:	0.000082	5.45	0.000160	10.65	0.000698	46.55
Youth 13-19:	0.000051	1.68	0.000125	4.17	0.000739	24.64
Adults 20-49:	0.000051	1.71	0.000134	4.48	0.001465	48.85
Adults 50-99:	0.000049	1.64	0.000134	4.46	0.001659	55.31
Female 13-49:	0.000047	1.58	0.000132	4.40	0.001454	48.48

Attachment 4

Chronic Food Plus Water Residue File

CHRONIC FOOD PLUS WATER RESIDUE FILE

California Dept of Pesticide Regulation Ver. 3.16, 03-08-d
DEEM-FCID Chronic analysis for METHOMYL
Residue file: H:\MyFiles\HAS docs\dietary exposure\DPR projects\methomyl 2012\DEEM runs\v4 deem runs\methomylchronicfoodpluswater.r08
Adjust. #2 NOT used
Analysis Date 08-16-2013 Residue file dated: 08-16-2013/11:20:24
Reference dose (RfD) = 0.03 mg/kg bw/day
Comment:Based on histopathologic abnormalities in the kidney and spleen in a chronic dog study

Food EPA Code	Crop Grp	Food Name	Residue (ppm)	Adj.Factors #1	#2
0401005000	4A	Amaranth, leafy	0.020451	1.000	1.000
1100007000	11	Apple, fruit with peel	0.000147	1.000	1.000
1100008000	11	Apple, peeled fruit	0.000147	1.000	1.000
1100008001	11	Apple, peeled fruit-babyfood	0.000147	1.000	1.000
1100009000	11	Apple, dried	0.000390	1.000	1.000
1100009001	11	Apple, dried-babyfood	0.000390	1.000	1.000
1100010000	11	Apple, juice	0.000476	1.000	1.000
1100010001	11	Apple, juice-babyfood	0.000476	1.000	1.000
1100011000	11	Apple, sauce	0.000230	1.000	1.000
1100011001	11	Apple, sauce-babyfood	0.000230	1.000	1.000
0103015000	1CD	Arrowroot, flour	0.005100	1.000	1.000
0103015001	1CD	Arrowroot, flour-babyfood	0.005100	1.000	1.000
0103017000	1CD	Artichoke, Jerusalem	0.005100	1.000	1.000
0401018000	4A	Arugula	0.020451	1.000	1.000
9500019000	O	Asparagus			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.000078	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.000078	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.000078	1.000	1.000
		222-Cooked; Frozen; Boiled	0.000078	1.000	1.000
		242-Cooked; Canned; Boiled	0.000254	1.000	1.000
9500020000	O	Avocado	0.100000	1.000	1.000
0902021000	9B	Balsam pear	0.004316	1.000	1.000
1500025000	15	Barley, pearled barley	0.004500	1.000	1.000
1500025001	15	Barley, pearled barley-babyfood	0.004500	1.000	1.000
1500026000	15	Barley, flour	0.004500	1.000	1.000
1500026001	15	Barley, flour-babyfood	0.004500	1.000	1.000
1500027000	15	Barley, bran	0.004500	1.000	1.000
0603030000	6C	Bean, black, seed	0.005200	1.000	1.000
0602031000	6B	Bean, broad, succulent	0.008670	1.000	1.000
0603032000	6C	Bean, broad, seed	0.005200	1.000	1.000
0602033000	6B	Bean, cowpea, succulent	0.008670	1.000	1.000
0603034000	6C	Bean, cowpea, seed	0.005200	1.000	1.000
0603035000	6C	Bean, great northern, seed	0.005200	1.000	1.000
0603036000	6C	Bean, kidney, seed	0.005200	1.000	1.000
0602037000	6B	Bean, lima, succulent	0.008670	1.000	1.000
0603038000	6C	Bean, lima, seed	0.005200	1.000	1.000
0603039000	6C	Bean, mung, seed	0.005200	1.000	1.000
0603040000	6C	Bean, navy, seed	0.005200	1.000	1.000
0603041000	6C	Bean, pink, seed	0.005200	1.000	1.000
0603042000	6C	Bean, pinto, seed	0.005200	1.000	1.000
0601043000	6A	Bean, snap, succulent			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.004003	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.004003	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.004003	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.004003	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.004003	1.000	1.000
		215-Cooked; Fresh or N/S; Boiled/baked	0.004003	1.000	1.000
		220-Cooked; Frozen; Cook Meth N/S	0.001780	1.000	1.000
		221-Cooked; Frozen; Baked	0.001780	1.000	1.000
		222-Cooked; Frozen; Boiled	0.001780	1.000	1.000
		232-Cooked; Dried; Boiled	0.004003	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.000708	1.000	1.000
		242-Cooked; Canned; Boiled	0.000708	1.000	1.000
0601043001	6A	Bean, snap, succulent-babyfood	0.000596	1.000	1.000
0101050000	1AB	Beet, garden, roots			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.001667	1.000	1.000

		212-Cooked; Fresh or N/S; Boiled	0.001667	1.000	1.000
		221-Cooked; Frozen; Baked	0.001667	1.000	1.000
		232-Cooked; Dried; Boiled	0.001667	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.003755	1.000	1.000
		242-Cooked; Canned; Boiled	0.003755	1.000	1.000
		250-Cooked; Cured etc; Cook Meth N/S	0.001667	1.000	1.000
0101050001	1AB	Beet, garden, roots-babyfood	0.003755	1.000	1.000
0200051000	2	Beet, garden, tops	6.000000	1.000	1.000
0101052000	1A	Beet, sugar	0.004100	1.000	1.000
0101052001	1A	Beet, sugar-babyfood	0.004100	1.000	1.000
0101053000	1A	Beet, sugar, molasses	0.004100	1.000	1.000
0101053001	1A	Beet, sugar, molasses-babyfood	0.004100	1.000	1.000
9500054000	O	Belgium endive	0.020451	1.000	1.000
1302057000	13B	Blueberry			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.004518	1.000	1.000
		120-Uncooked; Frozen; Cook Meth N/S	0.002579	1.000	1.000
		130-Uncooked; Dried; Cook Meth N/S	0.004518	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.004518	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.004518	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.004518	1.000	1.000
		214-Cooked; Fresh or N/S; Fried/baked	0.004518	1.000	1.000
		223-Cooked; Frozen; Fried	0.002579	1.000	1.000
		230-Cooked; Dried; Cook Meth N/S	0.004518	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.004518	1.000	1.000
1302057001	13B	Blueberry-babyfood	0.004518	1.000	1.000
0501061000	5A	Broccoli	0.000342	1.000	1.000
0501061001	5A	Broccoli-babyfood	0.000342	1.000	1.000
0501062000	5A	Broccoli, Chinese	0.001881	1.000	1.000
0502063000	5B	Broccoli raab	0.007677	1.000	1.000
0501064000	5A	Brussels sprouts	0.001881	1.000	1.000
0101067000	1AB	Burdock	0.004154	1.000	1.000
0501069000	5A	Cabbage	0.000296	1.000	1.000
0502070000	5B	Cabbage, Chinese, bok choy	0.001881	1.000	1.000
0501071000	5A	Cabbage, Chinese, napa	0.001881	1.000	1.000
0501072000	5A	Cabbage, Chinese, mustard	0.001881	1.000	1.000
0901075000	9A	Cantaloupe	0.003774	1.000	1.000
0402076000	4B	Cardoon	0.002764	1.000	1.000
0101078000	1AB	Carrot	0.000631	1.000	1.000
0101078001	1AB	Carrot-babyfood	0.000631	1.000	1.000
0101079000	1AB	Carrot, juice	0.000631	1.000	1.000
0103082000	1CD	Cassava	0.005100	1.000	1.000
0103082001	1CD	Cassava-babyfood	0.005100	1.000	1.000
0501083000	5A	Cauliflower	0.000249	1.000	1.000
0101084000	1AB	Celeriac	0.004154	1.000	1.000
0402085000	4B	Celery	0.002826	1.000	1.000
0402085001	4B	Celery-babyfood	0.002826	1.000	1.000
0402086000	4B	Celery, juice	0.002826	1.000	1.000
0402087000	4B	Celtuce	0.020451	1.000	1.000
0902088000	9B	Chayote, fruit	0.006274	1.000	1.000
0603098000	6C	Chickpea, seed	0.005200	1.000	1.000
0603098001	6C	Chickpea, seed-babyfood	0.005200	1.000	1.000
0603099000	6C	Chickpea, flour	0.005200	1.000	1.000
0101100000	1AB	Chicory, roots	0.004154	1.000	1.000
0902102000	9B	Chinese waxgourd	0.004316	1.000	1.000
0401104000	4A	Chrysanthemum, garland	0.020451	1.000	1.000
1001106000	10A	Citron	0.006500	1.000	1.000
1001107000	10A	Citrus hybrids	0.006500	1.000	1.000
1001108000	10A	Citrus, oil	0.006500	1.000	1.000
0502117000	5B	Collards	0.010077	1.000	1.000
1500120000	15	Corn, field, flour	0.001500	1.000	1.000
1500120001	15	Corn, field, flour-babyfood	0.001500	1.000	1.000
1500121000	15	Corn, field, meal	0.001500	1.000	1.000
1500121001	15	Corn, field, meal-babyfood	0.001500	1.000	1.000
1500122000	15	Corn, field, bran	0.001500	1.000	1.000
1500123000	15	Corn, field, starch	0.001500	1.000	1.000
1500123001	15	Corn, field, starch-babyfood	0.001500	1.000	1.000
1500124000	15	Corn, field, syrup	0.001500	1.000	1.000
1500124001	15	Corn, field, syrup-babyfood	0.001500	1.000	1.000
1500125000	15	Corn, field, oil	0.001500	1.000	1.000
1500125001	15	Corn, field, oil-babyfood	0.001500	1.000	1.000
1500126000	15	Corn, pop	0.001500	1.000	1.000

1500127000	15	Corn, sweet			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.001361	1.000	1.000
		140-Uncooked; Canned; Cook Meth N/S	0.001293	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.001361	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.001361	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.001361	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.001361	1.000	1.000
		220-Cooked; Frozen; Cook Meth N/S	0.001293	1.000	1.000
		221-Cooked; Frozen; Baked	0.001293	1.000	1.000
		222-Cooked; Frozen; Boiled	0.001293	1.000	1.000
		232-Cooked; Dried; Boiled	0.001293	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.001293	1.000	1.000
		242-Cooked; Canned; Boiled	0.001293	1.000	1.000
		243-Cooked; Canned; Fried	0.001293	1.000	1.000
1500127001	15	Corn, sweet-babyfood	0.001293	1.000	1.000
2003128000	20C	Cottonseed, oil	0.050000	1.000	1.000
2003128001	20C	Cottonseed, oil-babyfood	0.050000	1.000	1.000
0401133000	4A	Cress, garden	0.020451	1.000	1.000
0401134000	4A	Cress, upland	0.020451	1.000	1.000
0902135000	9B	Cucumber	0.000846	1.000	1.000
0401138000	4A	Dandelion, leaves	0.020451	1.000	1.000
0103139000	1CD	Dasheen, corm	0.005100	1.000	1.000
0802148000	8BC	Eggplant	0.001224	1.000	1.000
0401150000	4A	Endive	0.020451	1.000	1.000
0402152000	4B	Fennel, Florence	0.002764	1.000	1.000
0301165000	3A	Garlic, bulb	0.001806	1.000	1.000
0301165001	3A	Garlic, bulb-babyfood	0.001806	1.000	1.000
0103166000	1CD	Ginger	0.005100	1.000	1.000
0103166001	1CD	Ginger-babyfood	0.005100	1.000	1.000
0103167000	1CD	Ginger, dried	0.005100	1.000	1.000
0101168000	1AB	Ginseng, dried	0.005100	1.000	1.000
1304175000	13D	Grape	0.006504	1.000	1.000
1304176000	13D	Grape, juice	0.000280	1.000	1.000
1304176001	13D	Grape, juice-babyfood	0.000280	1.000	1.000
9500177000	O	Grape, leaves	0.007000	1.000	1.000
9500178000	O	Grape, raisin	0.004161	1.000	1.000
1304179000	13D	Grape, wine and sherry	0.000280	1.000	1.000
1003180000	10C	Grapefruit	0.007000	1.000	1.000
1003181000	10C	Grapefruit, juice	0.007000	1.000	1.000
0603182000	6C	Guar, seed	0.005200	1.000	1.000
0603182001	6C	Guar, seed-babyfood	0.005200	1.000	1.000
0901187000	9A	Honeydew melon	0.008369	1.000	1.000
9500188000	O	Hop	0.040000	1.000	1.000
0101190000	1AB	Horseradish	0.004154	1.000	1.000
0502194000	5B	Kale	0.005637	1.000	1.000
0501196000	5A	Kohlrabi	0.001881	1.000	1.000
1002197000	10B	Kumquat	0.006500	1.000	1.000
0302198000	3B	Leek	0.002079	1.000	1.000
1002199000	10B	Lemon	0.000064	1.000	1.000
1002200000	10B	Lemon, juice	0.000049	1.000	1.000
1002200001	10B	Lemon, juice-babyfood	0.000049	1.000	1.000
1002201000	10B	Lemon, peel	0.000064	1.000	1.000
0603203000	6C	Lentil, seed	0.005200	1.000	1.000
0401204000	4A	Lettuce, head	0.013652	1.000	1.000
0401205000	4A	Lettuce, leaf	0.013652	1.000	1.000
1002206000	10B	Lime	0.006500	1.000	1.000
1002207000	10B	Lime, juice	0.005000	1.000	1.000
1002207001	10B	Lime, juice-babyfood	0.005000	1.000	1.000
0502229000	5B	Mustard greens	0.007677	1.000	1.000
1202230000	12B	Nectarine	0.001090	1.000	1.000
1500231000	15	Oat, bran	0.004500	1.000	1.000
1500232000	15	Oat, flour	0.004500	1.000	1.000
1500232001	15	Oat, flour-babyfood	0.004500	1.000	1.000
1500233000	15	Oat, groats/rolled oats	0.004500	1.000	1.000
1500233001	15	Oat, groats/rolled oats-babyfood	0.004500	1.000	1.000
0802234000	8BC	Okra	0.006923	1.000	1.000
0301237000	3A	Onion, bulb	0.002129	1.000	1.000
0301237001	3A	Onion, bulb-babyfood	0.002129	1.000	1.000
0301238000	3A	Onion, bulb, dried	0.006000	1.000	1.000
0301238001	3A	Onion, bulb, dried-babyfood	0.006000	1.000	1.000
0302239000	3B	Onion, green	0.001298	1.000	1.000
1001240000	10A	Orange	0.000064	1.000	1.000
1001241000	10A	Orange, juice	0.000049	1.000	1.000
1001241001	10A	Orange, juice-babyfood	0.000049	1.000	1.000
1001242000	10A	Orange, peel	0.000064	1.000	1.000

0401248000	4A	Parsley, leaves			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.005700	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.005700	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.005700	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.005700	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.005700	1.000	1.000
		215-Cooked; Fresh or N/S; Boiled/baked	0.005700	1.000	1.000
		221-Cooked; Frozen; Baked	0.005700	1.000	1.000
		232-Cooked; Dried; Boiled	0.005700	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.000060	1.000	1.000
		242-Cooked; Canned; Boiled	0.000060	1.000	1.000
1901249000	19A	Parsley, dried leaves	0.005700	1.000	1.000
1901249001	19A	Parsley, dried leaves-babyfood	0.005700	1.000	1.000
0101250000	1AB	Parsley, turnip rooted	0.004154	1.000	1.000
0101251000	1AB	Parsnip	0.004154	1.000	1.000
0101251001	1AB	Parsnip-babyfood	0.004150	1.000	1.000
0602255000	6B	Pea, succulent			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.000863	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.000863	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.000863	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.000863	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.000863	1.000	1.000
		221-Cooked; Frozen; Baked	0.000863	1.000	1.000
		222-Cooked; Frozen; Boiled	0.000863	1.000	1.000
		232-Cooked; Dried; Boiled	0.000863	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.000060	1.000	1.000
		242-Cooked; Canned; Boiled	0.000060	1.000	1.000
0602255001	6B	Pea, succulent-babyfood	0.000060	1.000	1.000
0603256000	6C	Pea, dry	0.005200	1.000	1.000
0603256001	6C	Pea, dry-babyfood	0.005200	1.000	1.000
0601257000	6A	Pea, edible podded, succulent	0.000863	1.000	1.000
0603258000	6C	Pea, pigeon, seed	0.005200	1.000	1.000
0602259000	6B	Pea, pigeon, succulent			
		212-Cooked; Fresh or N/S; Boiled	0.000863	1.000	1.000
		242-Cooked; Canned; Boiled	0.000060	1.000	1.000
1202260000	12B	Peach			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.002296	1.000	1.000
		120-Uncooked; Frozen; Cook Meth N/S	0.002296	1.000	1.000
		130-Uncooked; Dried; Cook Meth N/S	0.002296	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.002296	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.002296	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.002296	1.000	1.000
		223-Cooked; Frozen; Fried	0.002296	1.000	1.000
		230-Cooked; Dried; Cook Meth N/S	0.002296	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.000299	1.000	1.000
1202260001	12B	Peach-babyfood	0.000299	1.000	1.000
1202261000	12B	Peach, dried	0.005400	1.000	1.000
1202261001	12B	Peach, dried-babyfood	0.005400	1.000	1.000
1202262000	12B	Peach, juice	0.002296	1.000	1.000
1202262001	12B	Peach, juice-babyfood	0.002296	1.000	1.000
9500263000	O	Peanut	0.050000	1.000	1.000
9500264000	O	Peanut, butter	0.005000	1.000	1.000
9500265000	O	Peanut, oil	0.005000	1.000	1.000
1400269000	14	Pecan	0.002500	1.000	1.000
0802270000	8B	Pepper, bell	0.010699	1.000	1.000
0802270001	8B	Pepper, bell-babyfood	0.010699	1.000	1.000
0802271000	8B	Pepper, bell, dried	0.010699	1.000	1.000
0802271001	8B	Pepper, bell, dried-babyfood	0.010699	1.000	1.000
0802272000	8BC	Pepper, nonbell	0.005461	1.000	1.000
0802272001	8BC	Pepper, nonbell-babyfood	0.005461	1.000	1.000
0802273000	8BC	Pepper, nonbell, dried	0.005461	1.000	1.000
9500275000	O	Peppermint	2.000000	1.000	1.000
9500276000	O	Peppermint, oil	2.000000	1.000	1.000
9500289000	O	Pomegranate	0.100000	1.000	1.000
0103296000	1C	Potato, chips	0.000127	1.000	1.000

0103297000	1C	Potato, dry (granules/ flakes)	0.005100	1.000	1.000
0103297001	1C	Potato, dry (granules/ flakes)-b	0.005100	1.000	1.000
0103298000	1C	Potato, flour	0.005100	1.000	1.000
0103298001	1C	Potato, flour-babyfood	0.005100	1.000	1.000
0103299000	1C	Potato, tuber, w/peel	0.000127	1.000	1.000
0103299001	1C	Potato, tuber, w/peel-babyfood	0.000127	1.000	1.000
0103300000	1C	Potato, tuber, w/o peel			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.000127	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.000127	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.000127	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.000127	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.000127	1.000	1.000
		221-Cooked; Frozen; Baked	0.000061	1.000	1.000
		223-Cooked; Frozen; Fried	0.000061	1.000	1.000
		232-Cooked; Dried; Boiled	0.000127	1.000	1.000
		233-Cooked; Dried; Fried	0.000127	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.000127	1.000	1.000
		242-Cooked; Canned; Boiled	0.000127	1.000	1.000
		252-Cooked; Cured etc; Boiled	0.000127	1.000	1.000
0103300001	1C	Potato, tuber, w/o peel-babyfood	0.000127	1.000	1.000
1003307000	10C	Pummelo	0.006500	1.000	1.000
0902308000	9B	Pumpkin	0.003370	1.000	1.000
0902309000	9B	Pumpkin, seed	0.003370	1.000	1.000
0401313000	4A	Radicchio	0.020451	1.000	1.000
0101314000	1AB	Radish, roots	0.004150	1.000	1.000
0101316000	1AB	Radish, Oriental, roots	0.004150	1.000	1.000
0502318000	5B	Rape greens	0.007677	1.000	1.000
0402322000	4B	Rhubarb	0.002764	1.000	1.000
0101327000	1AB	Rutabaga	0.004150	1.000	1.000
1500328000	15	Rye, grain	0.004500	1.000	1.000
1500329000	15	Rye, flour	0.004500	1.000	1.000
0101331000	1AB	Salsify, roots	0.004150	1.000	1.000
0302338500	3B	Shallot, fresh leaves	0.002079	1.000	1.000
1500344000	15	Sorghum, grain	0.001500	1.000	1.000
1500345000	15	Sorghum, syrup	0.001500	1.000	1.000
0600347000	6	Soybean, seed	0.001500	1.000	1.000
0603348000	6C	Soybean, flour	0.001500	1.000	1.000
0603348001	6C	Soybean, flour-babyfood	0.001500	1.000	1.000
0600349000	6	Soybean, soy milk	0.001500	1.000	1.000
0600349001	6	Soybean, soy milk-babyfood or in	0.001500	1.000	1.000
0600350000	6	Soybean, oil	0.001500	1.000	1.000
0600350001	6	Soybean, oil-babyfood	0.001500	1.000	1.000
9500352000	O	Spearmint	2.000000	1.000	1.000
9500353000	O	Spearmint, oil	2.000000	1.000	1.000
0401355000	4A	Spinach			
		110-Uncooked; Fresh or N/S; Cook Meth N/S	0.007158	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.007158	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.007158	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.007158	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.007158	1.000	1.000
		215-Cooked; Fresh or N/S; Boiled/baked	0.007158	1.000	1.000
		220-Cooked; Frozen; Cook Meth N/S	0.000551	1.000	1.000
		221-Cooked; Frozen; Baked	0.000551	1.000	1.000
		222-Cooked; Frozen; Boiled	0.000551	1.000	1.000
		232-Cooked; Dried; Boiled	0.007158	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.000566	1.000	1.000
		242-Cooked; Canned; Boiled	0.000566	1.000	1.000
0401355001	4A	Spinach-babyfood	0.000566	1.000	1.000
0902356000	9B	Squash, summer	0.000939	1.000	1.000
0902356001	9B	Squash, summer-babyfood	0.000939	1.000	1.000
0902357000	9B	Squash, winter	0.000337	1.000	1.000
0902357001	9B	Squash, winter-babyfood	0.000337	1.000	1.000
0103366000	1CD	Sweet potato	0.000619	1.000	1.000
0103366001	1CD	Sweet potato-babyfood	0.000903	1.000	1.000
0402367000	4B	Swiss chard	0.002764	1.000	1.000
1001369000	10A	Tangerine	0.005000	1.000	1.000
1001370000	10A	Tangerine, juice	0.005000	1.000	1.000
0103371000	1CD	Tanier, corm	0.005100	1.000	1.000
0801374000	8A	Tomatillo	0.002500	1.000	1.000
0801375000	8A	Tomato			
		110-Uncooked; Fresh or N/S; Cook Meth N/S			

			0.000189	1.000	1.000
		150-Uncooked; Cured etc; Cook Meth N/S	0.000189	1.000	1.000
		210-Cooked; Fresh or N/S; Cook Meth N/S	0.000189	1.000	1.000
		211-Cooked; Fresh or N/S; Baked	0.000189	1.000	1.000
		212-Cooked; Fresh or N/S; Boiled	0.000189	1.000	1.000
		213-Cooked; Fresh or N/S; Fried	0.000189	1.000	1.000
		214-Cooked; Fresh or N/S; Fried/baked	0.000189	1.000	1.000
		215-Cooked; Fresh or N/S; Boiled/baked	0.000189	1.000	1.000
		221-Cooked; Frozen; Baked	0.000189	1.000	1.000
		222-Cooked; Frozen; Boiled	0.000189	1.000	1.000
		232-Cooked; Dried; Boiled	0.000189	1.000	1.000
		240-Cooked; Canned; Cook Meth N/S	0.000490	1.000	1.000
		242-Cooked; Canned; Boiled	0.000490	1.000	1.000
		252-Cooked; Cured etc; Boiled	0.000189	1.000	1.000
0801375001	8A	Tomato-babyfood	0.000490	1.000	1.000
0801376000	8A	Tomato, paste	0.001162	1.000	1.000
0801376001	8A	Tomato, paste-babyfood	0.001162	1.000	1.000
0801377000	8A	Tomato, puree	0.001162	1.000	1.000
0801377001	8A	Tomato, puree-babyfood	0.001162	1.000	1.000
0801378000	8A	Tomato, dried	0.000004	1.000	1.000
0801378001	8A	Tomato, dried-babyfood	0.000004	1.000	1.000
0801379000	8A	Tomato, juice	0.000189	1.000	1.000
1500381000	15	Triticale, flour	0.004500	1.000	1.000
1500381001	15	Triticale, flour-babyfood	0.004500	1.000	1.000
0103387000	1CD	Turmeric	0.005100	1.000	1.000
0101388000	1AB	Turnip, roots	0.004150	1.000	1.000
0502389000	5B	Turnip, greens	0.007677	1.000	1.000
1400391000	14	Walnut	0.002500	1.000	1.000
8601000000	86A	Water, direct, all sources	0.000005	1.000	1.000
8602000000	86B	Water, indirect, all sources	0.000005	1.000	1.000
0901399000	9A	Watermelon	0.001359	1.000	1.000
0901400000	9A	Watermelon, juice	0.001359	1.000	1.000
1500401000	15	Wheat, grain	0.004500	1.000	1.000
1500401001	15	Wheat, grain-babyfood	0.004500	1.000	1.000
1500402000	15	Wheat, flour	0.004500	1.000	1.000
1500402001	15	Wheat, flour-babyfood	0.004500	1.000	1.000
1500403000	15	Wheat, germ	0.004500	1.000	1.000
1500404000	15	Wheat, bran	0.004500	1.000	1.000
0103406000	1CD	Yam, true	0.005100	1.000	1.000
0103407000	1CD	Yam bean	0.005100	1.000	1.000
0301338000	3A	Shallot, bulb	0.006000	1.000	1.000
0601349500	6AB	Soybean, vegetable	0.200000	1.000	1.000

Attachment 5

Chronic Analysis Reports

CHRONIC FOOD PLUS WATER RESULTS

```
California Dept of Pesticide Regulation                          Ver. 3.16, 03-08-d
DEEM-FCID Chronic analysis for METHOMYL                     NHANES 2003-2008 2-day
Residue file name: H:\MyFiles\HAS docs\dietary exposure\DPR projects\methomyl 2012\DEEM runs\v2
deem runs\methomylchronicfoodpluswater.r08
                                                 Adjustment factor #2 NOT used.
Analysis Date 06-26-2013/14:17:39     Residue file dated: 06-26-2013/09:34:44
Reference dose (RfD, Chronic) = .03 mg/kg bw/day
COMMENT 1: Based on histopathologic abnormalities in the kidney and spleen in a chronic dog study
===============================================================================
                    Total exposure by population subgroup
-------------------------------------------------------------------------------
```

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of PAD
Total US Population	0.000029	0.1%
Hispanic	0.000033	0.1%
Non-Hisp-White	0.000029	0.1%
Non-Hisp-Black	0.000024	0.1%
Non-Hisp-Other	0.000031	0.1%
Nursing Infants (.03*)	0.000020	0.1%
Non-Nursing Infants (.03*)	0.000028	0.1%
Female 13+ PREG (.03*)	0.000028	0.1%
Children 1-6 (.03*)	0.000059	0.2%
Children 7-12 (.03*)	0.000036	0.1%
Male 13-19 (.03*)	0.000026	0.1%
Female 13-19/NP (.03*)	0.000023	0.1%
Male 20+ (.03*)	0.000026	0.1%
Female 20+/NP (.03*)	0.000026	0.1%
Seniors 55+ (.03*)	0.000024	0.1%
All Infants (.03*)	0.000026	0.1%
Female 13-50 (.03*)	0.000025	0.1%
Children 1-2 (.03*)	0.000063	0.2%
Children 3-5 (.03*)	0.000058	0.2%
Children 6-12 (.03*)	0.000039	0.1%
Youth 13-19 (.03*)	0.000024	0.1%
Adults 20-49 (.03*)	0.000026	0.1%
Adults 50-99 (.03*)	0.000026	0.1%
Female 13-49 (.03*)	0.000025	0.1%

*PAD in mg/kg-bw-day

Attachment 6

Sensitivity Analysis (a)

(a) Note that some DEEM-FCID acute results indicate an FQPA safety factor of 2. All final calculations were made with an FQPA safety factor of 4.

California Dept of Pesticide Regulation
DEEM-FCID Acute Critical Exposure Contribution Analysis (Ver. 3.18, 03-08-d)
NHANES 2003-2008 2-Day
Residue file = H:\MyFiles\HAS docs\dietary exposure\DPR projects\methomyl 2012\DEEM runs\v4 deem runs\methomylacutefoodonly.r08
Acute report = H:\MyFiles\HAS docs\dietary exposure\DPR projects\methomyl 2012\DEEM runs\v4 deem runs\methomylacutefoodonly.AC8
Date and time of analysis: 08-16-2013 13:02:26
Food and foodform consumption evaluated by eating occasion.
Adjustment factor #2 not used.
Minimum exposure contribution = 1%
MC Iterations = 1000 Seed = 10 RNG = MS VB
CEC records generated for first 90 iterations.
Exposures divided by body weight

==

Total US Population

Low percentile for CEC records: 99 Exposure (mg/day) = 0.000177
High percentile for CEC records: 99.9 Exposure (mg/day) = 0.001493
Number of actual records in this interval: 44799

Critical foods with foodforms for this population (as derived from these records):
N=number of appearances in all records (including duplicates)
%=percent of total exposure for all records (including duplicates)

Food	FF	N	Percent	Food Name
0401204000	110	7047	13.15%	Lettuce, head-Uncooked; Fresh or N/S; Cook Meth N/S
9500020000	110	3023	13.13%	Avocado-Uncooked; Fresh or N/S; Cook Meth N/S
1304175000	110	3932	10.30%	Grape-Uncooked; Fresh or N/S; Cook Meth N/S
1100010000	110	9158	9.29%	Apple, juice-Uncooked; Fresh or N/S; Cook Meth N/S
9500263000	211	4879	4.44%	Peanut-Cooked; Fresh or N/S; Baked

Critical foods (without foodforms) for this population (as derived from these records):
N=number of appearances in all records (including duplicates)
%=percent of total exposure for all records (including duplicates)

Food	N	Percent	Food Name
9500020000	3330	14.14%	Avocado
0401204000	7546	14.09%	Lettuce, head
1304175000	4977	11.92%	Grape
1100010000	11053	10.27%	Apple, juice
9500263000	6941	4.78%	Peanut

==

Children 1-2

Low percentile for CEC records: 99 Exposure (mg/day) = 0.000402
High percentile for CEC records: 99.9 Exposure (mg/day) = 0.002327
Number of actual records in this interval: 2034

Critical foods with foodforms for this population (as derived from these records):
N=number of appearances in all records (including duplicates)
%=percent of total exposure for all records (including duplicates)

Food	FF	N	Percent	Food Name
1304175000	110	471	26.97%	Grape-Uncooked; Fresh or N/S; Cook Meth N/S
1100010000	110	602	13.53%	Apple, juice-Uncooked; Fresh or N/S; Cook Meth N/S
0901075000	110	187	7.38%	Cantaloupe-Uncooked; Fresh or N/S; Cook Meth N/S
0401204000	110	129	5.53%	Lettuce, head-Uncooked; Fresh or N/S; Cook Meth N/S
0901399000	110	102	4.26%	Watermelon-Uncooked; Fresh or N/S; Cook Meth N/S

Critical foods (without foodforms) for this population (as derived from these records):
N=number of appearances in all records (including duplicates)
%=percent of total exposure for all records (including duplicates)

Food	N	Percent	Food Name
1304175000	606	31.87%	Grape
1100010000	693	15.00%	Apple, juice
0901075000	187	7.38%	Cantaloupe
0401204000	137	5.87%	Lettuce, head
9500020000	67	4.54%	Avocado

==

Children 3-5

Low percentile for CEC records: 99 Exposure (mg/day) = 0.000307
High percentile for CEC records: 99.9 Exposure (mg/day) = 0.001977
Number of actual records in this interval: 2119

Critical foods with foodforms for this population (as derived from these records):
N=number of appearances in all records (including duplicates)
%=percent of total exposure for all records (including duplicates)

Food	FF	N	Percent	Food Name
1304175000	110	387	21.46%	Grape-Uncooked; Fresh or N/S; Cook Meth N/S
1100010000	110	474	10.04%	Apple, juice-Uncooked; Fresh or N/S; Cook Meth N/S
0401204000	110	241	8.67%	Lettuce, head-Uncooked; Fresh or N/S; Cook Meth N/S
9500263000	211	262	6.80%	Peanut-Cooked; Fresh or N/S; Baked
0901399000	110	142	6.05%	Watermelon-Uncooked; Fresh or N/S; Cook Meth N/S

Critical foods (without foodforms) for this population (as derived from these records):
N=number of appearances in all records (including duplicates)
%=percent of total exposure for all records (including duplicates)

Food	N	Percent	Food Name
1304175000	502	24.79%	Grape
1100010000	559	10.78%	Apple, juice
0401204000	265	9.53%	Lettuce, head
9500263000	301	6.86%	Peanut
0901399000	142	6.05%	Watermelon

ACUTE SENSITIVITY ANALYSIS, RESIDUE FILE

```
California Dept of Pesticide Regulation                    Ver. 3.18, 03-08-d
DEEM-FCID Acute analysis for METHOMYL
Residue file name: H:\MyFiles\HAS docs\dietary exposure\DPR projects\methomyl 2012\DEEM runs\v6
deem runs sens analysis food incl grape\methomylacutefoodonlyxnondetects.r08
Analysis Date 09-05-2013             Residue file dated: 09-05-2013/09:35:35
Reference dose (aRfD) = 0.003 mg/kg bw/day
---------------------------------------------------------------------------------
RDL indices and parameters for Monte Carlo Analysis:
Index Dist Parameter #1           Param #2    Param #3    Comment
  #   Code
----- ---- ------------           ----------- ----------- ----------
  1    6   H:\RDF files\apple juice.rdf
  2    6   H:\RDF files\apple sauce.rdf
  3    6   H:\RDF files\apple.rdf
  4    6   H:\RDF files\asparagus canned.rdf
  5    6   H:\RDF files\asparagus.rdf
  6    6   H:\RDF files\avocadotol5pct.rdf
  7    6   H:\RDF files\beans green bf.rdf
  8    6   H:\RDF files\beans green canned.rdf
  9    6   H:\RDF files\beans green fzn.rdf
  10   6   H:\RDF files\beans green.rdf
  11   6   H:\RDF files\beets canned..rdf
  12   6   H:\RDF files\blueberry fzn.rdf
  13   6   H:\RDF files\blueberry.rdf
  14   6   H:\RDF files\broccabb100pct.rdf
  15   6   H:\RDF files\broccoli.rdf
  16   6   H:\RDF files\cabbage.rdf
  17   6   H:\RDF files\cantaloupe.rdf
  18   6   H:\RDF files\cantaloupe100pct.rdf
  19   6   H:\RDF files\carrot.rdf
  20   6   H:\RDF files\carrot40pct.rdf
  21   6   H:\RDF files\carrot100pct.rdf
  22   6   H:\RDF files\cauliflower.rdf
  23   6   H:\RDF files\celery.rdf
  24   6   H:\RDF files\celery100pct.rdf
  25   6   H:\RDF files\collard greens.rdf
  26   6   H:\RDF files\collkale100pct.rdf
  27   6   H:\RDF files\corn sweet on cob.rdf
  28   6   H:\RDF files\corn sweet.rdf
  29   6   H:\RDF files\cucumber.rdf
  30   6   H:\RDF files\cucumber100pct.rdf
  31   6   H:\RDF files\eggplant.rdf
  32   6   H:\RDF files\eggplant100pct.rdf
  33   6   H:\RDF files\grape juice.rdf
  34   6   H:\RDF files\grape.rdf
  35   6   H:\RDF files\grapefruit.rdf
  36   6   H:\RDF files\green onion.rdf
  37   6   H:\RDF files\grnbeans100pct.rdf
  38   6   H:\RDF files\grnonion100pct.rdf
  39   6   H:\RDF files\kale.rdf
  40   6   H:\RDF files\lettuce.rdf
  41   6   H:\RDF files\nectarine.rdf
  42   6   H:\RDF files\nutstol2.5pct.rdf
  43   6   H:\RDF files\onion.rdf
  44   6   H:\RDF files\onion65pct.rdf
  45   6   H:\RDF files\orange juice.rdf
  46   6   H:\RDF files\orange.rdf
  47   6   H:\RDF files\pea snap.rdf
  48   6   H:\RDF files\peach canned.rdf
  49   6   H:\RDF files\peach.rdf
  50   6   H:\RDF files\peas sweet canned.rdf
  51   6   H:\RDF files\pepper hot.rdf
  52   6   H:\RDF files\pepper sweet bell.rdf
  53   6   H:\RDF files\potato fzn.rdf
  54   6   H:\RDF files\raisin.rdf
  55   6   H:\RDF files\soybean grain.rdf
  56   6   H:\RDF files\spinach canned.rdf
  57   6   H:\RDF files\spinach fzn.rdf
  58   6   H:\RDF files\spinach.rdf
  59   6   H:\RDF files\spinach1pct.rdf
  60   6   H:\RDF files\spincanned1pct.rdf
  61   6   H:\RDF files\spinlett100pct.rdf
  62   6   H:\RDF files\squash summer.rdf
  63   6   H:\RDF files\squash winter.rdf
  64   6   H:\RDF files\sweet potato bf.rdf
  65   6   H:\RDF files\sweet potato.rdf
  66   6   H:\RDF files\tomato canned.rdf
```

```
  67   6   H:\RDF files\tomato paste.rdf
  68   6   H:\RDF files\tomato.rdf
  69   6   H:\RDF files\watermelon.rdf
  70   6   H:\RDF files\wintersq10pct.rdf
  71   6   H:\RDF files\wintersq100pct.rdf
  72   6   H:\RDF files\potato.rdf

  EPA      Crop Food Name                        Def Res     Adj.Factors  RDL  Comment
  Code      Grp                                   (ppm)       #1     #2   Pntr
---------- ---- ------------------------------  ----------  ------ ------ ---  -------
0401005000 4A   Amaranth, leafy                   1.000000   1.000  1.000  61
1100007000 11   Apple, fruit with peel            1.000000   1.000  1.000   3
1100008000 11   Apple, peeled fruit               1.000000   1.000  1.000   3
1100008001 11   Apple, peeled fruit-babyfood      1.000000   1.000  1.000   3
1100009000 11   Apple, dried                      0.000390   1.000  1.000       2007 U
    Full comment: 2007 USEPA DEA
1100009001 11   Apple, dried-babyfood             0.000390   1.000  1.000       2007 U
    Full comment: 2007 USEPA DEA
1100010000 11   Apple, juice                      1.000000   1.000  1.000   1
1100010001 11   Apple, juice-babyfood             1.000000   1.000  1.000   1
0103015000 1CD  Arrowroot, flour                  0.005100   1.000  1.000
0103015001 1CD  Arrowroot, flour-babyfood         0.005100   1.000  1.000
0103017000 1CD  Artichoke, Jerusalem              0.005100   1.000  1.000
0401018000 4A   Arugula                           1.000000   1.000  1.000  61
9500019000 O    Asparagus
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000   5
                   212-Cooked; Fresh or N/S; Boiled
                                                  1.000000   1.000  1.000   5
                   213-Cooked; Fresh or N/S; Fried
                                                  1.000000   1.000  1.000   5
                   222-Cooked; Frozen; Boiled     1.000000   1.000  1.000   5
                   242-Cooked; Canned; Boiled     0.000000   1.000  1.000
9500020000 O    Avocado                           1.000000   1.000  1.000   6
0902021000 9B   Balsam pear                       1.000000   1.000  1.000  30
0603030000 6C   Bean, black, seed                 0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602031000 6B   Bean, broad, succulent            1.000000   1.000  1.000  37
0603032000 6C   Bean, broad, seed                 0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602033000 6B   Bean, cowpea, succulent           1.000000   1.000  1.000  37
0603034000 6C   Bean, cowpea, seed                0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603035000 6C   Bean,  great northern, seed       0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603036000 6C   Bean, kidney, seed                0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602037000 6B   Bean, lima, succulent             1.000000   1.000  1.000  37
0603038000 6C   Bean, lima, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603039000 6C   Bean, mung, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603040000 6C   Bean, navy, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603041000 6C   Bean, pink, seed                  0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603042000 6C   Bean, pinto, seed                 0.005200   1.000  1.000       1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0601043000 6A   Bean, snap, succulent
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000  10
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                  1.000000   1.000  1.000  10
                   211-Cooked; Fresh or N/S; Baked
                                                  1.000000   1.000  1.000  10
                   212-Cooked; Fresh or N/S; Boiled
                                                  1.000000   1.000  1.000  10
                   213-Cooked; Fresh or N/S; Fried
                                                  1.000000   1.000  1.000  10
                   215-Cooked; Fresh or N/S; Boiled/baked
                                                  1.000000   1.000  1.000  10
                   220-Cooked; Frozen; Cook Meth N/S
                                                  1.000000   1.000  1.000   9
                   221-Cooked; Frozen; Baked      1.000000   1.000  1.000   9
                   222-Cooked; Frozen; Boiled     1.000000   1.000  1.000   9
                   232-Cooked; Dried; Boiled      1.000000   1.000  1.000  10
                   240-Cooked; Canned; Cook Meth N/S
                                                  0.000000   1.000  1.000
                   242-Cooked; Canned; Boiled     0.000000   1.000  1.000
0601043001 6A   Bean, snap, succulent-babyfood    1.000000   1.000  1.000   7
0101050000 1AB  Beet, garden, roots
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                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  20
                   212-Cooked; Fresh or N/S; Boiled
                                                1.000000   1.000  1.000  20
                   221-Cooked; Frozen; Baked    1.000000   1.000  1.000  20
                   232-Cooked; Dried; Boiled    1.000000   1.000  1.000  20
                   240-Cooked; Canned; Cook Meth N/S
                                                0.000000   1.000  1.000
                   242-Cooked; Canned; Boiled   0.000000   1.000  1.000
                   250-Cooked; Cured etc; Cook Meth N/S
                                                1.000000   1.000  1.000  20
0200051000 2    Beet, garden, tops              6.000000   1.000  1.000
0101052000 1A   Beet, sugar                     0.004100   1.000  1.000
0101052001 1A   Beet, sugar-babyfood            0.004100   1.000  1.000
0101053000 1A   Beet, sugar, molasses           0.004100   1.000  1.000
0101053001 1A   Beet, sugar, molasses-babyfood  0.004100   1.000  1.000
9500054000 O    Belgium endive                  1.000000   1.000  1.000  61
1302057000 13B  Blueberry
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  13
                   120-Uncooked; Frozen; Cook Meth N/S
                                                1.000000   1.000  1.000  12
                   130-Uncooked; Dried; Cook Meth N/S
                                                1.000000   1.000  1.000  13
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  13
                   211-Cooked; Fresh or N/S; Baked
                                                1.000000   1.000  1.000  13
                   213-Cooked; Fresh or N/S; Fried
                                                1.000000   1.000  1.000  13
                   214-Cooked; Fresh or N/S; Fried/baked
                                                1.000000   1.000  1.000  13
                   223-Cooked; Frozen; Fried    1.000000   1.000  1.000  13
                   230-Cooked; Dried; Cook Meth N/S
                                                1.000000   1.000  1.000  13
                   240-Cooked; Canned; Cook Meth N/S
                                                1.000000   1.000  1.000  13
1302057001 13B  Blueberry-babyfood              1.000000   1.000  1.000  13
0501061000 5A   Broccoli                        1.000000   1.000  1.000  15
0501061001 5A   Broccoli-babyfood               1.000000   1.000  1.000  15
0501062000 5A   Broccoli, Chinese               1.000000   1.000  1.000  14
0502063000 5B   Broccoli raab                   1.000000   1.000  1.000  26
0501064000 5A   Brussels sprouts                1.000000   1.000  1.000  14
0101067000 1AB  Burdock                         1.000000   1.000  1.000  21
0501069000 5A   Cabbage                         1.000000   1.000  1.000  16
0502070000 5B   Cabbage, Chinese, bok choy      1.000000   1.000  1.000  14
0501071000 5A   Cabbage, Chinese, napa          1.000000   1.000  1.000  14
0501072000 5A   Cabbage, Chinese, mustard       1.000000   1.000  1.000  14
0901075000 9A   Cantaloupe                      1.000000   1.000  1.000  17
0402076000 4B   Cardoon                         1.000000   1.000  1.000  24
0101078000 1AB  Carrot                          1.000000   1.000  1.000  19
0101078001 1AB  Carrot-babyfood                 1.000000   1.000  1.000  19
0101079000 1AB  Carrot, juice                   1.000000   1.000  1.000  19
0103082000 1CD  Cassava                         0.005100   1.000  1.000
0103082001 1CD  Cassava-babyfood                0.005100   1.000  1.000
0501083000 5A   Cauliflower                     1.000000   1.000  1.000  22
0101084000 1AB  Celeriac                        1.000000   1.000  1.000  21
0402085000 4B   Celery                          1.000000   1.000  1.000  23
0402085001 4B   Celery-babyfood                 1.000000   1.000  1.000  23
0402086000 4B   Celery, juice                   1.000000   1.000  1.000  23
0402087000 4B   Celtuce                         1.000000   1.000  1.000  61
0902088000 9B   Chayote, fruit                  1.000000   1.000  1.000  71
0603098000 6C   Chickpea, seed                  0.005200   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603098001 6C   Chickpea, seed-babyfood         0.005200   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603099000 6C   Chickpea, flour                 0.005200   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0101100000 1AB  Chicory, roots                  1.000000   1.000  1.000  21
0902102000 9B   Chinese waxgourd                1.000000   1.000  1.000  30
0401104000 4A   Chrysanthemum, garland          1.000000   1.000  1.000  61
1001106000 10A  Citron                          0.006500   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for orange PDP
1001107000 10A  Citrus hybrids                  0.006500   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for orange PDP
1001108000 10A  Citrus, oil                     0.006500   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for orange PDP
0502117000 5B   Collards                        1.000000   1.000  1.000  25
1500127000 15   Corn, sweet
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  27
```

		140-Uncooked; Canned; Cook Meth N/S	0.000000	1.000	1.000		
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	27	
		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	27	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	27	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	27	
		220-Cooked; Frozen; Cook Meth N/S	0.000000	1.000	1.000		
		221-Cooked; Frozen; Baked	0.000000	1.000	1.000		
		222-Cooked; Frozen; Boiled	0.000000	1.000	1.000		
		232-Cooked; Dried; Boiled	0.000000	1.000	1.000		
		240-Cooked; Canned; Cook Meth N/S	0.000000	1.000	1.000		
		242-Cooked; Canned; Boiled	0.000000	1.000	1.000		
		243-Cooked; Canned; Fried	0.000000	1.000	1.000		
0401133000	4A	Cress, garden	1.000000	1.000	1.000	61	
0401134000	4A	Cress, upland	1.000000	1.000	1.000	61	
0902135000	9B	Cucumber	1.000000	1.000	1.000	29	
0401138000	4A	Dandelion, leaves	1.000000	1.000	1.000	61	
0103139000	1CD	Dasheen, corm	0.005100	1.000	1.000		
0802148000	8BC	Eggplant	1.000000	1.000	1.000	31	
0401150000	4A	Endive	1.000000	1.000	1.000	61	
0402152000	4B	Fennel, Florence	1.000000	1.000	1.000	24	
0103166000	1CD	Ginger	0.005100	1.000	1.000		
0103166001	1CD	Ginger-babyfood	0.005100	1.000	1.000		
0103167000	1CD	Ginger, dried	0.005100	1.000	1.000		
0101168000	1AB	Ginseng, dried	0.005100	1.000	1.000		
1304175000	13D	Grape	1.000000	1.000	1.000	34	
9500177000	O	Grape, leaves	1.000000	1.000	1.000	34	
1304179000	13D	Grape, wine and sherry	1.000000	1.000	1.000	33	
0603182000	6C	Guar, seed	0.005200	1.000	1.000		1/2LOD
Full comment: 1/2LOD for canned beans PDP							
0603182001	6C	Guar, seed-babyfood	0.005200	1.000	1.000		1/2LOD
Full comment: 1/2LOD for canned beans PDP							
0901187000	9A	Honeydew melon	1.000000	1.000	1.000	18	
9500188000	O	Hop	0.040000	1.000	1.000		LOD
0101190000	1AB	Horseradish	1.000000	1.000	1.000	21	
0502194000	5B	Kale	1.000000	1.000	1.000	39	
0501196000	5A	Kohlrabi	1.000000	1.000	1.000	14	
1002197000	10B	Kumquat	0.006500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for orange PDP							
0302198000	3B	Leek	1.000000	1.000	1.000	38	
0603203000	6C	Lentil, seed	0.005200	1.000	1.000		1/2LOD
Full comment: 1/2LOD for canned beans PDP							
0401204000	4A	Lettuce, head	1.000000	1.000	1.000	40	
0401205000	4A	Lettuce, leaf	1.000000	1.000	1.000	40	
1002206000	10B	Lime	0.006500	1.000	1.000		1/2LOD
Full comment: 1/2LOD for orange PDP							
1002207000	10B	Lime, juice	0.005000	1.000	1.000		1/2LOD
Full comment: 1/2LOD for oj PDP							
1002207001	10B	Lime, juice-babyfood	0.005000	1.000	1.000		1/2LOD
Full comment: 1/2LOD for oj PDP							
0502229000	5B	Mustard greens	1.000000	1.000	1.000	26	
1202230000	12B	Nectarine	1.000000	1.000	1.000	41	
0802234000	8BC	Okra	1.000000	1.000	1.000	32	
0301238000	3A	Onion, bulb, dried	0.006000	1.000	1.000		
0301238001	3A	Onion, bulb, dried-babyfood	0.006000	1.000	1.000		
0302239000	3B	Onion, green	1.000000	1.000	1.000	36	
1001240000	10A	Orange	1.000000	1.000	1.000	46	
1001241000	10A	Orange, juice	1.000000	1.000	1.000	45	
1001241001	10A	Orange, juice-babyfood	1.000000	1.000	1.000	45	
1001242000	10A	Orange, peel	1.000000	1.000	1.000	46	
0401248000	4A	Parsley, leaves					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	59	
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	59	
		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	59	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	59	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	59	
		215-Cooked; Fresh or N/S; Boiled/baked	1.000000	1.000	1.000	59	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	59	
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	59	

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                   240-Cooked; Canned; Cook Meth N/S
                                                1.000000   1.000  1.000  60
                   242-Cooked; Canned; Boiled   1.000000   1.000  1.000  60
1901249000 19A  Parsley, dried leaves           0.005700   1.000  1.000
1901249001 19A  Parsley, dried leaves-babyfood  0.005700   1.000  1.000
0101250000 1AB  Parsley, turnip rooted          1.000000   1.000  1.000  21
0101251000 1AB  Parsnip                         1.000000   1.000  1.000  21
0101251001 1AB  Parsnip-babyfood                1.000000   1.000  1.000  21
0602255000 6B   Pea, succulent
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  47
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  47
                   211-Cooked; Fresh or N/S; Baked
                                                1.000000   1.000  1.000  47
                   212-Cooked; Fresh or N/S; Boiled
                                                1.000000   1.000  1.000  47
                   213-Cooked; Fresh or N/S; Fried
                                                1.000000   1.000  1.000  47
                   221-Cooked; Frozen; Baked    1.000000   1.000  1.000  47
                   222-Cooked; Frozen; Boiled   1.000000   1.000  1.000  47
                   232-Cooked; Dried; Boiled    1.000000   1.000  1.000  47
                   240-Cooked; Canned; Cook Meth N/S
                                                0.000000   1.000  1.000
                   242-Cooked; Canned; Boiled   0.000000   1.000  1.000
0603256000 6C   Pea, dry                        0.005200   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0603256001 6C   Pea, dry-babyfood               0.005200   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0601257000 6A   Pea, edible podded, succulent   1.000000   1.000  1.000  47
0603258000 6C   Pea, pigeon, seed               0.005200   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for canned beans PDP
0602259000 6B   Pea, pigeon, succulent
                   212-Cooked; Fresh or N/S; Boiled
                                                1.000000   1.000  1.000  47
                   242-Cooked; Canned; Boiled   1.000000   1.000  1.000  50
1202260000 12B  Peach
                   110-Uncooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  49
                   120-Uncooked; Frozen; Cook Meth N/S
                                                1.000000   1.000  1.000  49
                   130-Uncooked; Dried; Cook Meth N/S
                                                1.000000   1.000  1.000  49
                   210-Cooked; Fresh or N/S; Cook Meth N/S
                                                1.000000   1.000  1.000  49
                   211-Cooked; Fresh or N/S; Baked
                                                1.000000   1.000  1.000  49
                   213-Cooked; Fresh or N/S; Fried
                                                1.000000   1.000  1.000  49
                   223-Cooked; Frozen; Fried    1.000000   1.000  1.000  49
                   230-Cooked; Dried; Cook Meth N/S
                                                1.000000   1.000  1.000  49
                   240-Cooked; Canned; Cook Meth N/S
                                                0.000000   1.000  1.000
1202261000 12B  Peach, dried                    0.005400   1.000  1.000      2007 U
    Full comment: 2007 USEPA DEA
1202261001 12B  Peach, dried-babyfood           0.005400   1.000  1.000      2007 U
    Full comment: 2007 USEPA DEA
1202262000 12B  Peach, juice                    1.000000   1.000  1.000  49
1202262001 12B  Peach, juice-babyfood           1.000000   1.000  1.000  49
9500263000 O    Peanut                          0.050000   1.000  1.000
9500264000 O    Peanut, butter                  0.005000   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for peanut butter PDP
9500265000 O    Peanut, oil                     0.005000   1.000  1.000      1/2LOD
    Full comment: 1/2LOD for peanut butter PDP
1400269000 14   Pecan                           1.000000   1.000  1.000  42
0802270000 8B   Pepper, bell                    1.000000   1.000  1.000  52
0802270001 8B   Pepper, bell-babyfood           1.000000   1.000  1.000  52
0802271000 8B   Pepper, bell, dried             1.000000   1.000  1.000  52
0802271001 8B   Pepper, bell, dried-babyfood    1.000000   1.000  1.000  52
0802272000 8BC  Pepper, nonbell                 1.000000   1.000  1.000  51
0802272001 8BC  Pepper, nonbell-babyfood        1.000000   1.000  1.000  51
0802273000 8BC  Pepper, nonbell, dried          1.000000   1.000  1.000  51
9500275000 O    Peppermint                      2.000000   1.000  1.000      tolera
    Full comment: tolerance
9500276000 O    Peppermint, oil                 2.000000   1.000  1.000      tolera
    Full comment: tolerance
9500289000 O    Pomegranate                     0.100000   1.000  1.000      2007 U
    Full comment: 2007 USEPA DEA
0103296000 1C   Potato, chips                   1.000000   1.000  1.000  72
0103297000 1C   Potato, dry (granules/ flakes)  0.005100   1.000  1.000
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0103297001	1C	Potato, dry (granules/ flakes)-b	0.005100	1.000	1.000		
0103298000	1C	Potato, flour	0.005100	1.000	1.000		
0103298001	1C	Potato, flour-babyfood	0.005100	1.000	1.000		
0103299000	1C	Potato, tuber, w/peel	1.000000	1.000	1.000	72	
0103299001	1C	Potato, tuber, w/peel-babyfood	1.000000	1.000	1.000	72	
0103300000	1C	Potato, tuber, w/o peel					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	72	
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	72	
		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	72	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	72	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	72	
		221-Cooked; Frozen; Baked	0.000000	1.000	1.000		
		223-Cooked; Frozen; Fried	0.000000	1.000	1.000		
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	72	
		233-Cooked; Dried; Fried	1.000000	1.000	1.000	72	
		240-Cooked; Canned; Cook Meth N/S	1.000000	1.000	1.000	72	
		242-Cooked; Canned; Boiled	1.000000	1.000	1.000	72	
		252-Cooked; Cured etc; Boiled	1.000000	1.000	1.000	72	
0103300001	1C	Potato, tuber, w/o peel-babyfood	1.000000	1.000	1.000	72	
1003307000	10C	Pummelo	0.006500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for orange PDP					
0902308000	9B	Pumpkin	1.000000	1.000	1.000	70	
0902309000	9B	Pumpkin, seed	1.000000	1.000	1.000	70	
0401313000	4A	Radicchio	1.000000	1.000	1.000	61	
0101314000	1AB	Radish, roots	1.000000	1.000	1.000	21	
0101316000	1AB	Radish, Oriental, roots	1.000000	1.000	1.000	21	
0502318000	5B	Rape greens	1.000000	1.000	1.000	26	
0402322000	4B	Rhubarb	1.000000	1.000	1.000	24	
0101327000	1AB	Rutabaga	1.000000	1.000	1.000	21	
0101331000	1AB	Salsify, roots	1.000000	1.000	1.000	21	
0302338500	3B	Shallot, fresh leaves	1.000000	1.000	1.000	38	
9500352000	O	Spearmint	2.000000	1.000	1.000		tolera
		Full comment: tolerance					
9500353000	O	Spearmint, oil	2.000000	1.000	1.000		tolera
		Full comment: tolerance					
0401355000	4A	Spinach					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	58	
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	58	
		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	58	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	58	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	58	
		215-Cooked; Fresh or N/S; Boiled/baked	1.000000	1.000	1.000	58	
		220-Cooked; Frozen; Cook Meth N/S	1.000000	1.000	1.000	57	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	57	
		222-Cooked; Frozen; Boiled	1.000000	1.000	1.000	57	
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	58	
		240-Cooked; Canned; Cook Meth N/S	0.000000	1.000	1.000		
		242-Cooked; Canned; Boiled	0.000000	1.000	1.000		
0902356000	9B	Squash, summer	1.000000	1.000	1.000	62	
0902356001	9B	Squash, summer-babyfood	1.000000	1.000	1.000	62	
0902357000	9B	Squash, winter	1.000000	1.000	1.000	63	
0902357001	9B	Squash, winter-babyfood	1.000000	1.000	1.000	63	
0402367000	4B	Swiss chard	1.000000	1.000	1.000	24	
1001369000	10A	Tangerine	0.005000	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for tangerine PDP					
1001370000	10A	Tangerine, juice	0.005000	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for tangerine PDP					
0103371000	1CD	Tanier, corm	0.005100	1.000	1.000		
0801374000	8A	Tomatillo	0.002500	1.000	1.000		1/2LOD
		Full comment: 1/2LOD for tomato PDP					
0801375000	8A	Tomato					
		110-Uncooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	68	
		150-Uncooked; Cured etc; Cook Meth N/S	1.000000	1.000	1.000	68	
		210-Cooked; Fresh or N/S; Cook Meth N/S	1.000000	1.000	1.000	68	

		211-Cooked; Fresh or N/S; Baked	1.000000	1.000	1.000	68	
		212-Cooked; Fresh or N/S; Boiled	1.000000	1.000	1.000	68	
		213-Cooked; Fresh or N/S; Fried	1.000000	1.000	1.000	68	
		214-Cooked; Fresh or N/S; Fried/baked	1.000000	1.000	1.000	68	
		215-Cooked; Fresh or N/S; Boiled/baked	1.000000	1.000	1.000	68	
		221-Cooked; Frozen; Baked	1.000000	1.000	1.000	68	
		222-Cooked; Frozen; Boiled	1.000000	1.000	1.000	68	
		232-Cooked; Dried; Boiled	1.000000	1.000	1.000	68	
		240-Cooked; Canned; Cook Meth N/S	0.000000	1.000	1.000		
		242-Cooked; Canned; Boiled	0.000000	1.000	1.000		
		252-Cooked; Cured etc; Boiled	1.000000	1.000	1.000	68	
0801375001	8A	Tomato-babyfood	1.000000	1.000	1.000	66	
0801378000	8A	Tomato, dried	0.000004	1.000	1.000		2007 U
Full comment: 2007 USEPA DEA							
0801378001	8A	Tomato, dried-babyfood	0.000004	1.000	1.000		2007 U
Full comment: 2007 USEPA DEA							
0801379000	8A	Tomato, juice	1.000000	1.000	1.000	68	
0103387000	1CD	Turmeric	0.005100	1.000	1.000		
0101388000	1AB	Turnip, roots	1.000000	1.000	1.000	21	
0502389000	5B	Turnip, greens	1.000000	1.000	1.000	26	
1400391000	14	Walnut	1.000000	1.000	1.000	42	
0901399000	9A	Watermelon	1.000000	1.000	1.000	69	
0901400000	9A	Watermelon, juice	1.000000	1.000	1.000	69	
0103406000	1CD	Yam, true	0.005100	1.000	1.000		
0103407000	1CD	Yam bean	0.005100	1.000	1.000		
0301338000	3A	Shallot, bulb	0.006000	1.000	1.000		
0601349500	6AB	Soybean, vegetable	0.200000	1.000	1.000		

ACUTE SENSITIVITY ANALYSIS

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California Dept of Pesticide Regulation                    Ver. 3.18, 03-08-d
DEEM-FCID ACUTE Analysis for METHOMYL                    NHANES 2003-2008 2-Day
Residue file: methomylacutefoodonlyxnondetects.r08
Adjustment factor #2 NOT used.
Analysis Date: 09-05-2013/09:40:03    Residue file dated: 09-05-2013/09:35:35
Acute Pop Adjusted Dose (aPAD) varies with population; see individual reports
RAC/FF intake reported by eating occasion
MC iterations = 10; MC list in residue file; MC seed = 1000; RNG = MS VB
Run Comment: ""
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Summary calculations--users:

	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	% aPAD	Exposure	% aPAD	Exposure	% aPAD
Total US Population:	0.000039	1.29	0.000149	4.97	0.001493	49.78
All Infants:	0.000068	4.50	0.000172	11.47	0.000656	43.76
Children 1-2:	0.000107	7.15	0.000337	22.43	0.001876	125.08
Children 3-5:	0.000087	5.79	0.000302	20.13	0.002650	176.70
Children 6-12:	0.000045	3.02	0.000155	10.36	0.001478	98.55
Youth 13-19:	0.000026	0.86	0.000109	3.63	0.000995	33.16
Adults 20-49:	0.000033	1.09	0.000121	4.05	0.001448	48.25
Adults 50-99:	0.000036	1.20	0.000130	4.33	0.001649	54.96
Female 13-49:	0.000031	1.04	0.000120	3.99	0.001452	48.38