METHYL BROMIDE

RISK CHARACTERIZATION DOCUMENT

Volume II

DIETARY EXPOSURE

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I.A. TOXICOLOGY PROFILE

The acute oral toxicity of methyl bromide in experimental animals included hypoactivity, ataxia, prostration, labored respiration, hypothermia, and mortality. Squamous cell hyperplasia in the stomach was reported in both acute and subchronic exposure studies with rats. This toxicity endpoint may be due to a direct irritation effect of methyl bromide on the stomach lining. Decreased food consumption and body weight gain were observed in the subchronic and chronic studies. Additional effects from chronic exposure were enlarged spleen in the rat and decreased hemoglobin and hematocrit levels in the dog. Methyl bromide has not been shown to be oncogenic in experimental animals.

I.B. RISK CHARACTERIZATION FOR DIETARY EXPOSURE

I.B.1. Hazard Identification for Dietary Exposure

For acute oral exposure, the critical NOEL was an estimated NOEL of 8 mg/kg for clinical signs after a single gavage dose of 80 mg/kg in rats. For chronic oral exposure, two endpoints were considered. The first endpoint was enlarged spleens with a NOEL of 0.02 mg/kg/day in rats. The other endpoint was decreased body weight with a NOEL of 2.2 mg/kg/day from the same study. This latter endpoint and NOEL were selected for chronic exposure risk characterization, as recommended by the National Research Council scientists.

The oncogenicity of methyl bromide by the oral route was not evaluated at this time because experimental studies did not provide sufficient evidence for oncogenic potential. There is evidence that methyl bromide causes damage to the genetic material in experimental animals and humans, which is generally considered to play a significant role in the process of tumor formation.

I.B.2. Dietary Exposure Assessment

The dietary exposure was estimated based on residue data for post-harvest fumigation and the consumption data from the 1989-1992 Continuing Survey of Food Intakes by Individuals. The potential acute dietary exposure of methyl bromide from all labeled uses ranged from 3.387 *u*g/kg/day to 8.195 *u*g/kg/day for the 95th percentile of user-days exposures for all population subgroups. Children (1-6 years) had the highest potential acute dietary exposure (8.195 *u*g/kg/day) to methyl bromide residues in the diet. The mean potential chronic dietary exposure for all population subgroups ranged from 0.014 *u*g/kg/day to 0.201 *u*g/kg/day. The population subgroup of children (1-6 years) also had the highest potential chronic exposure (0.201 *u*g/kg/day).

I.B.3. Risk Characterization for Dietary Exposure

For acute exposure, the lowest MOE was 980 for children 1-6 years old. Other children, infants, and adult groups had MOEs greater than 1500. For chronic exposure, the MOE was 11,000 for both children 1-6 years and 7-12 years old. The MOEs for infants were greater than

120,000. The MOEs for the adult subgroups were greater than 14,000.

I.C. RISK APPRAISAL FOR DIETARY EXPOSURE

The uncertainties associated with the hazard identification included the use of results from bolus dosing in the acute toxicity study, the estimation of the NOEL from the LOEL in the acute study, and the selection of the critical endpoints. Overall, these resulted in health protective NOELs for both acute and chronic toxicity assessments.

The dietary exposure estimate was based on fumigation chamber studies with residue levels reduced by processing factors and percent of crop treatment when data were available. The potential sources of overestimation included use of maximum label rate in the studies, 100% crop treatment, and no loss due to processing for some commodities. The use of the detection limit to assign residue levels for samples with residue levels at or below the detection limit or the use of surrogate data could either over- or under-estimate the exposure. The exposure might be underestimated because the samples were composites which could mask higher residue levels in individual units. There was no residue information for potential metabolites in the treated commodities.

For the risk characterization, two 10-fold default uncertainty factors were used to address the uncertainties associated with the extrapolation of data from experimental animals to humans and the variations in response to methyl bromide between individuals. Since there were no data to determine the magnitude of the factors, these factors could overestimate or underestimate the risks for human exposure to methyl bromide.

I.D. CONCLUSIONS FOR DIETARY EXPOSURE

The human health risk from potential dietary exposure to methyl bromide was evaluated in this Volume II of the Risk Characterization Document. The potential risks were evaluated based on clinical signs and decreased body weights observed in experimental animals given methyl bromide orally for acute and chronic exposures, respectively. The risks, expressed as margins of exposure, were calculated for human population subgroups based on region, age, and gender. For non-oncogenic effects based on animal data, the MOEs were compared with a benchmark of 100 to determine whether the exposure would be of a potential health concern.

The dietary exposures were considered reasonable estimates of actual exposures. The ranges of MOEs were 980 to 2360 and 10,930 to 162,600 for acute and chronic exposures, respectively. Other variables discussed in this document which potentially underestimate or overestimate actual dietary exposures should also be considered in the evaluation of these MOEs.

Since methyl bromide residues are found in treated commodities, there is a need for tolerances to be established for methyl bromide *per se* for food uses.

II. INTRODUCTION

This Volume II of the methyl bromide risk characterization document focuses on the potential risk of human exposure to methyl bromide residues in the diet. For general information such as the usage and regulatory history, the reader is referred to Section **II. INTRODUCTION** of the Risk Characterization Document (RCD) for inhalation exposure (DPR, 2001). A draft of the inhalation RCD (DPR, 1999) was reviewed by the National Research Council panel of scientists (NRC, 2000).

Methyl bromide residues are found primarily due to post-harvest fumigation of food commodities. Environmental fate studies showed crop residues were unlikely from methyl bromide preplant soil treatment use (Bolsa Research, 1988). The use of methyl bromide on food is currently regulated by the U.S. EPA based on inorganic bromide level because of the assumption that methyl bromide is degraded completely to bromide (Federal Register, 1991). However, residue studies have shown that fumigated commodities contain detectable levels (in ppm range) of methyl bromide *per se* especially immediately after fumigation. In 1986, the Methyl Bromide Industry Panel (MBIP) petitioned the U.S. EPA for tolerances for methyl bromide *per se* (U.S. EPA, 1986a). The proposed levels ranged from 0.1 ppm for certain vegetables to 5.0 ppm for green cocoa beans. To date, no tolerances have been established.

While the primary effect of methyl bromide after inhalation exposure is neurotoxicity, there is no information on the effects of acute and chronic oral exposures to low concentrations of methyl bromide in humans. The U.S. EPA has established an oral chronic reference dose (RfD) of 0.0014 mg/kg/day based on the no-observed-effect level (NOEL) of 1.4 mg/kg/day for forestomach epithelial hyperplasia in a rat oral subchronic study (Danse *et al.,* 1984) and an uncertainty factor of 1000 (IRIS, 2000). For methyl bromide in the drinking water, the one-day, ten-day, and longer-term health advisory for a child is 0.1 mg/L assuming 1 L/day water consumption for a 10-kg child (U.S. EPA, 1992). The longer-term health advisory for an adult is 0.5 mg/L assuming 2 L/day water consumption for a 70-kg adult. The lifetime health advisory is 0.01 mg/L assuming 20% of exposure by drinking water. Methyl bromide is classified as a "Group D" carcinogen (not classifiable as to human carcinogenicity) by U.S. EPA due to inadequate human and animal data (U.S. EPA, 1992).

III. TOXICOLOGY PROFILE

The complete pharmacokinetic and toxicology database for methyl bromide for all routes of exposure was presented in **Volume I** (**III. TOXICOLOGY PROFILE**) (DPR, 2001) and they are not repeated in this Volume. All the studies were included in the draft inhalation RCD (DPR, 1999) for the NRC to review. In this Volume, only those oral toxicity studies considered for critical endpoints in risk characterization are discussed in detail. NRC comments on specific studies are noted. A study is noted as supplemental information if the SB 950 data requirements are fulfilled by other toxicity studies, in particular, those conducted via the inhalation route. Available oral toxicity studies for the comparison of NOELs and endpoints are presented in Table 1.

III.A. ACUTE TOXICITY

There were two toxicity studies in the database to evaluate acute oral toxicity. The first

study was conducted in dogs (1/sex/group) given methyl bromide (1, 3, 5, 50, or 500 mg/kg) in capsules (Naas, 1990). There was no control group. Emesis was reported for 3 mg/kg and higher doses and described as white foamy, containing food, with partially dissolved capsules, and/or red material. No vomiting was observed during one week post-dosing observation period. Clinical signs were observed in the 50 and 500 mg/kg groups. At 50 mg/kg, both dogs showed hypoactivity, hypothermia (body cool to touch), no pain reflexes, and soft stools. Animals treated at 500 mg/kg showed prostration, rapid heart rates, hypothermia, and were dead within one day. Gross examination of the organs of these two dogs showed dark red adrenal glands (male only), dark red kidneys (both), slight hydrocephaly (female only), and marked reddened stomach mucosa (both). Necropsy was not performed on other dogs. Because of the few number of animals involved and that the effects may be due to dosing method, a NOEL was not determined. This study was considered supplemental information by DPR.

Albino rats (5/sex/group) were given methyl bromide (99.5% pure) either as a liquid in corn oil or microencapsulated mixed with corn oil (Kiplinger, 1994). In the liquid methyl bromide testing, methyl bromide was given once by gavage at 50, 100, or 150 mg/kg in initial testing and at 0, 80, 120 or 160 mg/kg in retesting. Only results from the retesting are presented in this Document. For the microencapsulated groups, the reported doses were 98, 146, or 195 mg/kg. Rats were fasted for 18-20 hours prior to dosing and feed was made available 3-4 hours after dosing. Rats were observed at approximately 1, 3, and 4 hours after dosing (post-dosing day 0) and once in the morning and once in the afternoon on post-dosing days 1 through 14 (day of scheduled sacrifice). As shown in Table 2, clinical signs and death were reported for all treated groups. The mortality incidences were 0 for control groups, 2/10 (corn oil) and 1/10 (microcapsules) for low dose, 6/10 (corn oil) and 7/10 (microcapsules) for the mid-dose, and 10/10 (corn oil) and 9/10 (microcapsules) for the high dose groups. The clinical signs observed before death included: hypoactivity, ataxia, prostration, labored respiration, hypothermia, and tremors. Other findings with increased incidences included wet yellow urogenital staining and mucoid feces in the treated animals. Rats died on or before post-dosing day 2 with one death on post-dosing day 4. The LD50s for the liquid methyl bromide group were 86 mg/kg and between 120 and 160 mg/kg for females and males, respectively (combined LD50 of 104 mg/kg). The LD50s for the microencapsulated group were 105 mg/kg and 159 mg/kg for females and males, respectively (combined LD50 was 133 mg/kg).

For both the liquid and microencapsulated methyl bromide groups, decreased food consumption and body weight gain were reported (Table 2). These effects were related to the dose in most cases. However, the food consumption reduction was greater for the first week than the second week. The stomach was the main organ affected regardless of how methyl bromide was mixed in corn oil. Hemorrhage, edema, and squamous cell hyperplasia were due to severe irritation of the stomach lining. To determine the relative toxicity between liquid and microencapsulated methyl bromide, DPR needs clarification on the following concerns: (1) whether the microcapsules dissolved before dosing and (2) whether the procedure for the methyl bromide content analyses was appropriate. The acute LOAELs were 80 mg/kg for liquid, and 98 mg/kg for microencapsulated methyl bromide for reduced food consumption, clinical signs, stomach lesions, and mortality in treated rats. This study was considered supplemental information by DPR.

Table 1. The No-Observed-Effect Levels (NOELs) and the Lowest-Observed-Effect Levels (LOELs) of methyl bromide from oral toxicity studies.

Species/route duration	NOEL/LOEL (ppm)	NOEL/LOEL (mg/kg/day)	Effects	Ref[a]
Acute Exposure				
Rat/gavage (liquid in corn oil in one dose)	-	(8.0)[b] / 80	Death, hypoactivity, ataxia, prostration, labored respiration, hypothermia, squamous cell hyperplasia in the stomach	1
Rat/gavage (microcapsules, one dose)	-	(9.8)[b] / 98	Death, squamous cell hyperplasia in the stomach	1
Subchronic Exposure				
Rat/gavage (5 d/w x 13 w)	-	2.0 / 10.0	Forestomach epithelial hyperplasia	2
Rat/gavage (5 d/w x 13, 17, 21 or 25w)	-	(5)[b] / 50	Forestomach epithelial hyperplasia for all duration	3
Rat/gavage (5d/w x 4 to 17 w)	-	(2.5)[b] / 25	Forestomach epithelial hyperplasia, cellular infiltration in glandular stomach	4
Chronic Exposure				
Rat/oral (microcapsules in feed, daily x 2 y)	0.5 / 2.5	0.02 / 0.11	Enlarged spleens (males only)	5*
Rat/diet (microcapsules in feed, daily x 2 y)	50 / 250	2.2 / 11.1	Decreased food consumption and body weight gain	5*
Dog/oral (fumigated feed,5 d/w x 1 y)	1.5 / 5.0	0.13 / 0.27	Decreased hemoglobin and/or hematocrit (males only)	6

a/ * = marginally acceptable to DPR. References: 1. Kiplinger, 1994; 2. Danse *et al.*, 1984; 3. Boorman *et al.*, 1986; 4. Hubbs, 1986; 5. Mertens, 1997; 6. Newton, 1996.

b/ Values in parenthesis are estimated NOELs based on the LOELs and a default uncertainty factor of 10-fold for the extrapolation.

Table 2. Clinical findings in rats after acute oral exposure.[a]

Clinical Findings	Control	80	120	160	98	146	195
	(---------- Corn oil----------)				(----- Microcapsules---)		
MALES							
Food Consumption	**Average (grams of feed /animal/day)**						
Week 0-1	22	2	2	1	4	2	6
Week 1-2	33	15	9	1	21	11	15
Body Weight Gain	**Average (grams/animal)**						
Week 0-2	+32	-6	-6	NA	-7	-6	+1
Clinical Signs	**Incidences[b]**						
Hypoactivity	0/5	4/5	4/5	5/5	0/5	4/5	5/5
Ataxia	0/5	1/5	2/5	3/5	0/5	1/5	2/5
Prostration	0/5	1/5	0/5	0/5	0/5	0/5	0/5
Labored respiration	0/5	1/5	1/5	1/5	0/5	1/5	0/5
Hypothermia	0/5	1/5	1/5	1/5	0/5	1/5	0/5
Tremors	0/5	0/5	0/5	1/5	0/5	1/5	0/5
Death	0/5	1/5	1/5	5/5	0/5	2/5	4/5
Histology- Stomach							
Squamous cell hyperplasia	0/5	3/5	4/5	0/5	4/5	3/5	1/5
Autolysis, hemorrhage, edema[c]	0/5	1/5	1/5	5/5	0/5	2/5	4/5
FEMALES							
Food Consumption	**Average (grams of feed /animal/day)**						
Week 0-1	15	2	1	NA	3	1	NA
Week 1-2	24	7	1	NA	9	NA	NA
Body Weight Gain	**Average (grams/animal)**						
Week 0-7	+6	-13	NA	NA	-7	NA	NA
Clinical Signs	**Incidences[b]**						
Hypoactivity	0/5	2/5	5/5	5/5	0/5	5/5	4/5
Ataxia	0/5	1/5	2/5	4/5	0/5	3/5	4/5
Prostration	0/5	0/5	2/5	1/5	0/5	1/5	2/5
Labored respiration	0/5	1/5	2/5	2/5	0/5	1/5	3/5
Hypothermia	0/5	1/5	2/5	2/5	0/5	1/5	2/5
Death	0/5	1/5	5/5	5/5	1/5	5/5	5/5
Histology- Stomach							
Squamous cell hyperplasia	0/5	4/5	0/5	0/5	3/5	0/5	0/5
Autolysis, hemorrhage, edema[c]	0/5	1/5	5/5	5/5	1/5	5/5	5/5

a/ Data from Kiplinger, 1994. NA=not available, the animals died.

b/ Incidences were expressed as number of animals affected/ total animals in the group. Death was observed on day 0 (day of dosing) to post-dose day 2 (2 days after dosing) except for one death noted on post-dose day 4. Effects were those observed during the day of dosing to post-dose day 4.

c/ These animals were found dead before scheduled sacrifice.

III.B. SUBCHRONIC TOXICITY

Subchronic toxicity studies are summarized since there is no distinct seasonal exposure to methyl bromide residues in the diet. Subchronic exposure of laboratory animals to methyl bromide via the oral route resulted in hyperplasia of the forestomach (Danse *et al.*, 1984; Boorman *et al.*, 1986; Hubbs, 1986). The NOELs ranged from 2.0 mg/kg/day to an estimated NOEL of 5 mg/kg/day from the three studies.

III.C. CHRONIC TOXICITY

Two studies were available to determine the chronic toxicity of methyl bromide (Newton, 1996; Mertens, 1997). In the Newton study (1996), beagle dogs (4/sex/dose except 8 dogs/sex at high dose) were given feed fumigated with methyl bromide 5 days per week for one year (Newton, 1996). Time-weighted average dosages (male/female) were: 0, 0.06/0.07, 0.13/0.12, and 0.27/0.27 mg/kg/day for target concentrations of 0, 0.5, 1.5 or 5.0 ppm. There were no clear effects on survival, cage side observations, body weight or food consumption. A possible treatment-related effect was decreased ($p<0.05$) hemoglobin and (or) hematocrit at 3, 6 and (or) 12 months only in the high-dose male group (Table 3). The average hemoglobin and hematocrit values in this group were about 90% of control values for all 3 time periods. The NOEL was 1.5 ppm (0.13 mg/kg/day for males) based on decreased hemoglobin and/or hematocrit at 5 ppm (0.27 mg/kg/day). This study was considered supplemental information by DPR. The U.S. EPA did not consider the reduction in hemoglobin and hematocrit to be biologically significant since the mean values were within 10% of control values and within the normal range (Hansen, 1998). U.S. EPA established a NOEL of $\geq$ 5 ppm for no effects in this study.

Table 3. Hematology effects in male dogs fed methyl bromide fumigated feed.[a]

Parameters	Months	Nominal concentration in the diet (ppm)			
		0	0.5	1.5	5.0
Males					
Hematocrit %	pretest[b]	(43.8-60.7)	(43.7-49.4)	(46.1-52.3)	(43.7-52.5)
	3	51.7 (50.3-54.3)	50.7 (49.7-51.1)	50.5 (46.4-55.3)	47.7* (44.6-49.5)
	6	50.8 (49.0-52.8)	51.0 (49.2-52.4)	49.1 (47.2-50.1)	46.8* (44.0-50.8)
	12	57.2 (54.5-60.0)	54.9 (54.4-55.4)	51.7 (42.7-58.6)	51.5* (45.9-55.7)
Hemoglobin g/dL	pretest	(14.5-19.5)	(14.7-16.3)	(15.0-16.8)	(14.4-17.0)
	3	17.4 (17.0-18.2)	17.1 (16.4-17.3)	17.0 (15.7-18.6)	16.2* (15.0-17.0)
	6	17.7 (17.1-18.4)	18.0 (17.0-18.5)	17.3 (16.6-17.5)	16.6* (15.5-18.0)
	12	19.1 (18.3-20.1)	18.3 (18.2-18.5)	17.5 (14.4-19.7)	17.3* (15.6-18.2)
RBC $10^6/u$L	pretest	(6.40-8.49)	(6.45-7.16)	(6.74-7.26)	(6.47-7.66)
	3	7.69 (7.48-8.13)	7.41 (7.07-7.70)	7.41 (7.23-7.74)	7.24 (6.54-7.78)
	6	7.64 (7.35-7.99)	7.62 (7.16-7.95)	7.40 (7.15-7.64)	7.23 (6.73-8.07)
	12	8.22 (7.93-8.68)	7.81 (7.65-8.00)	7.45 (6.44-8.04)	7.59 (6.74-8.33)
Females					
Hematocrit %	3	45.9	48.4	47.9	49.6
	6	45.4	45.3	49.5	48.9
	12	48.0	49.2	53.7*	48.3
Hemoglobin g/dL	3	15.6	16.4	16.3	16.8
	6	15.9	16.0	17.4	16.9
	12	15.8	16.3	18.0*	16.2
RBC $10^6/u$L	3	6.76	7.21	7.26	7.46
	6	6.80	6.82	7.53	7.33
	12	6.79	7.04	7.85*	7.03

a/ Data from Newton, 1996. *, ** Statistically different from control value at $p<0.05$ and $p<0.01$, respectively. There were 4 dogs/sex at all dose levels except 8 dogs/sex at the high dose.

b/ Values in parenthesis are range for all animals. Pre-test values for weeks -3, -2 and -1 before the start of the experiment were combined.

Another chronic toxicity study was conducted in Sprague-Dawley rats (70/sex/group, except for 0.5 and 2.5 ppm with 50/sex/group) given feed mixed with microencapsulated methyl bromide for two years (Mertens, 1997). Corn oil containing methyl bromide was micro-encapsulated using starch and sucrose. Two types of microcapsules were produced. One was a blend of 7 production runs; it had a methyl bromide content of 0.48% w/w. The second type was a blend of five production runs; its methyl bromide content was 3.44% w/w. The two types of microcapsules differed also in terms of corn oil, starch, and sucrose content and age of the material at start of testing. Nominal methyl bromide concentrations in the diet were as follows: 0 (basal diet), 0 (diet containing placebo microcapsules), 0.5 , 2.5, 50 or 250 ppm. The blend containing 0.48% methyl bromide was used to prepare the two low doses while the blend containing 3.44% was used to prepare the two high doses. The highest dose tested was selected on the basis of a two-week range-finding study. The daily ration of feed varied as follows: for test weeks 0-65, males and females each received 30 and 23 g, respectively; for test weeks 66 -104, males and females received 35 and 30 g, respectively. One outcome of this feeding strategy appeared to have been that a fraction of the animals in the control and 0.5 to 50 ppm groups had their feed consumption restricted during the first 65 weeks of the study. In test week 53, interim sacrifices were performed on 18-20 rats/sex for the following dose levels: 0 (basal diet), 0 (placebo microcapsules), 50 and 250 ppm. The reported dosages (male/female) were 0, 0.02/0.03, 0.11/0.15, 2.20/2.92, or 11.10/15.12 mg/kg/day for 0, 0.5, 2.5, 50, or 250 ppm, respectively.

Survival was statistically increased in the 250 ppm male group and in the 50 and 250 ppm female groups when compared to the placebo-microcapsule groups. Body weight was reduced in the 250 ppm groups; the reduction reached a maximum (about 90% of control) in the early weeks of testing in both sexes (Table 4). A further reduction in body weight relative to the controls (placebo-microcapsule groups) did not occur despite continued exposure and reduced food consumption throughout the study (Table 4). Since a reduction in feed consumption occurred in the 250 ppm groups (both sexes) starting with the first exposure week, the body weight reduction would appear to be due mainly to the reduced feed consumption.

No treatment-related effects were reported in the following areas: clinical observations, ophthalmology, hematology, serum chemistry or urinalysis. Effects on absolute organ weights (only brain, kidneys, liver, testes/ovaries were measured) and organ weights relative to body weight appeared to be due to the body weight reduction in the 250 ppm groups; this was true for animals sacrificed at test week 52 as well as for the survivors at the end of the study. An increased incidence of dark red areas was observed on the livers of the 50 ppm females surviving to test week 104 (0 ppm, basal: 5/20; 0 ppm, placebo: 3/19; 0.5 ppm: 8/22; 2.5 ppm: 4/24; 50 ppm: 14/27; and 250 ppm, 8/29). No statistical analyses were supplied for the histology data. Also, the lesion-incidence summary table did not present autolysis and lesion-grade data and may not have been corrected for tissues lost to autolysis. Possible treatment-related effects include: increased incidence of pancreatic acinar atrophy at 250 ppm (both sexes), increased incidence of adrenal cortical hypertrophy at 250 ppm (females), and increased incidence of pulmonary arterial mineralization at 50 ppm (females). Two rare tumor types, adenocarcinoma of the prostate and endometrial stromal sarcoma of the cervix, were seen at 4% incidence only at 250 ppm. By experimental design, the histological examinations of the pancreas, prostate, spleen, adrenal glands, cervix, and uterus at the 0.5 to 50 ppm dose levels were limited to those rats that did not survive to terminal sacrifice. Autolysis was a

frequent observation in the gastrointestinal organs in rats that did not survive to the end of the study (all groups, both sexes). While an increased incidence of spongiosis hepatis was seen in the 50 ppm females, the relationship of this lesion to angiectasis and the necropsy finding of dark red liver spots that also occurred at the 50 ppm dose level needs clarification.

A possible, treatment-related finding at necropsy was statistically increased incidences of enlarged spleens in the 2.5 ppm and 50 ppm groups, but not the 250 ppm group (Table 5). While the physical dimensions (length, width, and height) of the enlarged spleens were given, neither the criteria for enlargement nor the dimensions for non-enlarged spleens were stated in the report. Histological findings of the spleens included extramedullary hematopoiesis and congestion. One incident of lymphoma was found in the 2.5 ppm and 50 ppm groups; however, not all spleens were sectioned. The NOEL was 0.5 ppm (0.02 mg/kg/day for males) for increased incidences of enlarged spleens at 2.5 and 50 ppm. When first reviewed, the study was considered unacceptable pending the submission of the supplemental information regarding: range-finding study; analytical methods; cause and extent of autolysis; histological examinations for the lower dose groups; and clarification of liver gross and histological findings. Additional information was submitted and this study is considered marginally acceptable to DPR. The NRC in the review of the draft inhalation RCD (DPR, 1999) considered a NOAEL of 50 ppm for this study based on decreased body weight (NRC, 2000). The enlarged spleen was not considered to be treatment-related since there was no clear dose-response relationship, histological correlates in the spleen, and effects on hematology and clinical chemistry parameters. The U.S. EPA also established a NOEL of 50 ppm for this study based on reduced body weights, body weight gain, and food consumption in both genders during the first 18 months of the study (Gross, 1999).

Table 4. Food consumption and body weight gain in rats during chronic exposure to methyl bromide.[a]

Duration	Microcap	Methyl Bromide concentration (ppm)				
(weeks)	0 ppm	0.5	2.5	50	250 ppm	
Male	**0**	**0.02**	**0.11**	**2.20**	**11.10 mg/kg/day**	
Food Consumption (mean, g/animal/day)						% Control
0 to 1	26	26	26	25	23**	88
26 to 27	27	27	27	26	24**	89
52 to 53	27	27	28	27	25**	93
78 to 79	28	27	27	27	26	93
103 to104	25	25	19	23	23	92
Body Weight (mean, g)						
1	252	256	252	250	242**	96
26	589	600	589	575	521**	88
52	683	697	684	661	595**	87
78	760	773	762	737	691*	91
104	685	725	673	667	700	102
Female	**0**	**0.03**	**0.15**	**2.92**	**15.12 mg/kg/day**	
Food Consumption (mean, g/animal/day)						
0 to 1	18	18	18	19	17**	94
26 to 27	20	20	20	19	18**	90
52 to 53	21	21	21	21	20*	95
78 to 79	24	23	23	23	21	87
103 to104	20	20	19	19	19	95
Body Weight (mean, g)						
1	171	169	170	173	166	97
26	305	303	300	305	281**	92
52	360	359	353	359	330**	92
78	462	449	443	465	418	90
104	488	455	445	489	454	93

a/ Only selected values are presented in this Table (Mertens, 1997). There were 60 to 70 animals (Microcap, 50 ppm, and 250 ppm) or 48 to 50 animals (0.5 ppm and 2.5 ppm) per group for the first 53 weeks. From week 53 to week 104, the number of male rats per group decreased from 57 to 17 (Microcap), 49 to 16 (0.5 ppm), 50 to 16 (2.5 ppm), 59 to 22 (50 ppm), and 60 to 30 (250 ppm) for the groups. For week 53 to week 104, the number of female rats decreased from 59 to 19 (Microcap), 50 to 22 (0.5 ppm), 48 to 22 (2.5 ppm), 48 to 24 (50 ppm), and 59 to 30 ppm (250 ppm) for the groups. Statistical significance was based on the Dunnett's test with *, ** for $p < 0.05$ and $p < 0.01$, respectively. % Control was based on values for Microcapsules only as the control.

Table 5. Effects of methyl bromide in the spleens of rats fed microcapsules containing methyl bromide in the feed for two years.[a]

	Micro-capsules 0 ppm	Methyl Bromide Concentrations			
		0.5 ppm	2.5 ppm	50 ppm	250 ppm
		0.02	0.11	2.2	11.0 mg/kg/day
ALL EXAMINED SPLEENS					
Enlarged[b]					
Male	2/50 (4%) (p<0.05)+	7/50 (14%) (p=0.08)	10/50 (20%) (p=0.014)**	11/50 (22%) (p=0.007)**	3/50 (6%)
Female	6/50 (12%)	4/50 (8%)	4/50 (8%)	2/52 (4%)	5/50 (10%)
Congestion					
Male	1/47 (2%)	0/34 (0%)	2/35 (6%)	2/28 (7%)	1/50 (2%)
Female	2/50 (4%)	0/28 (0%)	0/24 (0%)	0/21 (0%)	0/49 (0%)
Extramedullary hematopoiesis					
Male	8/47(17%)	9/34(27%)	10/35(29%)	7/28(25%)	12/50(24%)
Female	14/50(28%)	11/28(39%)	6/24(25%)	3/21(14%)	12/49(25%)
Lymphoma/ Leukemia					
Male	0/47 (0%)	1/34 (3%)	1/35 (3%)	1/28 (4%)	0/50 (0%)
Female	0/50 (0%)	0/28 (0%)	0/24 (0%)	0/21 (0%)	0/49 (0%)
ENLARGED SPLEENS - Histological findings in male rats					
Extramedullary hematopoiesis	2/2	4/7	3/10	4/11	3/3
Congestion	0/2	0/7	0/10	2/11	0/3
Lymphoma/ Leukemia	0/2	1/7	1/10	1/11	0/3
Not Sectioned	0/2	2/7	6/10	4/11	0/3

a/ Data from Mertens, 1997.

b/ Incidence= number of animals affected/total animals examined. With the 250 ppm dose excluded, statistical significance was determined by the Fisher Exact Test with ** for p:< 0.01, and the Cochran-Armitage Trend test with * for p≤0.05. Histological examination of the spleens in the 0.5, 2.5, and 50 ppm groups was limited to those rats which did not survive to terminal sacrifice. The first male rat with enlarged spleen was in the 2.5 ppm group and was found dead on day 394 of the study. Spleen enlargement was determined by dimensions. Neither the criteria for enlargement nor dimensions for normal spleens were provided.

IV. RISK ASSESSMENT FOR DIETARY EXPOSURE

IV.A. HAZARD IDENTIFICATION FOR DIETARY EXPOSURE

There were no human data on the effects of oral exposure to methyl bromide. Results from animal studies were extrapolated to humans assuming that the effects observed in laboratory animals would also be observed in humans. There was a limited number of oral studies, compared to inhalation studies in experimental animals, since inhalation is the primary route of human exposure.

IV.A.1. Acute Toxicity

Oral studies with acute and 1-week observations were considered in the determination of the critical acute NOEL and endpoints for hazard identification. One possible acute endpoint was the decreased food consumption observed within the first week of exposure in the subchronic toxicity study (Tompkins, 1995) and chronic toxicity study (Mertens, 1997) with methyl bromide in microcapsules mixed in the feed. The reduction in food consumption, however, was similar (about 90%) regardless of exposure duration. This lack of duration-response relationship suggested that the food consumption decrease may be an acute effect. Methyl bromide at high concentration has been described to have a chloroform-like odor and a burning taste (The Merck Index, 1989). The decrease in food consumption may be a result of taste aversion as methyl bromide at high concentrations may have exceeded the odor threshold of 20.6 ppm and may be irritating to the palate.

A more appropriate endpoint for hazard identification was clinical signs observed in rats (Kiplinger, 1994) after oral (gavage) exposure to methyl bromide. In this study, at the lowest dose tested (80 mg/kg) with methyl bromide in the liquid form, rats showed hypoactivity, ataxia, prostration, labored respiration, hypothermia, and tremors (Table 2). At this dose, 2 of 10 animals died after 2 or more days of exposure. Some of the clinical signs may be due to stress from severe irritation to the stomach lining that resulted in squamous cell hyperplasia. The observation of tremors and ataxia, however, suggested the possibility of neurotoxicity from systemic absorption of methyl bromide. Similar clinical signs and mortality were also observed with microencapsulated methyl bromide at all doses tested (98 to 195 mg/kg) (Table 2). Since 80 mg/kg is the lowest dose tested, it was selected as the LOEL for the study. Using a default uncertainty factor of 10 for the extrapolation of an estimated NOEL (ENEL) from a LOEL, the critical ENEL was 8 mg/kg based on clinical signs and mortality at 80 mg/kg/day.

IV.A.2. Chronic Toxicity - Oral

In the chronic study with dogs, the NOEL was 1.5 ppm (0.13 mg/kg/day) with a LOEL of 5.0 ppm for decreased hemoglobin and (or) hematocrit levels at 3, 6 and (or) 12 months in male dogs fed fumigated feed (Newton, 1996) (Table 3). The biological significance of reduction in these levels for chronic toxicity is uncertain. The reduction was about the same magnitude (90%) for all durations and occurred only in the males. At 12 months, the ranges of hematocrit values were: 54.5-60.0% (control), 54.4-55.4% (0.5 ppm), 42.7-58.6% (1.5 ppm), and 45.9-55.7% (5.0 ppm). The ranges of hemoglobin values were: 18.3-20.1 (control), 18.2-18.5 (0.5

ppm), 14.4-19.7 (1.5 ppm), and 15.6-18.2 (5.0 ppm). The red blood cell counts for this group, measured by pretest, 3, 6, and 12 months, were lower (5-8%, not statistically significant) than that for the control throughout the experiment. Examination of the individual data showed that animals with low RBC counts at pretest also had low hemogloblin and hematocrit levels during pretest and throughout the experiment. This association suggested that the reduction in the hemogloblin and hematocrit may be variations within the normal range, as concluded by the U.S. EPA. Therefore, the reduction in hemoglobin and hematocrit was not considered an appropriate endpoint for risk characterization of chronic toxicity.

From the rat chronic toxicity study, two possible endpoints/NOELs were considered (Mertens, 1997). One endpoint was for enlarged spleens with a NOEL of 0.5 ppm (0.02 mg/kg/day) and a LOEL of 2.5 ppm (0.11 mg/kg/day) in male rats. In this rat chronic toxicity study, the number of animals with enlarged spleens increased significantly from 14% for 0.5 ppm to 22% for 50 ppm (Table 5). While an increase was not observed at 250 ppm, this effect observed at the lower doses (0.5 ppm, 2.5 ppm, and 50 ppm) was considered treatment related for several reasons. First, enlarged spleen was observed in 3 of the 4 treated groups. Histological findings showed lymphoma in one of the enlarged spleens from each group. Second, the increase was dose-related (Cochran-Armitage Trend Test p :< 0.05) and was statistically significant from the control (Fisher's Exact Test p :< 0.01). However, DPR has determined that this endpoint was not appropriate for risk assessment (Patterson, 2001) because of the following reasons:

1. The extent of the enlargement was not dose-related. A reexamination of the initial report showed that only the dimension (length, height, and width) was measured. Neither the dimension for normal spleen nor criteria for enlargement was given in the report. A research of the literature did not provide any historical database for spleen dimensions. The spleens were not weighed in this study. The enlargement was apparently defined by deviations of any of the physical dimensions (length, width, and height) of the spleen in the report. The dimensions of the enlarged spleens ranged from 52mm x 7mm x 5mm (one animal in 2.5 ppm) to 80 mm x 20 mm x 15 mm (another animal in 2.5 ppm group). The dimensions for the two enlarged spleens in the control group were 63 mm x 15 mm x 10 mm and 57 mm x 16 mm x 8 mm. There was no apparent correlation between the dose and the extent of the enlargement. The magnitude of the enlargement, if quantified as the product of dimensions (l x w x h), was varied within each group and the ranges were 7296 to 9750 mm^3 (control), 3300 to 14790 mm^3 (0.5 ppm), 1820 to 24,000 m^3 (2.5 ppm), and 3180 to14400 mm^3 (50 ppm).

2. The spleens of the treated female and the high dose male groups were not affected. There was no evidence for gender-specific responses from other studies. Also, although there was a 20-fold difference between 2.5 and 50 ppm, the incidence increased only by one animal. When a trend test (Cochran-Armitage) was run, excluding the high dose, the value was marginally significant (1.683 versus 1.65) to reach p <0.05.

3. The cause of the enlargement was unclear. Congestion and extramedullary hematopoiesis were reported for both normal and enlarged spleens. Blood content and age of the animal, independent of treatment, can also have an effect on the size of the spleen. While the finding of lymphoma only in enlarged spleens suggested that it may be the cause of the enlargement,

the incidences (one in each dose level) and the number of spleens sectioned were too low to determine a cause-and-effect relationship. Histological examination was conducted only on some of the enlarged spleens.

4. Neither the NRC nor the U.S. EPA considered this finding to be treatment related.

Another endpoint was reduced body weight with a NOEL of 2.2 mg/kg/day in the same above study (Table 4). The body weight reduction was associated with a decrease in food consumption observed as early as the first week of exposure and persisted for most of the study. For lack of other effects observed in these chronic toxicity studies, this effect on the body weight reduction was considered as the critical endpoint for risk characterization of chronic exposure.

IV.A.3. Oncogenicity

Positive findings in genotoxicity studies indicate that methyl bromide is potentially oncogenic. However, there was no clear evidence of oncogenicity under the experimental conditions used in the inhalation and oral oncogenicity and chronic toxicity studies (Reuzel *et al.*, 1987 and 1991; NTP, 1992; Eustis, 1992; Danse *et al.*, 1984; Boorman *et al.*, 1986; Hubbs, 1986). Therefore, oncogenic risk for methyl bromide was not considered based on the currently available data. More discussion on the this issue is in Volume I (DPR, 2001).

IV.B. DIETARY EXPOSURE ASSESSMENT

Introduction

The dietary assessment was conducted for acute and chronic exposures to commodities potentially treated with methyl bromide. There is no distinct seasonal exposure since most of the commodities may be consumed throughout the year. The potential exposure from methyl bromide in drinking water was not included in this assessment because residues have not been detected (<1 ppb) in the monitored wells (Golder Associates, Inc. 1985; **II.G. ENVIRONMENTAL FATE** in **Volume I**). Residues were assumed to be zero for preplant soil fumigation uses. Pre-plant studies showed that there were not detectable residues (LOD ca.~ 0.005 -0.01 ppm) of methyl bromide (Bolsa Research, 1988). The complete dietary exposure assessment is presented in Attachment A and is summarized in this section (Table 6).

Current tolerances for the use of methyl bromide were established for inorganic bromide. Since exposure to inorganic bromide is not the focus of this document, tolerance assessment was not conducted (**V. TOLERANCE ASSESSMENT**).

Methyl Bromide Residue Database

Methyl bromide residue data used to estimate the dietary exposure were submitted by The Methyl Bromide Industry Panel (complete references in Attachment A). U.S. EPA used these studies for the determination of proposed tolerances and dietary exposure (Perfetti, 1994; Schaible, 1995).

The samples were randomly collected under known fumigation conditions and were composited before analysis. The limits of detection (LOD) for methyl bromide ranged from 0.001 ppm (leaf lettuce) to 0.05 ppm (raw apple/grape and cheese). Most of the analyzed commodities had a LOD of 0.01 ppm as the LOD varied with the commodity type, processed food form, and the date of the analysis. When a commodity did not have any residue data, a residue value from another commodity in the same or similar crop group was used as a surrogate representative.

Over 230 commodities and their food forms (*i.e.* raw, baked, cooked, frozen) were included in the acute and chronic dietary exposures. For acute exposure, either the highest detected residue for the raw agricultural commodities (*i.e.*, whole apple, peach, etc.) or the average value for mixtures (juices, flour, etc.) were used. The average consisted of a simple average of all the detected values and the non-detectable residues reported at the LOD for the study. The chronic residue values in the dietary exposure assessment used the average of all the reported residues for both the raw agricultural commodities and mixtures. The chronic average consisted of a simple average of all the utilized residue values in the study and any non-detected level residue was reported as ½ of the LOD.

Table 6: Summary of residue values and factors used to estimate dietary exposure levels.[a]

Commodity	Acute Residue (ppm)			Chronic Residue (ppm)			Processing Factor			Percent Crop Treated Factor		
	raw	dried/ cured	juice	raw	dried/ cured	juice	raw	dried/ cured	juice	raw	dried/ cured	juice
Berries & Small Fruits[b]	0.017-2.14	0.77	0.017-2.14	0.013-1.62	0.71	0.013-1.62	0.01-0.16	1.0	0.09	0.6-1.0	1.0	0.01
Citrus[c]	0.99-1.55	0.99	0.87-1.36	0.005-1.36	0.89	0.87-1.36	0.29	0.29	0.36	0.01-0.14	0.01	0.01
Pome Fruits[d]	0.01-6.77	1.33-6.77	0.025-5.46	0.005-5.46	1.09-5.46	0.022-5.46	0.01-1.0	1.0	0.07-0.1	0.01-1.0	0.01-0.13	0.01
Other Fruits[e]	0.01-4.2	0.01-1.7	0.01-1.9	0.005-3.9	0.005-1.6	0.005-1.53	0.1-1.0	1.0	0.1-1.0	0.01-1.0	0.01-1.0	0.01
Vegetables[f]	0.004-5.33	0.01-5.33	0.07	0.002-2.7	0.005-2.7	0.025-0.042	0.02-1.0	0.02-1.0	1.0	0.01-1.0	0.01 or 1.0	0.01
Grains[g]	0.01-4.51			0.005-4.51			0.07-1.0			0.01		
Nuts[h]	0.01-15.2	4.7-15.2		0.005-11.9	2.9-11.9		1.0	1.0		1.0	1.0	
Walnut and Peanut	20.9	20.9	20.9 walnut oil 0.025 p. butter	13.3	13.3	13.3 walnut oil 0.025 p. butter	1.0	1.0	1.0	1.0	1.0	0.01
Herb & Spices[i]	0.01-4.14			0.005-4.14			1.0			1.0		
Meats & eggs[j]	0.01			0.005			1.0			0.01		
Pork	0.01	0.804		0.005	0.804		1.0	1.0		0.01	0.01	

Commodity	Acute Residue (ppm)			Chronic Residue (ppm)			Processing Factor			Percent Crop Treated Factor		
	raw	dried/ cured	juice	raw	dried/ cured	juice	raw	dried/ cured	juice	raw	dried/ cured	juice
Chocolate	0.069	0.069		0.069			1.0	1.0		0.01		
Gelatin	4.14			4.14			1.0			0.01		
Milk	0.125 (solids)	0.01 (sugar)	0.01 (water)	0.125 (solids)	0.005 (sugar)	0.005 (water)	1.0 (solids)	0.05 (sugar)	1.0 (water)	0.01 (solids)	0.01 (sugar)	0.01 (water)
Others[k]	0.01			0.005			1.0			0.01		

a Residues and factors for individual commodities are listed in Attachment A. Values in the table are the ranges for each group. Processing factor of less than 1 means loss of residues in time. Percent of crop treated factors ranged from 0.01 to 1.0 with 1.0=100% crop treated.

For the following footnotes, commodities without residue data are in parenthesis and are grouped with their surrogate commodities.

b Includes: blackberry (boysenberry, raspberry, dewberry, loganberry, youngberry), blueberry, grape (currant, elderberry, gooseberry, juneberry, mulberry, huckleberry), and strawberry.

c Includes: citrus citron, grapefruit, lemon (kumquat, lime), and orange (tangelos, and tangerine).

d Includes: apple (crabapple, quince), peach (apricot, nectarine), avocado, cherry, pear, and plum.

e Includes: banana, cantaloupe (casaba, honeydew, watermelon, wintermelon), coconut (jackfruit), date, fig, kiwi, papaya, and pineapple.

f Includes: asparagus, bean (dry and succulent), beet (root), broccoli (Brussel sprouts), cabbage (Chinese cabbage, kale, kohlrabi, savoy), carob, carrot (Jerusalem artichoke, burdock, taro root, salsify), cassia, cauliflower (collard), celery (chicory-French/Belgian endive, endive-curly and escarole), corn (sweet and pop), cucumber, garlic, leafy lettuce (Swiss chard, dandelion green, cress, fennel, parsley), head lettuce, onion (leek, shallot), parsnip, green pea (lentil, snow pea), spinach, peppers (sweet, chili, pimiento, and others), potato, jicama, cassava, radish-root, daikon, rutabagas, sesame seed, soybean-dry, squash, pumpkin, bitter melon, towel gourd, spaghetti squash, tomato, eggplant, turnip-root, and others (green onions, chives, mushrooms, okra, sugar beets, palm heart, soybean-sprouted, sunflower seeds, dried taro, sugar cane, flax seed, seaweed, guar beans).

g Includes: barley, oat, corn, rice, rye, sorghum, millet, wheatbran, and buckwheat.

h Includes: almond (Brazil nut, cashew, filbert, hickory nut, macadamia, pistachio, beechnut), chestnut, and pecan.

I Includes: allspice, cinnamon (chicory, caraway, anise, coriander, dill, mustard seed, nutmeg), marjoram (dried parsley, dried chives, bay, basil, mace, savory, peppermint, spearmint), black pepper, horseradish (ginger, clover), cumin, oregano, paprika (from data for capsicum), poppy seed, and sesame seed.

j Includes: beef, veal, turkey, poultry, and eggs.

k Includes: all oils (except walnut oil), coffee, tea, vinegar, distilled alcohol, yeast, aloe vera juice, and maple syrup.

Residue Adjustments

Processing and Dissipation Effects

Estimation of acute and chronic dietary exposures considered the potential loss or accumulation of residues during processing of the commodities. This is reasonable since methyl bromide is volatile and known to dissipate with time after fumigation (Eickhoff *et al*., 1998). In addition, processing studies showed that methyl bromide residues were reduced below the detection limits after various forms of processing (peeling, boiling, pasteurizing, cooking and baking) of the raw commodity (Eickhoff *et al*., 1998). Therefore, the processing factors for some commodities were <1 with the default factor as 1 for no dissipation of residues. This factor was zero for those food forms that are in packages (*i.e.* canned) during fumigation.

Percent of the Crop Treated

The current DPR chronic dietary exposure analysis default assumption is that 100% of any commodity is treated (percent crop treated factor of 1) with the pesticide under consideration. When use data are available, the residue value was adjusted by a factor of less than 1 which corresponded to the fraction treated. This adjustment factor applied only to the chronic dietary exposure analysis since there is a possibility of consuming untreated commodities over time. The minimum factor was 0.01 for at least 1% of the crop treated.

Consumption Data

The USDA directs the Nationwide Food Consumption Survey (NFCS) and the Continuing Survey of Food Intakes by Individuals (CSFII) (USDA, 1987-1988; USDA, 1989-1992). The NFCS is a geographically stratified probability sampling of U.S. households and is conducted every 10 years (1977-1978 and 1987-1988). The CSFII is an annual survey to collect current consumption data in particular those for vulnerable population subgroups (e.g., infants and children). The consumption analysis in this document used the three-year data (1989-1990, 1990-1991, and 1991-1992) from the CSFII (USDA, 1989-1992).

Dietary Exposure Analysis

Acute and chronic dietary exposure analyses were conducted with the Exposure-4™ and Exposure-1™ software programs, respectively (TAS, Technical Assessment Systems, Inc.). The Exposure-4™ program is used to estimate the distribution of user-day (consumer-day) exposure (acute exposure) for the U.S. population and specific subgroups (TAS, 1996a). A user-day is any day in which at least one food from the label-approved commodities is consumed. The Exposure-1™ program is used to estimate the annualized average exposure (chronic exposure) for all members of a designated population subgroup (TAS, 1996b).

The potential acute dietary exposure to methyl bromide from all labeled uses ranged from 3.387*u*g/kg/day to 8.195 *u*g/kg/day for the 95th percentile of user-days exposures for all population subgroups (Table 7). Children (1-6 years) had the highest potential acute dietary exposure (8.195 *u*g/kg/day) to methyl bromide residues in the diet. The mean potential chronic

dietary exposure for all population subgroups ranged from 0.014 *u*g/kg/day to 0.200 *u*g/kg/day (Table 7). The population subgroup of children (1-6 years) had the highest potential chronic exposure (0.200 *u*g/kg/day).

A critical commodity contribution analysis was conducted to determine the commodities with significant (5% or more of the total exposure) contributions to the diet (Attachment A). The analysis for infants showed a potential overestimation of exposure. In this analysis, oat, soybean, and taro root, along with apple, grape, and raisin were among the significant contributors. The exposures for raw soybean and raw oats were based on the assumption that processed soybeans and oats would have the same residue values as the raw form. This assumption was necessary since no processing data were available. Consequently, the contributions of soybean and oats to the total exposure are overestimated. Taro root was another commodity in which its contribution was likely to be overestimated. In the dietary exposure analysis, the residues for raw carrot were used to estimate that for taro root (in all food forms) and no adjustment for processing. Since taro root is consumed only after cooking, it is unlikely there are any residues left in the root.

The impact of these 3 commodities in the total exposure for each group was studied by excluding them in the analysis (Attachment A, Appendix C). The chronic dietary exposure for infants decreased 41% (0.017 *u*g/kg/day to 0.01 *u*g/kg/day) for nursing infants and 64% for non-nursing infants (0.014 *u*g/kg/day to 0.005 *u*g/kg/day). There was essentially no change in the exposure for the other age groups, who consumed a larger variety of food.

Table 7. Acute and chronic dietary exposure to methyl bromide residues.

Population subgroup	Acute Exposure 95th percentile (*u*g/kg/day)[a]	Chronic Exposure Annualized average (*u*g/kg/day)
US Population all seasons	4.892	0.127
Pacific Region	5.705	0.182
Hispanics	4.831	0.103
Non-Hispanic Whites	4.973	0.133
Non-Hispanic Blacks	4.116	0.090
Non-Hispanic Other	5.942	0.194
All Infants	3.896	0.015
Infants (nursing)	5.125	0.017
Infants (non-nursing)	3.504	0.014
Children (1-6 years)	8.195	0.200
Children (7-12 years)	5.138	0.199
Females (13-19 years) (not pregnant, not nursing)	3.387	0.060
Females (20+ years) (not pregnant, not nursing)	4.993	0.143
Females (13-50 years)	4.678	0.136
Females (13+ years) (pregnant, not nursing)	4.292	0.099
Females (13+ years) (nursing)	4.448	0.149
Males (13-19 years)	3.704	0.060
Males (20+ years)	4.433	0.093
Females and Males (16+ years)	4.649	na
Seniors (55+ years)	4.886	0.124

a/ Exposure levels have been rounded off to 3 significant figures and were based on the 1989-1992 Continuing Surveys of Food Intakes of Individuals surveys (Attachment A, Appendices A and B).

IV.C. RISK CHARACTERIZATION FOR DIETARY EXPOSURE

Risk to non-oncogenic effects was characterized in terms of a margin of exposure (MOE), defined as the ratio of the critical NOEL to the estimated human exposure levels. For acute exposures, the 95th percentile of human dietary exposure levels were used to calculate the margins of exposure (MOEs). For chronic exposure, the mean exposure values were used to determine the MOEs.

Based on a critical acute estimated NOEL of 8 mg/kg/day for clinical signs in rats (Kiplinger, 1994), the lowest MOE for acute exposure was 980 for children 1-6 years old (Table 8). Other children, infants, and adults groups had MOEs greater than 1500.

Based on a critical chronic NOEL of 2.2 mg/kg/day for reduced body weight in rats (Mertens, 1997), the MOEs were 11,000 for children 1-6 years and 7-12 years groups (Table 8). The MOEs for infants were greater than 120,000. The MOEs for the adult subgroups were greater than 14,000. If the three commodities (oats, soybean, and taro roots) were excluded from the exposure estimate, the MOEs for infants would increase about 2-fold and would be >200,000. The MOEs for the other population groups remained the same as when these 3 commodities were included.

Table 8. Margins of exposure for acute and chronic dietary exposures to methyl bromide.

Population subgroup	Acute MOE[a]	Chronic MOE[b]
US Population all seasons	1640	17310
Pacific Region	1400	12060
Hispanics	1660	21300
Non-Hispanic Whites	1610	16510
Non-Hispanic Blacks	1940	24420
Non-Hispanic Other	1350	11330
All Infants	2050	150620
Infants (nursing)	1560	128190
Infants (non-nursing)	2280	162600
Children (1-6 years)	980	10930
Children (7-12 years)	1560	11080
Females (13-19 years) (not pregnant, not nursing)	2360	36470
Females (20+ years) (not pregnant, not nursing)	1600	15430
Females 13-50 years	1710	16180
Females (13+ years) (pregnant, not nursing)	1860	22290
Females (13+ years) (nursing)	1800	14790
Males (13-19 years)	2160	36560
Males (20+ years)	1810	23680
Females and Males (16+ years)	1720	na
Seniors (55+ years)	1640	17760

a/ The Margin of Safety was calculated based on estimated NOEL of 8 mg/kg for clinical signs in rats (Kiplinger, 1994).

b/ The Margin of Safety was calculated based on NOEL of 2.2 mg/kg/day for reduced body weight in rats (Mertens, 1997).

V. RISK APPRAISAL FOR DIETARY EXPOSURE

V.A. INTRODUCTION

Risk assessment is the process used to evaluate the potential for human exposure and the likelihood that adverse effects of a substance will occur in humans under specific exposure conditions. Every risk assessment has inherent limitations on the application of existing data to estimate the potential risk to human health. Therefore, certain assumptions and extrapolations are incorporated into the hazard identification, dose-response assessment, and exposure assessment processes. This, in turn, results in uncertainty in the risk characterization which integrates all the information from the previous three processes. Qualitatively, risk assessments for all chemicals have similar uncertainties. However, the degree or magnitude of the uncertainty can vary depending on the availability and quality of the data, and the types of exposure scenarios being assessed. Specific areas of uncertainty associated with this dietary risk assessment of methyl bromide are delineated in the following discussion. A comparison of the critical NOELs and endpoints for oral and inhalation exposures are shown in Table 9.

V.B. HAZARD IDENTIFICATION FOR DIETARY EXPOSURE

V.B.1. Acute Toxicity

The acute critical NOEL was estimated from a LOEL of an oral gavage study with rats (Table 2) (Kiplinger, 1994). The animals were severely affected as some died and others showed ataxia, prostration, labored respiration and tremors. There was some uncertainty on selection of this LOEL because of the method of administration. Since methyl bromide is an irritant, gavage of a bolus dose could damage the gastrointestinal tract. The stomach was reported to show hemorrhage, edema, and squamous cell hyperplasia due to irritation of the lining. This may have resulted in more methyl bromide absorbed, and hence increased toxicity, than if methyl bromide were given in the feed, which would more closely simulate the human exposure scenario. Therefore, the ENEL (8 mg/kg/day) is likely an overestimate of the toxicity. Humans are exposed to a variety of food items in a day at methyl bromide residue levels unlikely to cause damage to the gastrointestinal tract. This likelihood of overestimation is also suggested when the oral critical NOEL is compared to that for the inhalation route, the most direct route for exposure. The critical oral ENEL of 8 mg/kg/day was lower than the critical NOEL for inhalation, if the absorbed doses, are compared (Table 9). For oral exposure, the exposure dose is the same as the absorbed dose since oral absorption is 100% based on studies with rats (Medinsky *et al.*, 1984). For inhalation exposure, the NOEL of 40 ppm for developmental toxicity in rabbits was equivalent to an absorbed dose of 11 mg/kg/day with inhalation absorption factor of 50% (Medinsky *et al.*, 1985; Raabe, 1986 and 1988).

V.B.2. Chronic Toxicity

One uncertainty in the selection of the critical NOEL of 2.2 mg/kg/day (Mertens, 1997) to evaluate chronic oral exposure is the use of reduced body weight as the critical endpoint. This endpoint was selected because no other significant treatment-related effects were observed. Since this effect was observed as early as the first week, it may be an overestimate of the NOEL after chronic exposure. The uncertainty regarding spleen enlargement from this study

has already been discussed (**IV.A.2. Chronic Toxicity - Oral**). Using an uncertainty factor of 100, the reference concentration for the reduced body weight is 0.02 mg/kg/day based on a NOEL of 2.2 mg/kg/day (Mertens, 1997). This values is higher than the U.S. EPA established reference dose of 0.0014 mg/kg/day (IRIS, 2000) based on a NOEL of 1.4 mg/kg/day for epithelial hyperplasia in the forestomach in rats exposed to methyl bromide by gavage for 14 weeks (Danse *et al.*, 1984). An uncertainty factor of 1000 was applied to account for lack of a chronic study, interspecies extrapolation, and intraspecies variations. The RfD was established in 1991 and U.S. EPA has not updated the evaluation with the more recent chronic toxicity studies. When compared to the inhalation exposure, the oral chronic critical NOEL of 2 mg/kg/day was higher than the inhalation chronic ENEL (0.3 ppm; adjusted dose of 0.14 mg/kg/day) for nasal epithelial hyperplasia and degeneration in rats (Table 9, Reuzel *et al.*, 1987 and 1991).

V.B.3. Extrapolation of Estimated No-Observed-Effect Level from the Lowest-Observed-Effect Level

The acute NOEL was estimated from a LOEL of 80 mg/kg for clinical signs in rats (Table 2) (Kiplinger, 1994) using a default uncertainty factor of 10-fold. This default factor is considered appropriate since the toxicity is significant and there is insufficient information to derive another factor or use other approaches.

Table 9. Comparison of critical NOELs and endpoints for oral and inhalation exposures.

Exposure	Oral[a]	Inhalation
Acute	ENEL= 8 mg/kg/day Absorbed dose= 8 mg/kg/day Clinical signs in rats (Kiplinger, 1994)	NOEL=40 ppm (21 mg/kg/day)[1] Absorbed dose=11 mg/kg/day Developmental Toxicity (Breslin *et al.*, 1990)
Chronic	NOEL= 2.2 mg/kg/day Absorbed dose= 2.2 mg/kg/day Reduced body weight in rats (Mertens, 1997)	ENEL=0.3 ppm (0.28 mg/kg/day)[2] Absorbed dose= 0.14 mg/kg/day Nasal epithelial hyperplasia and degeneration (Reuzel *et al.*, 1987 and 1991)

a/ Absorption by the oral route is 100%.

[1]The critical NOEL (40 ppm) was converted to mg/kg/day unit by the following equation accounting for inhalation rate of rabbits and amortization for daily exposure. Using a default value of 50% absorption, the absorbed dose is 11 mg/kg/day.

$$40 \text{ ppm} \times 0.54 \text{ m}^3 / \text{kg} / \text{day} \times \frac{94.95}{24.45} \times \frac{6 \text{ hours}}{24 \text{ hours}} = 21 \text{ mg} / \text{kg} / \text{day}$$

[2]The critical ENEL (0.3 ppm) was converted to mg/kg/day unit by the following equation accounting for inhalation rate of rats and amortization for daily exposure. Using a default value of 50% absorption, the absorbed dose is 0.14 mg/kg/day.

$$0.3 \text{ ppm} \times 0.96 \text{ m}^3 / \text{kg} / \text{day} \times \frac{94.95}{24.45} \times \frac{6 \text{ hours}}{24 \text{ hours}} = 0.28 \text{ mg} / \text{kg} / \text{day}$$

V.C. DIETARY EXPOSURE ASSESSMENT

Dietary exposure analyses were conducted for more than 200 commodities and their food forms (Attachment A). For acute exposure, the highest residue value for a crop or the average value for a mixture was adjusted with processing factors when data were available. For chronic exposure, the combined average residue value for a crop or mixture was adjusted both with processing factor and percent of crop treated data, if available. The residue levels of processed forms of most commodities were reduced because methyl bromide dissipated with cooking (such as boiling, pasteuring, and baking). The percentage of crop treatment ranged from 1% (majority of the commodities) to 68% (fresh plum) based on multi-year marketing data. While this approach provided a reasonable estimate of actual exposures, there were potential sources of overestimation of exposure because of limitations in the data. For example, the residues for several major contributors (walnut, almond, raisin, pineapple, grape, and apple) to the total dietary exposures were based on fumigation using the maximum label rate of 4 lbs/1000 ft^3. Depending on the circumstance, the actual use rate may be lower. Another source of overestimation was the assumption, in the absence of data, of no loss of residue during processing and 100% of crop treated for some commodities such as spices, some dried beans, and some vegetables. Most of these commodities had low consumption rates and are not major contributors to the total exposure. However, the assumption of no loss in processing had a major impact on commodities with significant contribution. As discussed in **IV.B.5. Dietary Exposure Analysis**, the exposures of infants were overestimated by about 2-fold if raw soybean, oats, and taro in uncooked form were included in the diet.

The use of detection limit to assign residue levels for samples with residue levels at or below the detection limit or the use of surrogate data could either over- or under-estimate the exposure. The total exposure may be an underestimate since composite samples were analyzed. This approach masked potential higher residue values of single units that a consumer may encounter in an acute exposure. Single-unit residue data were not available. One area of uncertainty is that the exposure did not consider the presence of metabolites. There were no residue data on the metabolites of methyl bromide in the treated commodities. Based on studies with methyl chloride and glutathione reactions, some of the metabolites of potential concerns are methanethiol, formaldehyde, and formate (Kornburst and Bus, 1983). In addition, methyl bromide is an alkylating agent and has been shown to form adducts with proteins and nucleic acids.

Additional routes of oral exposure such as ingestion of treated soil and breast milk have been suggested as potential sources of oral exposure to methyl bromide residues. The exposure from ingestion of treated soil can be considered negligible. Methyl bromide, once injected into the soil, undergoes biotransformations and transport (see **Volume I** on **II.G. Environmental Fate**). It is decomposed within the soil matrix, hydrolyzed, and degraded by soil bacteria. There is a measurable amount of methyl bromide in the soil air; however, the level is relatively low. The soil gas concentrations were < 1 ppm after 7 days (Williams *et al.*, 1999) or a maximum concentration of 2 g methyl bromide/m^3 of soil found at 0.5 meter deep (Yates *et al.*, 1996) after the tarp was removed. Using a bulk density of 1.65 g/cm^3, this maximum concentration is equivalent to 1.2 *u*g of methyl bromide per gram of dry soil. Assuming a 10-kg child ingests the soil and the methyl bromide at the upper percentile soil ingestion rate of 400 mg/day (U.S. EPA, 1997a), the estimated exposure from soil ingestion

was 0.048 ug/kg/day [3]. This exposure level is more than 100-fold lower than those (5-8 *u*g/kg/day) estimated for direct dietary exposure for children (Table 6).

There are currently no data available on the potential for exposure to methyl bromide via the breast milk. Studies on the potential for exposure to pesticides in the breast milk focused primarily on organochlorines such as DDT and metabolites, dieldrin, lindane, and hexachlorobenzene (NRC, 1993). One study with sodium bromide in rats suggested that off-spring were exposed to inorganic bromide via the milk (Disse *et al.*, 1996). In a review on human exposure to inorganic bromide, the authors compared the bromide ion levels in the breast milk measured in two studies conducted in The Netherlands (van Leeuwen and Sangster, 1987). There was an apparent decrease in levels with time as the mean levels were 2.7 mg/L (range 1.1 to 9.7 mg/L) and 1.6 mg/L (range 0.3 to 4.4 mg/L) for the 1974 and 1985 studies, respectively. The authors associated this apparent decrease with the reduced use of methyl bromide in The Netherlands. The validity of this association is questioned since these values came from two different studies. There was no information on other factors which may influence the measured levels such as change in the background level of bromide ion, other sources of bromide ion exposure, and methyl bromide exposure levels.

V.D. RISK CHARACTERIZATION FOR DIETARY EXPOSURE

The MOEs for potential acute and chronic exposures were based on ENEL or NOEL for toxicity observed in laboratory animals. When the NOEL for non-oncogenic effects is based on animal data, a MOE of 100 is generally considered adequate for protection against potential acute or chronic toxicity of a chemical. This benchmark of 100 includes an uncertainty factor of 10 for interspecies extrapolation and a factor of 10 for intraspecies variability. These uncertainty factors assume that the average human is 10 times more sensitive to the effects of a chemical than the most sensitive laboratory animal, and that a sensitive individual is 10 times more susceptible than an average individual (Davidson *et al.*, 1986; Dourson and Stara, 1983).

V.D.1. Interspecies Extrapolation

The sensitivity of humans and laboratory animals to methyl bromide toxicity could not be compared since there are no data on human oral exposure. The only interspecies factor considered was consumption rate differences in the determination of dietary exposure for humans and exposure dosages in animals. In the absence of data, the current DPR default for interspecies extrapolation is a factor of 10-fold with respect to the dose.

V.D.2. Intraspecies Extrapolation

For intraspecies variation in the response to the toxicity of methyl bromide, the DPR default uncertainty factor of 10-fold was used since there are no data to quantify the variation. The potential differences in exposure levels were accounted for by addressing the dietary exposures of many subgroups based on age, gender, ethnicity, and region (Table 6). In the

[3] $\frac{400 \text{ mg soil}}{\text{day}} \times \frac{1.2 \text{ ug mebr}}{\text{g soil}} \times \frac{1 \text{ g}}{1000 \text{ mg}} \times \frac{1}{10 \text{ kg child}} = 0.048 \text{ ug / kg / day}$

inhalation RCD (DPR, 2001), the interaction of methyl bromide and glutathione-S-transferase (GST), and human GST polymorphism were discussed. The conclusion was that the polymorphism of GST-theta (GSTT) in the human population is important to consider. At this time, it was not possible to conclude that GSTT polymorphism would lead to increased susceptibility to methyl bromide toxicity and to determine whether or not the variation is sufficiently addressed by the 10-fold default intra-individual uncertainty factor.

V.E. ISSUES RELATED TO THE FOOD QUALITY PROTECTION ACT

For inhalation exposure to methyl bromide, there was some evidence for increased sensitivity to the prenatal and post-natal toxicity of methyl bromide when NOELs for developmental or reproductive toxicity were compared with those for maternal toxicity (see **Volume I** section **V.E.**). The National Research Council scientists did not recommend an additional uncertainty factor for the inhalation exposure since the critical NOELs were considered conservative (NRC, 2000).

For oral exposure, the current database did not suggest increased sensitivity to methyl bromide by infants and children. A NOEL could not be established in the oral reproductive toxicity study (Kaneda *et al.*, 1993) where rats were given methyl bromide fumigated feed and the actual dose was not determined. No developmental toxicity was observed in rabbits (gestation day 6-18) and rats (gestation day 6-15) given methyl bromide by gavage (Kaneda *et al.*, 1998). The highest doses tested were 30 mg/kg/day in the rat and 10 mg/kg/day in the rabbit. In comparison, these doses are similar to the equivalent dose for the NOEL (40 ppm or absorbed dose of 10.5 mg/kg/day[4]) for developmental toxicity in the rabbit by inhalation (Breslin *et al.*, 1990).

V.E.2. Aggregate Exposure

There could be a potential for aggregate exposure from occupation or residential exposures and dietary exposures. Aggregate exposure is addressed in **Volume III**.

V.E.3. Cumulative Toxicity

Since the mechanism of methyl bromide toxicity from oral exposure is unknown, it is not possible to consider cumulative toxicity at this time.

V.E.4. Endocrine Effects

Based on the studies reviewed, methyl bromide has not been shown to cause endocrine disruption effects.

[4] 40 ppm x 3.89 mg/m^3/ppm x 0.54 m^3/kg/day x 6 hours/24 hoursx50% = 10.5 mg/kg/day

VI. TOLERANCE ASSESSMENT

VI.A. INTRODUCTION

VI.A.1. U.S. EPA

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). A tolerance is the legal maximum residue concentration of pesticide which is allowed in a raw agricultural commodity and processed food. The 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). 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). The 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).

For methyl bromide, the established tolerances of methyl bromide are based on inorganic bromide. They are in the range of 5 ppm for apples to 240 ppm for pop corn (Federal Register, 1991). The toxicological database for the establishment of the tolerances included three studies with inorganic bromide: (1) a 20-month rat feeding study with a NOEL of 235 ppm or 11.75 mg/kg, (2) a 52-week rabbit feeding study with a NOEL of 90 ppm or 2.7 mg/kg, and (3) a 1-year dog feeding study with a NOEL of 2900 ppm or 72.5 mg/kg (U.S. EPA, 1983 a and b). In the 1986 Reregistration Standard, U.S. EPA stated that inorganic bromide was not of toxicological concern and required residue studies based on methyl bromide *per se* (U.S. EPA, 1986b). In response to the Standard, the registrant developed a residue database for multiple crop groups and tolerance proposals (U.S. EPA, 1986a). The proposed tolerances ranged from 0.1 ppm (vegetables, small fruits and berries, and stone fruits) to 50 ppm (green cocoa beans). However, the U.S. EPA has yet to establish the tolerances on methyl bromide *per se.*

In 1996, the Food Quality Protection Act (FQPA) amended the overall regulation of pesticide residues under FIFRA and FFDCA (U.S. EPA, 1997b and c). One major change was the removal of the Delaney Clause that prohibited residues of cancer-causing pesticides in processed foods. The 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 U.S. EPA determined, based on reliable data, that a different margin would be safe. In addition, the 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. Previously, U.S. EPA reassessed tolerances as part of its reregistration and Special Review processes. In the

evaluation of tolerances, the U.S. EPA uses a tiered approach and the assessment includes all label-use commodities. Methyl bromide is among the non-organophosphate pesticides with risk assessments to be completed by the U.S. EPA in fiscal year of 2001 (U.S. EPA, 2000).

VI.A.2. California

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. In these assessments, the tolerance for each specific commodity is evaluated individually. Since there is no tolerance established for methyl bromide, *per se*, in treated commodities, a tolerance assessment was not conducted for this document.

VII. CONCLUSIONS FOR DIETARY EXPOSURE

The human health risk from potential dietary exposure was evaluated in this Volume II of the Risk Characterization Document. The potential risks of dietary exposure to methyl bromide were evaluated based on clinical signs and reduced body weight observed in animal studies for acute and chronic exposures, respectively. The risks, expressed as margins of exposure, were calculated for human population subgroups based on region, age, and gender.
For non-oncogenic effects based on animal data, the MOEs were compared with a benchmark of 100 to determine whether the exposure would be of a potential health concern.

The dietary exposures were considered reasonable estimates of actual exposures. The range of MOEs were 980 to 2360 and 10,930 to 162,600 for acute and chronic exposures, respectively. Other variables discussed in this document which potentially underestimate or overestimate actual dietary exposures should also be considered in the evaluation of these MOEs.

Since methyl bromide residues are found in treated commodities, there is a need to establish tolerances for the parent compound on these commodities.

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IX. ATTACHMENTS

ATTACHMENT A

Dietary Exposure Assessment

METHYL BROMIDE (Bromogas 7, Terr-O-Gas 7)

DIETARY EXPOSURE ASSESSMENT

Wesley C. Carr, Jr.

HEALTH ASSESSMENT SECTION

MEDICAL TOXICOLOGY BRANCH

CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

October 4, 2001

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I. Summary

An acute and chronic dietary exposure assessment was performed for the pesticide methyl bromide. No lifetime dietary exposure analysis was conducted since there was no clear evidence of cancer in experimental animal studies. Over 230 raw agricultural commodity (RACs) residues were included in the assessment. The residue data were derived exclusively from registrant supplied pre-plant field and post-harvest fumigation residue data (Table 1).

Exposures were calculated for an acute dietary exposure intake using the combined RACs residue values which had been adjusted to reflect processing factors. The acute dietary scenario was evaluated using the acute estimated-no-effect-level (ENEL) of 8.0 mg/kg/day based on clinical signs from a rat oral gavage study. The acute exposure values at the 95th% ranged from 0.003387 mg/kg/day, females 13-19 years, to 0.008195, children 1-6 years (Table 3).

Exposures were calculated for a chronic dietary exposure intake using combined averaged RACs. The dietary scenario was evaluated using the chronic no-observed-effect-level (NOEL) of 2.2 mg/kg/day based on reduced body weight observed in a 2 year rat study. The residue data used in the chronic dietary assessment included a percent of the crop treated (PCT) adjustment for almost all of the commodities. The percent crop treated adjustment factors ranged from 1% treated (majority of commodities) to 68% treated for the national fresh plum crop. The methyl bromide percent crop treated calculations were based on registrant supplied multi-year marketing data. The chronic dietary exposure analysis was also modified by commercial processing data. The chronic dietary exposures ranged from 0.000014 mg/kg/day, non-nursing infants, to 0.0002 mg/kg/day, children 1-6 years of age population subgroups (Table 4).

An acute tolerance assessment using the U.S. EPA tolerances maximum residue contribution (MRC) level was not performed on individual commodities since there are no tolerances established for methyl bromide. Current tolerances on these commodities are based on inorganic bromide levels.

II. Introduction

Acute and chronic dietary exposure assessments were conducted for methyl bromide. All available methyl bromide raw agricultural commodities (RAC) residue data were evaluated (Table 1). A tolerance assessment was not conducted since there is currently not an established 40 CFR 180 tolerance that characterizes methyl bromide. The listed tolerances of 40 CFR 180.123, 180.199 and 185.3700 are only for the inorganic bromide which is toxicologically different than methyl bromide (CFR, 1999).

Most of the federal and state regulatory pesticide residues monitoring programs do not routinely analyze for methyl bromide or the inorganic bromide. These include the Food and Drug Administration (FDA) monitoring program (McMahannon and Wirtz, 1998, 1999), the United States Department of Agriculture (USDA) Food Safety Inspection Service (FSIS) and the Pesticide Data Program (PDP) (USDA, 1996 - 2000 PDP references).

Residues analyzed by the FDA regulatory monitoring surveillance program (statistically based commodity survey) for inorganic bromide were collected through the early 1990s for domestic and imported commodities. The FDA has not monitored for methyl bromide; therefore, no FDA residue data were considered for use in the DPR dietary exposure analysis (Y. Lee, 1998). The FDA multiple screen residue databases for 1997 and 1998 were reviewed. The residue screens are located on the FDA homepage and must be downloaded to use. The FDA residue methods do not screen for methyl bromide residues (McMahonnan and Wirtz, 1998, 1999).

The USDA does not currently monitor for methyl bromide using either their multi-residue screen or individual analyte programs, and therefore no data are available or reported in their annual surveys for the Pesticide Data Program (PDP) nor the Food Safety Inspection Service (FSIS). The PDP program targets specific raw agricultural commodities that are likely to be heavily consumed by infants and children (USDA, 1997c, 1998c,d and 2000). The FSIS monitors for chemical residues, including some pesticides, on various commercial meat animals, such as cattle, pork, poultry and sheep (USDA, 1994).

The DPR does not routinely monitor for methyl bromide in its market basket surveillance or priority pesticide programs (DPR, 1997,1998, 1999a). As a special project, the DPR added methyl bromide to the DPR priority pesticide program for 1996 and 1997. Methyl bromide is not part of a DPR multiple residue screen analysis program and is measured using a single analyte methodology. The range for the limits of detection (LOD) was between 0.005 ppm for peaches to 0.05 ppm for dates. There were 5 other commodities (almond, cherry, prune, strawberry and walnut) analyzed under the priority program all with a LOD of 0.01 ppm (DPR, 1998, 1999a).

The commodity residue values obtained from the 1996 and 1997 DPR priority pesticide program were evaluated but not used in this dietary exposure assessment. The DPR data were not used primarily because the samples were measured at different times after fumigation. The chambers were not certified for detection levels and accuracy after each commodity fumigation cycle as required for "good laboratory practices" standards. These factors increased the variability in the methyl bromide residue data.

The Methyl Bromide Industry Panel (MBIP) is an industry group consisting of Albemarle Corp., Ameribrom, Inc., Great Lakes Chemical, Co. and Trical, Inc. The pesticide name used in the submitted field and post-harvest fumigation residue studies is methyl bromide (Trade Names: Bromogas 7, Terr-O-Gas 7, etc.) or bromomethane (IUPAC). Methyl bromide as an active ingredient is a colorless and odorless gas. Methyl bromide products are frequently found combined with chloropicrin. Chloropicrin, a pesticide itself, increases the overall efficacy of the registered product when combined with methyl bromide and also functions as a warning odorant to the presence of methyl bromide.

As of July 2000, there are 54 active product registrations of methyl bromide approved for use in California. The product registrations are only for agricultural (pre-plant field or post-harvest commodity fumigation) or professional home fumigation end uses. The agricultural products are for broad- spectrum pest control (bacteria, fungi, insects, nematodes and vertebrate

control) in pre-plant field preparation or post-harvest fumigation of raw agricultural commodities. The professional applicator structural fumigation registrations are used for the control of structural pests (termites and other wood destroying organisms). The percentages of methyl bromide in product formulations range from a low of 45% (Trical pre-plant soil fumigant) to a maximum of 100% (several quarantine fumigant products). The soil fumigant's agricultural pre-plant crop interval on a field is set at either 365 or 730 days depending on the crop that is going to be planted into the treated fallow field. The typical post harvest fumigation interval for warehoused commodities was 0 days for almost all labeled uses except sweet potato (3 days).

A total of 17,565,348 pounds (lbs.) of methyl bromide was used in California during 1995 (DPR, 1996). There were 16,022,069 lbs. applied during 1996 and for 1997, 15,663,832 lbs. (DPR, 1999a,b). A total of 13,569,875 lbs. was applied during 1998 and for 1999 (preliminary data), 15,342,080 lbs. (DPR, 2000a,b). The 5-year California average (1995 - 1999) of total methyl bromide use is 15,632,641 lbs. per year. The top four California sites (DPR PUR definition) receiving methyl bromide applications over the 1995-99 period were strawberry (average of 4,418,786 pounds/year), soil application-pre-plant-outdoor and/or fallow agricultural land (average of 1,858,801 lbs./yr.), non-outdoor container/field grown plants (average of 1,057,556 lbs./yr.), and wine grapes (average of 974,045 lbs./yr.). These four sites account, on average, for approximately 52% of the total methyl bromide applied in California.

III. Methyl Bromide Residues

A. Methyl Bromide Residue Database

The methyl bromide residue data used in the DPR dietary exposure assessment were entirely submitted by the MBIP taskforce. The May, 2000 submitted data were the most extensive particularly with regard to the fumigation chamber protocols and verification of limits of detection and time intervals for post-fumigation sampling. More than 200 registrant methyl bromide residue studies were received and evaluated by the DPR staff. Most of the older studies (more than 100) were ultimately not used because they were replaced by more recent studies for the same commodities. The more recent studies had lower limits of detection and more precise data validation (Table 1).

Almost all of the fresh commodities analyzed for methyl bromide residues were collected from the contiguous United States and were fumigated and processed primarily in California. Several commodities originated in Hawaii (e.g. pineapple) and a few were imported from Chile to represent the United States winter season fresh fruit market. In all cases, the imported commodities were still fumigated and analyzed at the California facilities. All composite samples (domestic and foreign origin) were randomly selected before extraction and chemical analysis. The methyl bromide protocols for certifying the fumigation chambers concentration levels, accuracy, temperature and holding times were included in the post-harvest fumigation reports.

None of the commodity residue values used in the dietary exposure assessment came from pre-plant soil fumigation field studies. All of the residues were derived from post-harvest fumigation studies provided by the MBIP registrants. The MBIP registrants did supply methyl

bromide pre-plant soil fumigation field studies for labeled commodities (i.e. root crops, Brassica) which indicated that there were not detectable residues (LOD ca. 0.005 - 0.01 ppm) of methyl bromide (Bolsa Research, 1988).

Methyl bromide residues for the commodities used in the dietary exposure assessment were analyzed by contract laboratories (ABC Laboratories, Inc. or Bolsa Reseach, Inc.) or from published government data (California Department of Food and Agriculture laboratory - Fresno, California) and then cited in the submitted studies. The registrant limit of detection (LOD) for methyl bromide ranged from 0.001 ppm (leaf lettuce) to 0.05 ppm (raw apple/grape and cheese). Most of the analyzed commodities had a residue LOD of 0.01 ppm depending on the commodity or processed food form and the age of the residue study (Table 1). The registrant methyl bromide residues were derived using the King, *et al.* (1981) rapid head-space assay method. Methyl bromide raw and processed agricultural commodity residue data used to conduct the DPR dietary exposure analyses are presented in Table 1. When a commodity did not have any residue data, a residue value from another commodity in the same or similar USEPA "crop group" was used as a surrogate representative. For example, carrot was used as the surrogate commodity residue to represent other root crop vegetables (USEPA crop group 1 - root vegetables) such as garden beets and rutabagas (CFR, 1999).

The Health Assessment Section (HAS) of the Medical Toxicology Branch of the DPR has a set of guidelines to help interpret and determine what data sources (field study or market basket) and which measures (highest, average, etc.) of the residues to use to represent the anticipated acute and chronic dietary exposure pesticide residue levels. All the residue data used in the dietary exposure assessment came from registrant field trial, post harvest fumigation studies. No registrant or government regulatory agencies market basket survey residue data were used.

The DPR default guideline is to select the highest detected residue for a raw agricultural commodity (i.e., whole apple, peach, etc.) or the acute average for mixtures (juices, flour, etc.) to represent a commodity for acute dietary exposure. The highest detected residue value for each RAC was selected since none of the registrant studies had more than 15 analyzed samples. The acute average was used to represent acute mixtures and consisted of a simple average of all the detected values together with the non-detectable residues reported at the limit of detection (LOD).

The chronic residue values in the dietary exposure assessment used the average of all the reported residues for both the raw agricultural commodities (i.e., whole apple, peach, etc.) and mixtures (juices, oils, flour, etc.). The chronic average consisted of a simple average of all the utilized residue values in the study. Any non-detect residues were reported as 1/2 the LOD.

All of the residue values used in the dietary exposure assessment were derived from composited samples. The analyzed replicate subsamples were taken from composites of multiple, randomized selections which were equally distributed within the fumigated commodities. These subsamples range from several grams to several pounds (five pounds), depending on the commodity. Commodities which have liquid food forms (e.g. juices, oils) also used the same sampling methodology.

B. Commodity Residue Studies

Over 230 commodities and food forms were included and analyzed in both the acute and chronic portions of the DPR dietary exposure assessment. The residue information presented in Table 1 is in summary form for most of the commodities analyzed in the dietary exposure assessment. Commodities which are major contributors to the dietary exposure are discussed in greater detail.

Walnut

Raw, dried walnut can be a very significant dietary exposure contributor to the Pacific region of the U.S. (ca. 40%), non-Hispanic other (ca. 32%), and children 1-6 years (ca. 33%) population subgroups if methyl bromide is applied. Dried walnuts, both the bulk and packaged forms, are generally consumed raw. The majority of raw, dried walnuts consumed in the United States are produced exclusively in California, with some commercial imports. Domestically grown raw, dried walnuts are generally stored in warehouses for a period of time prior to commercial distribution. It is during this period when fumigation occurs. Methyl bromide could be found as a residue on raw, dried walnuts if applied during warehouse storage. Any raw, dried walnuts imported into the continental United States would require quarantine fumigation as a condition to entry, and therefore, would also be a potential residue source.

The raw, dried walnut residue values were generated from a California Department of Food and Agriculture post-harvest fumigation study cited by the MBIP registrant (Hartsell and Hurley, 1995). A post-production fumigation study using both bulk and packaged raw, dried walnuts, conducted during 1995, was used for the dietary exposure assessment. The LOD value for the study was 0.1 ppm. The maximum label fumigation chamber rate of 4 lbs. per 1000 cubic feet was used with timed measurements taken at 0, 1, 3 and 14 days post-fumigation. The bulk and packaged raw, dried walnut residue values were combined and used for the dietary assessment. This was done because there were differences reported by the authors in sample handling and logistics that may have resulted in the slightly higher residues between the packaged and bulk walnut forms. Therefore, the 14 days post-fumigation combined bulk and packaged residue values were used in the dietary exposure assessment to account for the variations between bulk and packaged forms. The 14 day time period residues ranged from 7.9 - 20.9 ppm (N = 12) with a mean value of 13.3 ppm (SD: 5.47) (Hartsell and Hurley, 1995). The residue values used for raw, dried walnut were 20.9 ppm (highest) for the acute dietary exposure and 13.3 ppm (average) for the chronic dietary exposure.

Almond

Raw, dried almond is a significant dietary exposure contributor to the Pacific region of the U.S. (ca. 12%), non-Hispanic other (ca. 8%), and children 1-6 years (ca. 9%) population subgroups when methyl bromide is applied. Raw, dried almonds are typically consumed raw. The majority of raw, dried almonds consumed in the United States are produced in California, with some commercial imports. Domestically grown raw, dried almonds are generally stored in warehouses for a period of time prior to commercial distribution. It is during this period when fumigation occurs. Methyl bromide could be found as a residue on raw, dried almonds if applied during storage. Any raw, dried almonds imported into the continental United States would

require quarantine fumigation as a condition to entry, and therefore, would also be a potential residue source.

The raw, dried almond residue value was generated from a California Department of Food and Agriculture post-harvest fumigation study cited by the MBIP registrant (Hartsell and Hurley, 1995). A post-harvest fumigation study using both bulk and packaged raw dried almonds, conducted during 1995, was used for the dietary exposure assessment. The LOD value for the study was 0.1 ppm. The maximum label fumigation chamber rate of 4 lbs. per 1000 cubic feet was used with measurements taken at 0, 1, 3 and 15 days post-fumigation. The bulk raw, dried almond residue values were used for the dietary exposure assessment rather than the packaged raw, dried almonds. The bulk form have slightly higher residues and are also the predominant storage form. The 15 days post-fumigation bulk and packaged residue values were all non-detectable. The 3rd day post-fumigation residue values were used in the dietary exposure assessment. The 3rd day post fumigation residues ranged from 10.0 - 15.2 ppm (N = 6) with a mean value of 11.91 ppm (SD: 2.14) (Hartsell and Hurley, 1995). The residue values used for raw, dried almond were 15.2 ppm (highest) for the acute dietary exposure and 11.9 ppm (average) for the chronic dietary exposure.

Raisin

Another significant dietary exposure contributor for the Non-Hispanic-Others (ca. 9%), non-nursing infants (ca. 13%) and children 1-6 years (ca. 17%) population subgroups is raisin. Raisins are typically consumed raw. The majority of raisins consumed in the United States are grown and dried in California. Domestically grown raisins are routinely stored in warehouses before distribution and sales. These warehoused raisins could be treated with methyl bromide during storage. Methyl bromide could be found as a residue on raisins if applied during storage. Any raisins imported into the continental United States would also require quarantine fumigation as a condition to entry.

The raisin residue value was generated from a registrant post-harvest fumigation study (Hartsell and Hurley, 1993). A post-production fumigation study using both bulk and packaged raisins, conducted during 1993, was used for the dietary exposure assessment. The LOD value for the study was 0.01 ppm. The maximum label fumigation chamber rate of 4 lbs. per 1000 cubic feet was used with measurements taken at 0, 1 and 3 days post-fumigation. The bulk raisin residue values were used for the dietary assessment rather than packaged raisins because bulk raisins are the predominate form stored. The 3rd day post-fumigation residue values were used in the dietary exposure assessment. These residues ranged from 0.64 - 0.77 ppm (N = 6) with a mean value of 0.71 ppm (SD; 0.064) (Fieser and Noland, 1993). The post- fumigation residue values used for raisins were 0.77 ppm (highest) for the acute dietary exposure and 0.71 ppm (average) for the chronic dietary exposure.

Pineapple

Raw pineapple is a potentially significant source of dietary exposure contribution for the Pacific region of the United States (ca. 9%), Non-Hispanic-Other (ca. 12%), and children 1-6 years (ca. 5%) population subgroups. Because pineapple is an imported commodity into the continental United States, quarantine treatments, including fumigation, are required as a

condition to product entry. Methyl bromide residues could be found since pineapple is routinely consumed in the raw form and not subject to processing that would decrease residue levels.

The raw pineapple residue value was generated from a registrant post-harvest fumigation study (Fieser and Conrath, 1993f). A single post-harvest pineapple fumigation study was conducted during 1993. The LOD value for the study was 0.01 ppm. The maximum label fumigation chamber rate of 4 lbs. per 1000 cubic feet was used with measurements taken at 0, 4, 8 and 24 hours post-fumigation. The 24 hour residues ranged from 2.21 - 3.86 ppm (N = 6) with a mean value of 2.98 ppm (SD; 0.683) (Fieser and Conrath, 1993f). The residue values used for raw pineapple were 3.86 ppm (highest) for the acute exposure and 2.98 ppm (average) for the chronic dietary exposure.

Grape

Another significant dietary exposure contributor for the nursing infants population subgroup (ca. 52%) is raw grape. Fresh table grapes are typically consumed raw. The vast majority of fresh table grapes consumed in the United States are grown domestically; however, a significant tonnage is imported primarily during the winter months. Domestically grown fresh table grapes are unlikely to be stored in warehouses for any length of time before distribution, and therefore, would not likely be exposed to methyl bromide storage fumigation. The only exceptions would be to meet quarantine requirements for interstate commerce to exclude pests (i.e. glassy-winged sharpshooter). Fresh table grapes imported into the United States would require quarantine fumigation as a condition to product entry and sale. Imported table grapes would be treated with methyl bromide prior to United States distribution. Therefore, methyl bromide could be found as a residue on imported table grapes.

The raw grape residue values were generated from a post-harvest fumigation study (Fieser and Noland, 1993). There was also a quarantine fumigation study for imported Chilean fruits (including grape), as a requirement for importation into the United States (Marulli and Lee, 1993). In the Chilean import study, the maximum time in which methyl bromide residues were measured was 24-hours. The actual post-fumigation time would likely be longer because the grapes would be fumigated and off-gassed prior to export from Chile and arrival in the United States. Therefore, the domestic table grape post-harvest fumigation study (Fieser and Noland, 1993) was used for the dietary exposure assessment. The LOD value for the study was 0.01 ppm. The maximum label fumigation chamber rate of 4 lbs. per 1000 cubic feet was used with measurements taken at 0, 4, 8 and 24 hours post-fumigation. The 24 hour residues ranged from 1.2 - 2.14 ppm (N = 6) with a mean value of 1.62 ppm (SD; 0.349). The 24-hour post-fumigation residue values were used in the dietary exposure assessment. The residue values used for raw grape were 2.14 ppm (highest) for the acute dietary exposure and 1.62 ppm (average) for the chronic dietary exposure.

Apple

A significant dietary exposure contributor for the nursing infants population subgroup (ca. 7%) is raw apple. Methyl bromide, when applied, likely could be found as a residue because apples are routinely consumed raw. The majority of apples consumed in the United States are primarily domestically grown; however, a significant amount is imported from Chile (Marulli and Lee, 1993). Domestically grown apples are frequently stored in post-harvest warehouses

before distribution and therefore could be treated with methyl bromide. Methyl bromide could be found as a residue on apples if applied during storage. Any fresh apples imported into the continental United States would also require quarantine treatment as a condition to product entry.

The raw apple residue value was generated from a registrant post-harvest fumigation study (Fieser and Conrath, 1993f). There was also a quarantine fumigation study for imported Chilean fruits (apple not measured) as a requirement for importation into the United States (Marulli and Lee, 1993). A single post-harvest apple fumigation study was conducted during 1993. The LOD value for the study was 0.01 ppm. The maximum label fumigation chamber rate of 4 lbs. per 1000 cubic feet was used with measurements taken at 0, 4, 8 and 24 hours post-fumigation. The 24 hour residues ranged from 3.46 - 6.77 ppm (N = 7) with a mean value of 5.46 ppm (SD; 1.1) (Fieser and Conrath, 1993f). The 24-hour post-fumigation residue value was used in the dietary exposure assessment. The residue value used for raw apple was 6.77 ppm (highest) for the acute dietary exposure and 5.46 ppm (average) for the chronic dietary exposure.

Table 1. Summary of Methyl Bromide Residues

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Alcohol (distilled)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct	1%
Allspice	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, acute = LOD of sampling	--
Almond	MBIP (Hartsell,Hurley,1995)	15.2	11.9	6	Bulk nuts, LOD=0.01 ppm, processed pct shown	1%
Aloe vera (juice)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct	1%
Anise	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, 192 hrs post-fume	--
Apple, fresh (+ dried)	MBIP (Fieser,Conrath,1993)	6.77	5.46	7	24 hr. post fumigation, Acute = hi num (#)	1 or 7%
Apple, juice	MBIP (Fieser,Conrath,1993)	5.46	5.46	7	Mixture = acute average, processed pct	1%
Apricot (fresh/juice)	MBIPsur (H. Lee, 1993)	0.025	0.022	6	Peach as surrogate, processed pct shown	1%
Apricot (dried)	MBIPsur (Hartsell,Hurley,1995)	1.33	1.09	6	Prune as surrogate, cookd pct shown	1%
Artichoke (Jeru.)	MBIPsur (H. Lee, 1993)	2.34	1.49	6	Carrot as surrogate, acute (Ac) = hi #	--
Asparagus	MBIP (Fieser,Conrath,1993)	0.021	0.016	6	Ac = hi #, 1 day Post Fume, canned pct shown	1%
Avocado	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not labeled, warehouse fumigation pct	1%
Banana (dried only)	MBIP (Eickhoff *et al.*, 1998)	1.33	1.09	-	Warehouse fumigation @	1%
Banana (fresh form)	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Non labeled use, presume warehouse fumigation	1%
Barley (raw/dried only)	MBIPsur (Fieser,Conrath,1993)	0.98	0.98	6	Wheat as surrogate (mixture).	1%
Basil	MBIPsur (Ussary *et al*, 1993)	1.63	1.63	4	Raw sage as surrogate, 192 hrs post-fumigation	--
Bay leaf	MBIPsur (Ussary *et al*, 1993)	1.63	1.63	4	Raw sage as surrogate, 192 hrs post-fumigation	--
Bean, dried	MBIP (Fieser,Conrath,1993)	0.65	0.51	6	Ac = hi #, LOD=0.01ppm, processed pct shown	1%
Bean, succulent	MBIP (Fieser,Conrath,1993)	0.007	0.0035	6	Ac = LOD (0.007ppm), processed pct shown	1%
Beechnut	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Beet root (garden)	MBIPsur (H. Lee, 1993)	1.1	0.99	6	Sugar beet, .03Adjustment Factor [d](AF#1), cooked=	1%
Bitter melon	MBIPsur (Fieser,Conrath,1993)	0.15	0.11	6	Squash as surrogate, 0.47 AF#1	--
Blackberry	MBIP (Fieser, Noland,1993)	0.36	0.309	6	Acute = hi #, 0.16 AF#1, processed pct shown	1%
Blueberry	MBIP (Fieser,Conrath,1993)	0.38	0.22	6	Blueberries, Ac=hi #, 0.16 AF#1, process % shown	1%
Boysenberry	MBIPsur (Fieser, Noland,1993)	0.36	0.309	6	Blkberry as surrogate, 0.16 AF#1, process% shown	1%
Brazil nut	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Broccoli	MBIP (Fieser, Conrath,1993)	0.008	0.004	6	Non detect, Ac=LOD, 0.47 AF#1,process % shown	1%
Brussels Sprout	MBIPsur (Fieser, Conrath,1993)	0.008	0.004	6	Broccoli as surrogate, 0.47 AF#1.	--
Buckwheat	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect. Warehouse fumigation	1%
Burdock	MBIPsur (H. Lee, 1993)	2.34	1.49	6	Carrot as surrogate residue.	--
Butter nut	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Cabbage (all)	MBIP (Fieser, Conrath,1993)	0.608	0.346	15	Acute = hi #, 0.47 AF#1, canned/cured pct shown	1%

(continued)

Table 1. Summary of Methyl Bromide Residues (Continued)

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Canola oil	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect. Warehouse fumigation	1%
Caraway	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, 192 hrs post-fume	--
Carob	MBIPsur (H. Lee, 1993)	0.069	0.069	3	Chocolate as surrogate. processed pct % shown	1%
Carrot	MBIP (H. Lee, 1993)	2.34	1.49	6	Acute = hi #, 0.03 AF#1, processed pct% shown	1%
Cashew nut	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Cassava	MBIPsur (H. Lee, 1993)	1.56	1.31	6	Potato as surrogate. 0.03 AF#1, process % shown	1%
Cassia	MBIP (Ussary *et al*, 1993)	0.92	0.92	4	Ac = avg, LOD=0.05 ppm, 192 hrs pst-fumigation	--
Cattle (fat, meat)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Cattle includes veal, warehouse fumigation	1%
Cattle (kidney, mbyp)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Cattle (liver)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Cauliflower	MBIP (Fieser, Conrath,1993)	0.027	0.022	6	Acute = hi #, 0.47 AF#1, processed pct % shown	1%
Celery	MBIP (H. Lee, 1993)	0.07	0.042	8	1 day post fumigation, processed forms pct shown	1%
Chicory	MBIPsur (H. Lee, 1993)	0.07	0.042	8	Celery as surrogate RAC.	--
Cherry (raw/juice)	MBIP (H. Lee, 1993)	0.058	0.031	7	Ac = hi #, avg 4 juice, 0.07/0.04 AF#1, processed =	1%
Cherry (dried fruit)	MBIPsur (Hartsell,Hurley,1995)	1.33	1.09	6	Dried prune as surrogate, processed pct % shown	1%
Chestnut	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detected residues.	--
Chicory	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, 192 hrs post-fumigation	--
Chives	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, processed forms fumigation pct shown	1%
Chocolate	MBIP (Lee, Natta, 1993)	0.069	0.069	3	Mix = acute avg., 27 days PF, process pct shown	1%
Cinnamon	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, 192 hrs post-fume	--
Citrus citron	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect. 0.29 AF#1. warehouse fumigation	1%
Clove	MBIPsur (Ussary *et al*, 1993)	1.23	1.23	4	Onion powder as surrogate,192 hrs pst-fumigation	--
Cocoa butter	MBIP (Lee, Natta, 1993)	0.0	0.0	3	Not detected, 27 days P-fume, process pct% shown	1%
Coconut (all forms)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not labeled, warehouse fumigation pct =	1%
Coffee	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not labeled, not detected, warehouse fumigation	1%
Collards	MBIPsur (Fieser, Conrath,1993)	0.027	0.022	6	Cauliflower as surrogate.	--
Coriander	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, 192 hrs post-fumigation	--
Corn (grain)	MBIP (Fieser, Conrath,1993)	3.6	2.74	6	Ac=hi #, cooked is 0.04 AF#1, all forms pct shown	1%
Corn (grain oil)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Residues not detected.	--
Corn (pop)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Residues not detected.	--
Corn (sweet)	MBIP (Fieser, Conrath,1993)	0.19	0.099	7	Acute = hi #, processed PCT fumigation is:	1%
Cottonseed meal (continued)	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Not labeled, all cooked forms w/o residues, all pct	1%

Table 1. Summary of Methyl Bromide Residues (Continued)

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Cottonseed oil	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct shown	1%
Cranberry (+ juice)	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Non labeled use, presume warehouse fumigation	1%
Cress (garden/upland)	MBIPsur (H. Lee, 1993)	0.011	0.0048	9	leaf lettuce as surrogate.	--
Cucumber	MBIP (Fieser,Conrath, 1993)	3.4	2.7	6	Ac = hi #, 0.47 AF#1, 0.01 ppm LOD. All pct.	1%
Cumin	MBIP (Ussary *et al*, 1993)	1.92	1.92	4	Ac = avg, LOD=0.05 ppm, 192 hrs pst-fumigation	--
Currant	MBIPsur (Fieser, Noland,1993)	2.14	1.62	6	Grape as surrogate, 0.01 AF#1, raw pct shown	60%
Dandelion greens	MBIPsur (H. Lee, 1993)	0.011	0.0048	9	Leaf lettuce as surrogate.	--
Date	MBIP (Hartsell,Hurley,1995)	0.67	0.64	6	Ac = hi #, 0.07 AF#1 cooked form, processed shown	1%
Dewberry	MBIPsur (Fieser, Noland,1993)	0.36	0.309	6	Blackberry surrogate, 0.16 AF#1.	--
Dill	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, 192 hrs post-fumigation	--
Egg	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Eggplant	MBIPsur (Fieser, Conrath,1993)	5.33	4.7	6	Tomato as surrogate, 0.33 AF#1, all forms pct	1%
Elderberry	MBIPsur (Fieser, Noland,1993)	2.14	1.62	6	Grape as surrogate, 0.16 AF#1	--
Endive	MBIPsur (H. Lee, 1993)	0.07	0.042	8	Celery as surrogate RAC.	--
Fennel	MBIPsur (H. Lee, 1993)	0.011	0.0048	9	Leaf lettuce as surrogate.	--
Fig (raw & dried)	MBIP (Hartsell,Hurley,1995)	1.7	1.6	6	Ac = hi #, 0.04/0.07 AF#1, cooked pct shown	1%
Filbert (hazelnut)	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Fish (fresh & salt water)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct	--
Flax seed	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct	1%
Garlic	MBIP (Fieser,Conrath:1993)	0.05	0.022	7	Acute = hi #, 0.02 AF#1	--
Gelatin (powdered)	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame spice as surrogate, 192 hrs pst-fume	--
Ginger	MBIPsur (Ussary *et al*, 1993)	1.23	1.23	4	Onion powder as surrogate,192 hrs pst-fume	--
Goat (fat, meat)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, Warehouse fumigation	1%
Goat (kidney, mbyp)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, Warehouse fumigation	1%
Goat (liver)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, Warehouse fumigation	1%
Gooseberry	MBIPsur (Fieser, Noland,1993)	2.14	1.62	6	Grape as surrogate residue, 0.16 AF#1	--
Grape, (fresh fruit)	MBIP (Fieser,Conrath:1993)	2.14	1.62	6	Grape, Ac=hi #, 0.01/ AF#1, proc pct = 1%, raw =	60%
Grape, juice	MBIP (Fieser,Conrath:1993)	1.62	1.62	6	Grape mixture, 0.09/0.01/0.0 AF#1 used.	1%
Grape, raisin (raw)	MBIP (Hartsell,Hurley,1995)	0.77	0.71	6	Ac=hi #, AF#1 = 0.09, processed pct % =	1%
Grapefruit (fruit/peel)	MBIP (Fieser,Conrath:1993)	1.16	0.87	7	Acute = hi #, 0.29 AF#1 used, proc pct = 1%, raw =	5%
Grapefruit (juice) (continued)	MBIP (Fieser,Conrath:1993)	0.87	0.87	7	Ac = mix, from fruit, 0.36/0.12 AF#1 used, all pct =	1%

Table 1. Summary of Methyl Bromide Residues (Continued)

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Guar bean	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not labeled, non detect, warehouse fumigation	1%
Guava	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Non labeled use, presume warehouse fumigation	1%
Hickory nut	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Honey	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Not labeled, presume warehouse fumigation	1%
Horse (all)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Horseradish	MBIPsur (Ussary *et al*, 1993)	1.23	1.23	4	Onion powder as surrogate,192 hrs pst-fume	--
Huckleberry	MBIPsur (Fieser, Noland,1993)	2.14	1.62	6	Grape as surrogate residue, 0.16 AF#1	--
Jackfruit	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detected residues, warehouse fumigation	1%
Juneberry	MBIPsur (Fieser, Noland,1993)	2.14	1.62	6	Grape as surrogate residue, 0.16 AF#1	--
Kale	MBIPsur (Fieser, Conrath,1993)	0.608	0.346	15	Cabbage as surrogate residue	--
Kiwi	MBIP (Fieser, Conrath,1993)	4.2	3.9	6	Acute = hi #, processed pct value shown	6%
Kohlrabi	MBIPsur (Fieser, Conrath,1993)	0.608	0.346	15	Cabbage as surrogate residue	--
Kumquat	MBIPsur (Fieser, Noland,1993)	1.55	1.36	6	Lemon as surrogate residue	--
Leek	MBIPsur (Fieser,Conrath,1993)	1.2	0.84	6	Bulb onion as surrogate, 0.02 AF#1	--
Lemon (fruit/peel)	MBIP (Fieser, Noland,1993)	1.55	1.36	6	Ac = hi #, 0.29/0.12 AF#1. Process = 1%, raw =	5%
Lemon (juice)	MBIP (Fieser, Noland,1993)	1.36	1.36	6	Mix = ac avg, 0.36/0.29/0.12 AF#1. Process shown	1%
Lentil (whole/split)	MBIPsur (Fieser, Conrath, 1993)	0.004	0.002	6	Succulent pea as surrogate residue.	--
Lettuce, head	MBIP (H. Lee, 1993)	0.26	0.16	6	Ac = hi #, 1 day post fumigation	1%
Lettuce, leaf	MBIP (H. Lee, 1993)	0.011	0.0048	9	Ac = hi #, 1 day post fumigation	--
Lime (fruit/peel)	MBIPsur (Fieser, Noland,1993)	1.55	1.36	6	Lemon as surrogate. Raw fruit pct shown	14%
Lime (juice)	MBIPsur (Fieser, Noland,1993)	1.36	1.36	6	Lemon as surrogate. Juice based on raw fruit	1%
Loganberry	MBIPsur (Fieser, Noland,1993)	0.36	0.309	6	Blkberry as surrogate, 0.16 AF#1.	--
Macadamia nut	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Mace	MBIPsur (Ussary *et al*, 1993)	1.63	1.63	4	Sage as surrogate, 192 hrs post-fumigation.	--
Mango	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Non labeled use, presume warehouse fumigation.	1%
Maple syrup	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct	1%
Marjoram	MBIPsur (Ussary *et al*, 1993)	1.63	1.63	4	Sage as surrogate, 192 hrs pst-fume, process	--
Meat (game species)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detected, warehouse fumigation.	--
Melon (all varieties)	MBIP (Fieser,Conrath,1993)	1.9	1.53	6	Ac = hi #, cantaloupe, 0.47 AF#1. Fumigation %	1%
Milk (fat/nonfat solids)	MBIP (Eickhoff *et al.*, 1998)	0.125	0.125	-	Raw, 0.05 AF#1, processed = 0 resi. Fume%	1%
Milk (sugar)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Millet (continued)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%

Table 1. Summary of Methyl Bromide Residues (Continued)

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Mulberry	MBIPsur (Fieser, Noland,1993)	2.14	1.62	6	Grape as surrogate residue, 0.16 AF#1	--
Mung bean	MBIPsur (Fieser,Conrath,1993)	0.007	0.0035	6	Succulent beans as surrogate.	--
Mushroom	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, acute = LOD, warehouse fumigation.	1%
Mustard seed	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, processed pct shown	1%
Nectarine	MBIPsur (H. Lee, 1993)	0.025	0.022	6	Peach as surrogate. Fresh pct value shown.	45%
Nutmeg	MBIPsur (Ussary *et al*, 1993)	4.14	4.14	4	Sesame seed as surrogate, 192 hrs post-fume	--
Oat (includes bran)	MBIPsur (Fieser,Conrath,1993)	0.98	0.98	6	Wheat as surrogate (mixture).	1%
Okra	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non labeled, non detect @ LOD, processed pct =	1%
Olive	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected @ LOD, process% fumigation	1%
Onion, bulb	MBIP (Fieser,Conrath,1993)	1.2	0.84	6	Ac = hi #, 0.02 AF#1, processed pct shown	1%
Onion, green	MBIP (Fieser,Conrath,1993)	0.012	0.005	7	Ac = hi #, LOD=0.008ppm, processed pct shown	1%
Orange (fruit/peel)	MBIP (Fieser, Conrath,1993)	0.99	0.89	6	Ac = hi #, 0.29/0.12 AF#1. Process 1%, raw pct =	5%
Orange (juice)	MBIP (Fieser, Conrath,1993)	0.89	0.89	6	Mix = ac avg, 0.36/0.29/0.12 AF#1. Processed pct =	1%
Oregano	MBIP (Ussary *et al*, 1993)	0.43	0.43	4	Ac = avg, LOD=0.05 ppm, 192 hrs pst-fume	--
Palm heart	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct =	1%
Palm oil	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct =	1%
Papaya (juice & pulp)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not labeled, non detect, warehouse fumigation pct =	1%
Paprika	MBIPsur (Ussary *et al*, 1993)	0.22	0.22	4	Capsicum powder as surrogate, dried form pct =	1%
Parsley	MBIPsur (H. Lee, 1993)	0.011	0.0048	9	Leaf lettuce as surrogate.	--
Parsnip	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, 0.03 AF#1.	--
Passion fruit (nectar)	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Not labeled, not detected, cooked pct shown	1%
Peach	MBIP (H. Lee, 1993)	0.025	0.022	6	Acute = hi #, juice = 0. Canned pct =1% / fresh pct =	45%
Peanut (bulk shelled)	MBIPsur (Hartsell,Hurley,1995)	20.9	13.3	12	Walnut as surrogate nut, 14 day post-fumigation	1%
Peanut (whole nut & oil)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected.	--
Peanut butter	MBIP (Ussary *et al.*, 1995)	0.025	0.025	3	Ac = mixture, use LOD, warehouse fumigation	1%
Pear (fresh & dried)	MBIP (Fieser, Conrath, 1993)	3.88	3.11	7	Acute = hi #, 0.01/0.04 AF#1, dried pct shown	1%
Pear (juice)	MBIP (Fieser, Conrath, 1993)	3.11	3.11	7	Ac. mix = avg , 0.04/0.1 AF#1, processed pct shown	1%
Peas (dried)	MBIP (Fieser, Conrath, 1993)	0.0	0.0	6	All forms are cooked with no residues.	--
Peas (succulent)	MBIP (Fieser, Conrath, 1993)	0.004	0.002	6	Acute = LOD, processed pct fumigation showm	1%
Pecan nut (shelled)	MBIP (Hartsell,Hurley,1995)	4.7	2.9	6	Ac = hi #, 9 days post fume, processed pct shown	1%
Pepper (black, ground)	MBIP (Ussary *et al*, 1993)	1.65	1.65	4	Ac = avg, LOD=0.05 ppm, 192 hrs pst-fume	--
Pepper (bell & chili) (continued)	MBIP (H. Lee, 1993)	0.46	0.41	6	Ac = hi #, 0.33 AF#1, percent crop treated =	1%

Table 1. Summary of Methyl Bromide Residues (Continued)

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Peppermint (leaf)	MBIPsur (Ussary *et al*, 1993)	1.63	1.63	4	Sage as surrogate, 192 hrs pst-fumigation	--
Peppermint (oil)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, processed pct % shown	1%
Pimento	MBIPsur (H. Lee, 1993)	0.46	0.41	6	Bell pepper as surrogate, processed pct =	1%
Pineapple (fresh)	MBIP (Fieser, Conrath,1993)	3.86	2.98	6	Ac. = hi #, 0.04 AF#1, process pct = 1%, raw % =	40%
Pineapple (dried)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, processed pct% =	1%
Pineapple (juice)	MBIP (Fieser, Conrath,1993)	0.0	0.0	6	Cooked = 0 residue, 0.04 AF#1, processed pct =	1%
Pistachio nut	MBIPsur (Hartsell,Hurley,1995)	15.2	11.9	6	Almond as surrogate nut residue.	--
Plantain	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Not labeled, not detected, warehouse fumigation	1%
Plum (fruit)	MBIP (H. Lee, 1993)	2.78	2.45	7	Ac. = hi #, 0.07/0.04 AF#1, raw fruit pct shown	68%
Pomegranates	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Not labeled, not detected, processed pct% shown	1%
Poppy (seed)	MBIP (Ussary *et al*, 1993)	2.43	2.43	4	Acute = average residue	--
Pork (fat, meat)	MBIP (Ussary *et al.*, 1995)	0.804	0.804	2	Country ham residues, warehouse fumigation	1%
Pork (kidney, mbyp)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Pork (liver)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Potato	MBIP (H. Lee, 1993)	1.56	1.31	6	Ac = hi #, 0.03 AF#1, processed pct % =	1%
Poultry (fat, meat)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect (N.D.), Cooked = 0 value, fume	1%
Poultry (kidney, mbyp)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	N.D., cooked = 0, warehouse fume	1%
Poultry (liver)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	N.D., cooked = 0, warehouse fume	1%
Prune	MBIP (Hartsell,Hurley,1995)	1.33	1.09	6	Ac. = hi #, 0.04 AF#1, cooked pct = 1%, raw pct =	13%
Pumpkin	MBIPsur (Fieser,Conrath,1993)	0.15	0.11	6	Squash as surrogate, processed forms pct	1%
Quince	MBIPsur (Fieser,Conrath,1993)	6.77	5.46	7	Apple as surrogate, percent crop treated shown	7%
Rabbit (all)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, Warehouse fumigation	1%
Radish (root)	MBIP (H. Lee, 1993)	0.015	0.012	7	Ac = hi #, 0.03 Adjustment factor #1	--
Raspberry	MBIPsur (Fieser, Noland,1993)	0.36	0.309	6	Blackberry surrogate, 0.16 AF#1, processed forms =	1%
Rice (grain)	MBIP (Fieser, Noland,1993)	0.405	0.405	6	Ac = avg resi #, warehouse fume pct rate @	1%
Rosemary	MBIP (Ussary *et al*, 1993)	0.0	0.0	4	Cooked form 0 residue, processed form pct	1%
Rutabaga (root)	MBIPsur (H. Lee, 1993)	2.34	1.49	6	Carrot as surrogate residue, 0.03 AF#1.	--
Rutabaga (greens)	MBIPsur (H. Lee, 1993)	0.011	0.0048	9	Leaf lettuce as surrogate residue	--
Rye (rough/germ only)	MBIPsur (Fieser,Conrath,1993)	0.98	0.98	6	Wheat as surrogate (mixture).	1%
Rye (flour)	MBIPsur (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non Detect, warehouse fumigation	1%
Safflower oil	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct =	1%
Sage	MBIP (Ussary *et al*, 1993)	0.0	0.0	4	Cooked = 0 residue, raw form as leaf surrogate	--
Salsify (continued)	MBIPsur (H. Lee, 1993)	2.34	1.49	6	Carrot as surrogate residue, 0.03 AF#1.	--

Table 1. Summary of Methyl Bromide Residues (Continued)

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Savory	MBIPsur (Ussary *et al*, 1993)	1.63	1.63	4	Raw sage as surrogate residue	--
Seaweed	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not labeled, non detect. dried, raw form pct	1%
Seeds (edible)	MBIP (Eickhoff *et al.*, 1998)	0.0	0.0	-	Non labeled use, presume warehouse fumigation	1%
Sesame (oil)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct =	1%
Sesame (seed)	MBIP (Ussary *et al.*, 1993)	4.14	4.14	4	Acute=avg resi. Raw form as seed surrogate	--
Shallots	MBIPsur (Fieser,Conrath,1993)	1.2	0.84	6	Onion as surrogate residue, 0.02 AF#1	--
Sheep (fat, meat)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Sheep (kidney, mbyp)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Sheep (liver)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Sorghum (grain)	MBIP (Fieser, Conrath, 1993)	4.51	4.51	7	Acute = mixture. 2 days post-fume.	1%
Soybean	MBIP (Fieser, Conrath, 1993)	1.06	1.06	7	Acute = average #. Cooked forms pct shown	1%
Soybean oil	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detected. Warehouse fumigation pct shown	1%
Spearmint (leaf)	MBIPsur (Ussary *et al*, 1993)	1.63	1.63	4	Sage as surrogate, 192 hrs pst-fume.	--
Spearmint (oil)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, processed pct %shown	1%
Spinach	MBIP (H. Lee, 1993)	0.004	0.002	6	Non detect, Ac = LOD. processed pct shown	1%
Squash, summer/winter	MBIP (Fieser, Conrath, 1993)	0.15	0.11	6	Ac =hi #, 0.47 AF#1, 0.01 ppm LOD, Proc pct =	1%
Strawberry (& juice)	MBIP (Fieser, Conrath: 1993)	0.017	0.013	6	Ac=hi #, 0.16/0.09 AF#1. processed pct shown	1%
Sugar beet (refined sugar)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, Acute = LOD, warehouse fume	1%
Sugar cane (refined sugar)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, Acute = LOD, warehouse fumigation	1%
Sunflower (oil & seed)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct shwon	1%
Sweet Potato	MBIPsur (H. Lee, 1993)	0.0	0.0	-	All cooked forms have 0 residue, proc.% shown	1%
Swiss Chard	MBIPsur (H. Lee, 1993)	0.011	0.0048	9	Leaf lettuce as surrogate.	--
Tangelo	MBIPsur (Fieser, Conrath,1993)	0.99	0.89	6	Orange fruit as surrogate residues	1%
Tangerine	MBIPsur (Fieser, Conrath,1993)	0.99	0.89	6	Orange fruit as surrogate residues	1%
Taro root	MBIPsur (H. Lee, 1993)	2.34	1.49	6	Carrot as surrogate, 0.03 AF#1	--
Taro, dried	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Tea	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not labeled, not detected, warehouse fumigation	1%
Thyme	MBIPsur (Ussary *et al*, 1993)	0.0	0.0	-	Cooked form has 0 residue	--
Tomato (whole fruit)	MBIP (H. Lee, 1993)	5.33	4.7	6	Ac = hi #, 0.33 AF#1, percent crop treated value =	1%
Tomato (processed forms) (continued)	MBIP (H. Lee, 1993)	0.0	0.0	-	Cooked forms have 0 residues	1%

Table 1. Summary of Methyl Bromide Residues (Continued)

RAC	Source [a] (Reference/Year)	Residue (PPM) Acute	Chronic	N [b]	Additional Information	PCT [c]
Towelgourd	MBIPsur (Fieser,Conrath,1993)	0.15	0.11	6	Squash as surrogate, 0.47 AF#1.	--
Turmeric	MBIPsur (Ussary *et al*, 1993)	0.0	0.0	-	Cooked form has 0 residue	--
Turnip (greens)	MBIP (H. Lee, 1993)	0.0	0.0	-	Cooked forms have 0 residues, process pct shown	1%
Turnip (root)	MBIP (H. Lee, 1993)	0.36	0.24	7	Ac = hi #, 0.03 AF#1, process pct % shown	1%
Vinegar	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, processed pct % shown	1%
Walnut (bulk shelled)	MBIP (Hartsell,Hurley,1995)	20.9	13.3	12	Ac = hi #, 14 day post fume, processed pct shown	1%
Waterchestnut	MBIP (H. Lee, 1993)	0.0	0.0	-	Cooked forms have 0 residues, cooked pct shown	1%
Wheat (bran only)	MBIP (Fieser,Conrath,1993)	0.98	0.98	6	Mixture = acute average	1%
Wheat (germ oil)	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Non detect, warehouse fumigation	1%
Yambean Tuber	MBIPsur (H. Lee, 1993)	1.56	1.31	6	Potato as surrogate residue, 0.03 AF#1	--
Yeast	MBIP (Eickhoff *et al.*, 1998)	0.01	0.005	-	Not detected, warehouse fumigation pct shown	1%
Youngberry	MBIPsur (Fieser, Noland,1993)	0.36	0.309	6	Blackberry surrogate, 0.16 AF#1, processed shown	1%

List of Abbreviations: **LOD**, Limit of Detection; **hi num**, high number; **pct**, percentage of the crop treated; **Ac**, acute; **Jeru**, Jerusalem artichoke.
a/ **MBIP** = Methyl Bromide Industry Panel residue studies, **MBIPsur** = surrogate data used (similar crop types) from the registrant field residue study.
b/ **N** = The number of RAC composite samples analyzed from the selected submitted studies. N.D. = non detected.
c/ **PCT** = Percent of the crop treated adjustment made to chronic dietary residues when sufficient use data are available.
d/ **AF#1** = Default Adjustment Factor #1 value from the commodity residue file has been modified with processing or residue dissipation data.

IV. Residue Adjustments

A. Processing and Dissipation Effects

The TAS® Dietary Exposure program residue file contains two adjustment factors (AF#1 and AF#2) which can be used to modify the residue concentrations used in the assessment. Adjustment factor #1 (AF#1 in Table #1) in the program commodity residue file is set to a specific default value depending on the commodity and its food form (fresh, dried, etc.). The default values range from 1.0 for most raw commodities to14.3 for dried tomato and are based on those values used by USEPA in its DRES® (Dietary Residue Evaluation System) dietary exposure program (TAS, 1999). These default values account for the potential concentration of pesticide residues in processed foods (e.g. concentrated fruit juices, peels and dried forms) due primarily to the removal of water (TAS, 1999). Since methyl bromide is relatively volatile, the concentration of residues from processing procedures such as drying, is unlikely. There potentially may be a concentration of methyl bromide as a result of repeated warehouse fumigation of some oily crops such as tree nuts and peanuts. This situation could occur if the nuts are not sealed in airtight containers impermeable to methyl bromide. All of the stored commodities reported in Table 1 were in their final market forms (fresh and dried fruit, nuts, canned products, etc.) and were in warehouses awaiting market distribution.

The Methyl Bromide Industry Panel (MBIP) registrants provided a number of commodity studies showing methyl bromide dissipation factors after post harvest fumigation applications (Eickhoff *et al.*, 1998). Also included was information related to the effects of commodity processing on methyl bromide residues. Most of the juices and other processed forms were based on residues measured after fumigation of the raw, whole fruit (i.e. apple, orange); therefore, processing factors dependent on the extent of preparation of the raw commodity into a processed form were also determined. Most methyl bromide residues are reduced to below the detection limit after various forms of processing (peeling, boiling, pasteurizing, cooking and baking) are performed on the raw commodity (Eickhoff *et al.*, 1998). Also, any raw commodity that was processed into another food form (baked, cooked, concentrated juice, etc.) and then sealed into a can would be impermeable to fumigation exposure. Therefore, AF#1 was not used for both canned and processed food forms for some specific commodities in the dietary exposure assessment.

Commodities destined for commercial processing (prepared tomato products, instant potatoes, concentrated fruit juices, etc.) are not likely to receive fumigation, but instead proceed directly to the commercial processor. However, if these pre-commercially processed commodities did receive a fumigation treatment while in their raw form, the AF#1 processing and dissipation reductions presented in Table 1 would still apply.

Table 2 contains the list of modifications made to adjustment factor #1 for a number of commodities analyzed in the dietary exposure assessment. The changes can include both the effects of processing and methyl bromide residue dissipation over time. Dissipation or processing residue reduction data, when available for one commodity in a crop group, were applied to related

commodities in that crop group. For example, the potato dissipation value of 0.03 (i.e. 3% of the original residue level) was used for all other tuber crops in the same crop group and appears in the residue file as an adjustment factor #1 change.

B. Percent of the Crop Treated

The current DPR chronic dietary exposure analysis default assumption is that 100% of any commodity is treated with the pesticide under consideration. When data are available that indicate less than 100% of a commodity is treated with a specific pesticide, exceptions to the default assumption are made on an individual crop and pesticide combination basis. The percent crop treated adjustment was not made to any commodities for the acute non-distributional dietary exposure analysis. The DPR premise is that a reasonable probability exists that any commodity analyzed may have a pesticide residue during an acute exposure period. The second adjustment factor (AF#2) in a chronic exposure analyses is always set to a default percent of the crop treatment value of 1.0 (assumes 100% of the crop treated). This value can be changed to less than 1.0 if percent of the crop treated commodity data are available. The percent of the crop treated adjustment is made if multiple year data indicate that less than 100% of a crop is treated with the pesticide on an annual or longer basis. An adjustment factor #2 value of 0.05, for example, would indicate that only 5% of the specified crop was treated with methyl bromide either during pre-plant or post-harvest fumigation.

The basic assumption in chronic exposure is that people under daily eating patterns would be continuously exposed to the averaged residue level of a pesticide for every labeled commodity for either for 1 year (chronic) or 70 years (lifetime). This exposure level based on an average residue and a 1/2 the non-detect as a residue value does not take into account the fact that a significant amount of a commodity may be untreated with the pesticide under consideration. The actual percentage of the crop treated with a specific pesticide varies from year to year depending upon biotic and abiotic factors. Using the existing percent crop treated data, it is reasonable to reduce the 100% treatment using more realistic pesticide treatment rates and use patterns. Commodities that used residues obtained from registrant field trial or state and federal monitoring data in the chronic dietary exposure assessment were considered for percent of the crop treated adjustments.

The percent of the crop treated adjustment method has been employed for most of the commodities in the chronic dietary exposure assessment. Many of the commodities have reported methyl bromide use at the federal and state levels for pre-plant, post-harvest or quarantine (import/export) activities. There are very little usable and comprehensive use data available from the DPR Pesticide Use Reports, CDFA crop statistics or the USDA Agricultural Field Crops Summary annuals because much of the methyl bromide use is for post-harvest fumigation which is not consistently reported. The MBIP supplied chronic dietary exposure analysis utilized percent of the crop treated (PCT) adjustments based on sales information available to the MBIP registrants. Refer to Table 1 for a list of commodities that have PCT adjustments made to their chronic dietary residues. The PCT adjustment would appear as a less than 1.0 value under the column titled "Adjustment Factor #2" in the TAS® chronic dietary exposure file printout (Appendices B and C).

Table 2. Residue File Adjustment Factor #1 Changes Based on Post Fumigation Dissipation/Processing Effects.

COMMODITY [a]	FACTOR [b]	SOURCE [c]
Apple (whole)	0.01	Apple dissipation data. Post fumigation residue decline curve. The same 0.01x factor was used for pear, crabapple and quince.
Apple juice (raw)	0.1	Raw apple juice processing adjustment. The 0.1x factor used for raw pear/apricot juice.
Apple juice (processed)	0.04	Processed apple juice adjustment used for cooked/canned forms & processed pear juice.
Apricot (processed)	0.04	Processed apple juice adjustment used for cooked/canned apricot food forms.
Apricot (whole)	0.07	Least reduced post fumigation residue dissipation factor used (range: 0.01 - 0.07). Derived from apricot and used as surrogate for the following whole stonefruits: cherry and plum.
Blackberry	0.16	Cane berry (*Rubus* spp.) dissipation. Post fumigation residue decline curve. Same 0.16x factor was used for the other types of cane berries (raspberries etc.).
Broccoli (raw)	0.47	Broccoli dissipation factor. Surrogate for all *Brassica* spp. vegetables.
Cantaloupe (raw)	0.47	Cantaloupe dissipation factor. Surrogate for all melons and other cucurbits.
Cherry (raw)	0.07	Cherry dissipation factor for raw fruit.
Cherry (processed)	0.04	Processing residue adjustment for the cooked/canned food forms.
Citrus (canned/cooked)	0.12	Processing residue adjustment for the cooked or canned food forms. Applied to other cooked/canned food forms of citrus (kumquat, lemon, limes, oranges, tangelos and tangerines).
Citrus (processed)	0.29	Used concentrated citrus juice processing adjustment for the baked/fried food forms. Applied to other baked/fried citrus food forms (kumquat, lemon, limes, oranges, tangelos and tangerines).
Citrus (whole)	0.29	Least reduced post fumigation residue dissipation factor used (range: 0.09 - 0.29). Derived from grapefruit and used as surrogate for all other raw citrus whole fruit and peels (kumquat, lemon, limes, oranges, tangelos and tangerines).
Citrus juice (conc.)	0.12	Cooked/canned concentrated citrus juice processing adjustment. Applied to other conc. citrus juice forms (lemon, limes, oranges,tangelos and tangerines).
Citrus juice (raw)	0.36	Raw citrus juice processing adjustment. Applied to other raw citrus juice forms (lemon, limes, oranges, tangelos and tangerines).
Cranberry	0.16/0.09	Cane berry value. Raw grape juice factor as surrogate for cranberry juice.
Grape (fruit)	0.01	Grape post fumigation dissipation curve. Also currant surrogate.
Grape (juice)	0.09/0.01/0.0	Grape processing residue reduction. Cooked juice had no residues.
Grape (raisin)	1.0/0.09	Cooked forms used processing reduction of 0.09x. "Raw" raisins set to 1.0x and have no specific reduction other than the default 4.3x value was not used since actual raisins were measured and no adjustment from fresh (grape) to dried form (raisin) needed.

(continued)

Table 2. Residue File Adjustment Factor #1 Changes (continued)

COMMODITY [a]	FACTOR [b]	SOURCE [c]
Milk	0.05	Registrant supplied residue reduction factor. Used for raw milk food forms.
Oat (bran)	0.08	Based on wheat processing factor.
Onion	0.02	Dry bulb onion dissipation factor. Surrogate for all bulb commodities.
Peach (raw)	0.01	Peach dissipation factor for raw fruit. Surrogate for nectarines.
Peach (dried)	1.0/0.07	Cherry dissipation factor used for cooked dried fruit. "Raw" dried form at 1.0x.
Plum (fresh)	0.07/0.04	Plum dissipation factor for raw fruit. Use 0.04x for processed forms.
Plum (dried)	1.0/0.04	Cooked/canned forms processing adjustment (0.04x). "Raw" dried form at 1.0x.
Potato (whole)	0.03	Potato dissipation factor. Surrogate for all root and tubers commodities.
Rice (bran)	0.07	Based on rice bran processing factor.
Strawberry	0.16/0.09	Strawberry dissipation data. Post fumigation residue decline curve. Raw grape juice (0.09) value used as surrogate for raw strawberry juice.
Tomato (whole)	0.33	Tomato dissipation factor. Surrogate for eggplant and peppers.
Wheat (oil)	0.08	Based on wheat processing factor.

a. The commodity name and, when necessary, the specific food form (i.e. cooked, juice, dried).
b. Residue reduction factor value used (all ,; 1.0). Derived from residue dissipation curves or processing (baking, cooking, etc.) reductions. Zero residue RAC food forms with an adjustment factor #1 modification are not included or described in this table. Non-labeled RACs are also excluded.
c. Explains reduction value origin together with if used as surrogate for other commodities.

V. Dietary Exposure

A. Acute Dietary Exposure

The complete acute dietary exposure analysis includes all current U.S. EPA label approved methyl bromide uses. The acute dietary exposure values are presented in Table 3 (TAS, 1996a, USDA, 1989-91). The margins of exposure (MOE) are based on an acute ENEL of 8.0 mg/kg/day (clinical signs, rat oral gavage study) and are reported for the 95th percentile of anticipated dietary exposure (Kiplinger, 1994). The default DPR policy is to use the 95th percentile of exposure for an acute dietary when a commodity residue is represented by a point estimate value. The 95th percentile MOEs are reported for methyl bromide because these values approximate the upper bound (2 standard deviations) distribution of the acute dietary exposure. The acute dietary exposure data for most commodity food forms were modified to reflect lower and/or lack of residues due to processing or non-use (zero residues). The 95th percentile acute dietary exposures ranged from 0.008195 mg/kg/day, (children 1-6 years old) to 0.003387 mg/kg/day, (females 13-19 years not pregnant/not nursing).

B. Seasonal Dietary Exposure

Methyl bromide, because of its extensive use on post-harvest commodity and pre-plant soil fumigations together with structural pest control, presents a clearly defined seasonal exposure scenario. This seasonal exposure can impact both residents living near fields and chambers and to workers applying the pesticide to fallow fields or operating fumigation chambers. The population subgroup females 20^{+} years (not pregnant, not nursing) was used as the surrogate population subgroup to represent anticipated exposure for residents and workers in the subchronic dietary exposure.

The TAS® dietary exposure program does not calculate subchronic duration exposure; therefore, the DPR uses either acute or chronic dietary exposure values to represent the sub-chronic dietary exposure. The choice is dependent on the approximate time frame of exposure which is based on the anticipated duration of the seasonal exposure. If the duration likely is to be less than 1 week, then an acute dietary exposure value would be used. A chronic exposure value would be used if the subchronic duration is expected to be >1 week to three months. The population subgroup selected to represent seasonal exposure should best represent the potential exposure to workers and also indicate relative exposure to other population subgroups. The females 20^{+} years (not pregnant, not nursing) population subgroup chronic exposure value was selected to best represent occupational exposure and also the general U.S. population. The seasonal calculated dietary exposure was 0.000143 mg/kg/day (Table 4).

Table 3. Acute Dietary Exposures from Anticipated Methyl Bromide Residues on Raw Agricultural Commodities.

	Acute Dietary Exposure [a]	
Population Subgroups	**95 th Percentile Exposure (mg/kg/day)**	**(Margins of Exposure) [b]**
U.S. Population, all seasons	0.004892 mg/kg/day	(MOE: 1,640)
Western Region	0.005483	(1,460)
Pacific Region	0.005705	(1,400)
Hispanics	0.004831	(1,660)
Non-Hispanic Whites	0.004973	(1,610)
Non-Hispanic Blacks	0.004116	(1,940)
Non-Hispanic Other	0.005942	(1,350)
All Infants	0.003896	(2,050)
Infants (nursing, < 1 year)	0.005125	(1,560)
Infants (non-nursing, < 1 year)	0.003504	(2,280)
Children (1-6 years)	0.008195	(980)
Children (7-12 years)	0.005138	(1,560)
Females (13-19 years) (not pregnant, not nursing)	0.003387	(2,360)
Females (20+ years) (not pregnant, not nursing)	0.004993	(1,600)
Females (13-50 years)	0.004678	(1,710)
Females (13+ years) (pregnant, not nursing)	0.004292	(1,860)
Females (13+ years) (nursing)	0.004448	(1,800)
Males (13-19 years)	0.003704	(2,160)
Males (20+ years)	0.004433	(1,810)
Seniors (55+ years)	0.004886	(1,640)
U.S. Population (16^{+} years) [C]	0.004649 mg/kg/day	(MOE: 1,720)

a/ Exposure levels rounded to 3 significant figures, based on the 1989-1992 Continuing Survey of Food Intakes of Individuals (CSFII). Anticipated residue values used for the commodities.

b/ MOE = NOEL ÷ Exposure. The acute ENEL value of 8.0 mg/kg/day was used (rat oral gavage study: clinical signs, Kiplinger, 1994).

c/ Custom population not available in the chronic dietary exposure program.

C. Chronic Dietary Exposure

The chronic dietary exposure values are presented in Table 4 (Mertens, 1997, TAS, 1996b, USDA, 1989-91). The chronic dietary exposure data for most commodities were modified with percent of the crop treated adjustments based on registrant marketing data. The commodity food form changes reflect lower and/or lack of residues due to processing effects or non-use. The changes made to the commodity food forms were based on registrant supplied processing and/or methyl bromide residue dissipation data. The data indicate that methyl bromide residues dissipate over time (post fumigation) and are also removed by the effects of processing (baked, canned, cooked, fried, etc.). When dissipation and/or processing data were supplied, then the food forms of many commodities were modified to reflect the reduced levels or the complete lack of methyl bromide residues. These extensive food form adjustments (residue file adjustment factor #1 set to between 1 and zero) only slightly reduce the over-all potential dietary exposure compared to the unmodified forms since the majority of residues are found in the raw and dried commodity food forms. The impact of percent of the crop treated adjustments to the commodities food form residues was much more significant. The percent of the crop treated values were derived from available comprehensive methyl bromide sales information. The percentages of the crop treated adjustment (PCT) factors for the chronic dietary exposure were based on this information source for each commodity. There were two chronic dietary exposure scenarios produced. The MOEs are based on a chronic NOEL of 2.2 mg/kg/day (reduced body weight, rat 2 year feeding study) and are reported as the average anticipated dietary exposure (Mertens, 1997). The first chronic dietary exposure scenario set all the processed food forms of a commodity equal to zero residue. The second chronic dietary exposure scenario was the same as the first except that 3 commodities were removed (soybean flour, oat, and taro root) to reflect elimination of these theoretical residues. The first (processed food form equals zero residue) chronic dietary exposure scenario ranged from 0.000201 mg/kg/day, (children 1-6 years) to 0.000014 mg/kg/day, (non-nursing infants) (Table 4). The second chronic dietary exposure scenario, modified by the removal of 3 additional commodities (soybean flour, oats, and taro root), was also run. The chronic dietary exposure ranged from 0.000201 mg/kg/day, (children 1-6 years) to 0.000005 mg/kg/day, (non-nursing infants). Refer to the Critical Commodity Contribution paragraph of the Commodity Contribution Effects (section D.) for details.

Table 4. Chronic Dietary Exposures from Anticipated Methyl Bromide Residues on Raw Agricultural Commodities.

Population Subgroup	Chronic Dietary Exposure [a] Annualized Averages Exposure (mg/kg/day)	(Margins of Exposure) [b]
U.S. Population, all seasons	0.000127 mg/kg/day	(MOE: 17,310)
Western Region	0.000176	(12,480)
Pacific Region	0.000182	(12,060)
Hispanics	0.000103	(21,300)
Non-Hispanic Whites	0.000133	(16,510)
Non-Hispanic Blacks	0.000090	(24,420)
Non-Hispanic Other	0.000194	(11,330)
All Infants	0.000015	(150,620)
Infants (nursing, < 1 year)	0.000017	(128,190)
Infants (non-nursing, < 1 yr.)	0.000014	(162,600)
Children (1-6 years)	0.000201	(10,930)
Children (7-12 years)	0.000199	(11,080)
Females (13-19 years) (not pregnant, not nursing)	0.000060	(36,470)
Females (20+ years) (not pregnant, not nursing)	0.000143	(15,430)
Females (13-50 years)	0.000136	(16,180)
Females (13+ years) (pregnant, not nursing)	0.000099	(22,290)
Females (13+ years) (nursing)	0.000149	(14,790)
Males (13-19 years)	0.000060	(36,560)
Males (20+ years)	0.000093	(23,680)
Seniors (55+ years)	0.000124 mg/kg/day	(MOE: 17,760)

a/ The chronic residue files used anticipated residue values for the commodities and are based on the 1989-1992 Continuing Survey of Food Intakes of Individuals (CSFII), USDA.
b/ MOE = NOEL ÷ Exposure. The chronic NOEL value of 2.2 mg/kg/day was used (rat; 2 year: decreased body weight, Mertens, 1997). Residue values are adjusted for percent of the crop treated. The modification is to adjustment factor 2 in the chronic residue file.

D. Commodity Contribution Effects

Five populations were selected to best characterize the significant groups of interest for the anticipated dietary exposures to methyl bromide. The following population subgroups were selected: Pacific region of the United States, non-Hispanic-others, nursing infants, non-nursing infants <1 year and children 1-6 years of age. The Pacific region of the U.S. (California, Oregon and Washington states) population represents the most appropriate exposure group to characterize all Californians. The non-Hispanic-others population subgroup represents primarily Asians and can account for dietary exposure from the consumption of fruits and vegetables at a higher rate than that of a traditional Western style diet. The nursing and non-nursing infants <1 year population groups are populations of interest especially in light of the USEPA Food Quality Protection Act (FQPA) mandates. The highest chronic dietary exposure value for any of the populations listed in Table 4 came from the children 1-6 years of age population subgroup (0.0002 mg/kg/day).

A *Critical Commodity Contribution Analysis* (TAS® program) was done for the selected representative population subgroups to ascertain which commodities were contributing significant exposure to the chronic DPR dietary exposure analysis (TAS, 1996b, USDA, 1989-91). There remained several commodities that are significant contributors to chronic dietary exposure after all of the processing, residue dissipation and percent of the crop treated adjustments were made to the chronic dietary residue food file.

The following commodities contributed 5 % or more to the total chronic dietary exposure for five representative populations: **raw dried almond** (Pacific, non-Hispanic-others and children 1-6 years), **raw dried walnut** (Pacific, non-Hispanic other and children 1-6 years), **raw pineapple** (Pacific, non-Hispanic-others and children 1-6 years), **raisin** (non-Hispanic-others, non-nursing infants and children 1-6 years), **raw grape** (nursing infants), **raw apple** (nursing infants), **raw oat** (nursing and non-nursing infants), **raw soybean flour** (nursing and non-nursing infants) and **taro root** (non-nursing infant). Residue data sources for some commodities are described in III. B. Commodity Residue Studies.

Three of these contributing commodities, in reality, are unlikely to contribute significantly to the overall dietary burden. The exposure contribution of raw soybean flour to both nursing (ca. 9% contribution) and non-nursing (ca. 36%) infants would likely be much lower because soybean flour is essentially never consumed raw and soybeans are also processed (milled) into flour. Both cooking and milling would likely reduce methyl bromide residues that were detected on the raw soybean. The residues used in the dietary exposure assessment were obtained directly from raw soybeans and were used as the default values. DPR did not have available processing data indicating that ready to eat soybeans would have lower or zero residues; therefore, a conservative assumption was made which used the raw form as being representative for the processed flour food form. Edible soybeans would be baked, boiled or cooked in home applications and in commercial baby food preparations would either not be treated or undergo the same previously mentioned preparation methods prior to consumption. More significantly, the source of the methyl bromide residue value was obtained from post-

harvest fumigated raw, whole soybeans and not actual soybean flour (Fieser and Conrath, 1993e). Based on reductions reported for other processed commodities, there would likely be a reduction in the methyl bromide residues when whole soybeans are processed into flour.

The exposure contribution of raw oats to both nursing and non-nursing infants (ca. 31% and ca.15% respectively) would be much lower because raw oats are essentially never consumed without being milled and cooked. DPR had no registrant processing data indicating that all "ready-to-eat" forms of oats would have lower (or zero) residue levels. Therefore, DPR made a health conservative assumption using the raw oat residues (inedible form) to represent cooked/prepared oats. Raw oats would be baked, boiled, or cooked prior to home consumption. In addition, commercial baby foods would undergo many of the same preparations as home use and also would not have been fumigated. Most significantly, the source of the raw milled oats residue value was obtained from post-harvest fumigated surrogate raw whole wheat (Fieser and Conrath, 1993c). These residues would likely be greatly reduced or eliminated during the course of milling raw oats into the flour form.

Taro root exposure contribution to non-nursing infants (ca. 10%) would likely be much lower or even zero because taro root is essentially not consumed without being in a cooked form. The MBIP registrants used a raw carrot residue value as the surrogate for taro root in its dietary exposure assessment. This approach was followed in the DPR assessment. Substituting another root crop (i.e. potato) for taro root (as surrogate) would not make any difference in the exposure since the other root crop commodity residues were also measured in their raw forms. The taro root value, due to a lack of food form information, was used in the DPR dietary exposure analysis without breakdown into its substituent food forms as a conservative default adjustment. The taro root food forms available are all baked, cooked or fried prior to consumption. These forms, based on other processed commodity data, would likely have substantially reduced methyl bromide residues when compared to the raw root surrogate values. Also, the consumption data for taro root is very limited (USDA, 1989-91). There was recorded consumption only for non-nursing infants and children 1-6 years in the CSFII database. Both populations' consumption percentages were less than 0.5%. The non-nursing infants per capita average consumption rate of 0.03% g/kg (average per consumer rate of 7 g/kg). Consumption rates below 5% for any population subgroup in the CSFII survey can be very unreliable and any reporting error (i.e. decimal errors) or over estimation could greatly impact the accuracy of the population consumption results.

Another chronic dietary exposure analysis which excluded three commodities was constructed. The commodities were removed so that the impact of suspected theoretical residues could be measured.. Soybean flour (all 3 forms), oats, and taro root were excluded to illustrate their impact on the dietary exposure of the nursing and non-nursing infants population subgroups. Methyl bromide would not likely be present in these commodities due to their elimination via processing and cooking. A similar decrease in residue levels was reported in numerous other commodity studies measuring methyl bromide residues that were then commercially processed and/or cooked. As expected, the two population subgroups chronic dietary exposures were much lower when the theoretical residues for the three commodities were excluded. The nursing infants population subgroup chronic dietary exposure was 0.00001

mg/kg/day (vs. 0.000017 mg/kg/d, a 41% ↓) and the non-nursing infants was 0.000005 mg/kg/day (vs. 0.000014 mg/kg/d, a 64% ↓). These decreases show the significance of including the 3 commodities with theoretical residues. The only other subgroup (excluding All Infants) out of the 21 populations analyzed that changed was the population subgroup Hispanic which decreased from 0.000103 mg/kg/day to 0.000102 mg/kg/day.

VI. Acute Tolerance Assessment

An acute tolerance assessment was not performed for methyl bromide residues using the U.S. EPA tolerances. There are no current 40 CFR 180 tolerances for methyl bromide listed by the U.S. EPA, only inorganic bromide tolerances exist (40 CFR 180.123, 180.199 and 185.3700) (CFR, 1999).

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APPENDIX A
Acute Dietary Exposure

Appendix is available by request at publicrecords@cdpr.ca.gov

APPENDIX B
Chronic Dietary Exposure All Commodities

Appendix is available by request at publicrecords@cdpr.ca.gov

APPENDIX C
Chronic Dietary Exposure
Excludes Three Processed Commodities

Appendix is available by request at
publicrecords@cdpr.ca.gov

ATTACHMENT B

Comments and Responses to Comments from the Office of Environmental Health Hazard Assessment

M E M O R A N D U M

TO: Gary Patterson, Ph.D., Chief
Medical Toxicology Branch
Department of Pesticide Regulation
P.O. Box 4015
Sacramento, California 95812-4015

FROM: Anna M. Fan, Ph.D., Chief
Pesticide and Environmental Toxicology Section

DATE: July 27, 2001

SUBJECT: COMMENTS ON THE DEPARTMENT OF PESTICIDE REGULATION'S DRAFT METHYL BROMIDE RISK CHARACTERIZATION DOCUMENT FOR DIETARY EXPOSURE

We have reviewed the draft methyl bromide risk characterization document (RCD) for dietary exposure prepared by the Department of Pesticide Regulation (DPR). Methyl bromide is a multipurpose fumigant used for pest control in structures such as warehouses, ships, freight cars, and homes and in postharvest treatment of commodities. It is also used in the preplant treatment of soil in fields and greenhouses to control insects, nematodes, weeds, bacteria, and fungi. On an average, 17 million pounds of methyl bromide is used annually in California. Approximately 96 percent is for soil fumigation, 3 percent is for structural use and 1 percent is for commodity and nursery fumigation.

Methyl bromide is a known stratospheric ozone depleter. Under the United Nations Montreal Protocol, it is scheduled to be phased out of use in the United States by 2005. In California, it is regulated under: Health and Safety Code Sections 39650 to 39670 (Toxic Air Contaminants, Assembly Bill 1807), Food and Agriculture Code Section 13134 (Dietary Risk Assessment, Assembly Bill 2161); Birth Defect Prevention Act of 1984 (Senate Bill 950), and Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65).

The draft methyl bromide RCD for dietary exposure submitted by DPR for the Office of Environmental Health Hazard Assessment's (OEHHA's) review is volume II of the projected three-volume document. The first volume on risk characterization for inhalation exposure was reviewed by OEHHA in August 1999. The third volume on risk characterization for aggregate exposure will be developed after completion of volumes I and II. The draft RCD for dietary exposure consists of two parts: a main document and an attachment with two appendices. The two parts discuss acute and chronic dietary analysis, respectively.

A summary of our comments is presented below. More detail is provided in the attachment.

1. We recommend that the draft dietary RCD for methyl bromide include the ranges of methyl bromide concentrations for particular commodities which are health protective for all consumer groups, especially for children. Such ranges could serve as a reference source in the future to see whether the proposed or approved tolerance values meet the safety requirements.

2. We recommend that the draft dietary RCD include a brief discussion on subpopulations at greater risk from methyl bromide exposure in the diet.

3. We recommend that the draft dietary RCD include a brief discussion comparing the pharmacokinetics, toxicity, and the lowest levels of methyl bromide causing adverse effects from inhalation and dietary exposure. Alternatively, this discussion could be included in volume III.

4. A discussion on polymorphism in glutathione transferase activity among humans and its implications on toxicity of methyl bromide in exposed individuals would enhance the risk characterization of this chemical. In addition, the lack of correlation between the strong mutagenic activity and the negative results in cancer bioassays for methyl bromide should be discussed. We recommend these topics be included in volume III.

Thank you for the opportunity to review the draft RCD for dietary exposure to methyl bromide prepared as volume II of a three volume set for this active ingredient. If you have any questions regarding our comments, or would like to set up a meeting to discuss them, feel free to contact me or Dr. Michael J. DiBartolomeis at (510) 622-3200.

Attachment

cc: Val F. Siebal
Chief Deputy Director
Office of Environmental Health Hazard Assessment

Michael J. DiBartolomeis, Ph.D., Chief
Pesticide and Food Toxicology Unit
Pesticide and Environmental Toxicology Section
Office of Environmental Health Hazard Assessment

Keith Pfeifer, Ph.D.
Senior Toxicologist
Medical Toxicology Branch
Department of Pesticide Regulation

bcc: G. Alexeeff

A T T A C H M E N T

Comments on the Draft Methyl Bromide Risk Characterization Document for Dietary Exposure

Methyl bromide is a multipurpose fumigant used for pest control in structures such as warehouses, ships, freight cars and homes and in postharvest treatment of commodities. It is also used in the preplant treatment of soil in fields and greenhouses to control insects, nematodes, weeds, bacteria, and fungi. On an average, 17 million pounds of methyl bromide are used annually in California for pest control. Approximately 96 percent is for soil fumigation, 3 percent is for structural use and 1 percent for commodity and nursery fumigation.

COMMENTS

Dietary versus inhalation exposure risks

The toxicological database for methyl bromide allows for the assessment of risk from exposures to methyl bromide from different routes of exposure. The risks from inhalation exposures (volume 1) were based on studies with inhalation exposures. The risks from dietary exposure to methyl bromide (volume 2, currently under review) was based on studies with oral exposures. In general, we support this approach. We also believe that the overall health risks from all routes of exposure to methyl bromide will be based on the absorbed doses of methyl bromide from all routes of exposures. According to the draft dietary risk characterization document (RCD), aggregate exposures will be assessed in volume III of the RCD.

The comparison of critical no-observed-adverse-effect-levels (NOAELs) and endpoints chosen for risk assessment for oral and inhalation exposures showed that these two parameters are very different for the two routes of exposure (see Table 8 on page 25). For oral exposure, both acute and chronic NOAELs (8 mg/kg and 0.02 mg/kg-day, respectively) selected for risk assessment were lower than acute and chronic NOAELs for inhalation exposure (11 mg/kg and 0.14 mg/kg-day, respectively). The toxicological endpoint used for acute oral exposure was clinical signs in rats while the endpoint for inhalation exposure was developmental toxicity. For chronic oral exposure the most sensitive toxicological endpoint used in risk assessment was enlarged spleens in rats while the most sensitive endpoints for chronic inhalation exposure were nasal epithelial hyperplasia and degeneration.

We recommend that the RCD include a comparison of the pharmacokinetics, toxicity, and the lowest levels causing adverse effects from exposure to methyl bromide via inhalation or in the diet. Alternatively, this discussion might be more appropriate for volume III, the aggregate exposure assessment.

Tolerance assessment

The draft dietary RCD does not include an assessment of tolerances because the existing tolerances established by the United States Environmental Protection Agency (U.S. EPA) for methyl bromide are based on inorganic bromide which U.S. EPA believes to be of no toxicological concern. There are no current official tolerances established for methyl bromide. However, there are prepared tolerances submitted to U.S. EPA by the registrant that could be presented. They range from 0.1 ppm (vegetables, small fruits and berries, and stone fruits) to 50 ppm (green cocoa beans). (Note: tolerance assessment issues are addressed in the draft RCD on pages 30 and 31.)

We recommend that the dietary RCD provide the range of methyl bromide concentrations for particular commodities which are health protective for all consumer groups, including but not limited to children and infants. Such ranges could serve as a reference source in the future to see whether the proposed or approved tolerance values meet the safety requirements.

Susceptible populations

The draft dietary RCD does not identify groups of people more susceptible to the toxic effects of methyl bromide. In the first volume of the draft RCD for methyl bromide from inhalation exposure, the issue of the increased sensitivity of the young to methyl bromide was addressed under the heading Pre-and Post-natal Sensitivity (as noted in volume II, pages 123 and 124). Dietary exposure analyses presented in volume II showed that children one to six years old had the highest potential acute and chronic dietary exposure to methyl bromide residues in the diet among the 20 groups analyzed. Although the risks for this group from the dietary exposure to methyl bromide were still within the acceptable range, we recommend that a brief discussion of the issue be included in the dietary RCD.

Conjugation of methyl bromide with glutathione

The conjugation with glutathione appears to be an important part of metabolism and the toxification/detoxification process for monohalomethanes including methyl bromide (Hallier et al., 1990). This reaction is catalyzed by glutathione transferase. There is a broad genetically determined polymorphism in glutathione transferase activity among humans (Hallier at al., 1993). Approximately 75 percent of people have red blood cells with a form of this enzyme (GST1-1), which is selective for the conjugation of methyl bromide with glutathione (fast conjugators) (Garnier et al., 1996). About 25 percent of the population does not have this enzyme phenotype (slow conjugators) (Garnier et al., 1996). There are ethnic differences in the prevalence of the genotype (Nelson et al., 1995).

The polymorphism of glutathione transferase activity may result in different dose responses among individuals in a population with varying toxic responses to methyl bromide exposure. Therefore, these differences in metabolism (conjugation) may be a factor in identifying susceptible subpopulations that would require more consideration in the risk assessment.

Although the amount of data on the subject matter is limited, we recommend that such a discussion be included in volume III.

Genotoxic and oncogenic effects of methyl bromide

The oncogenic potential of methyl bromide has been studied extensively through inhalation (two long-term chronic toxicity studies in rats) as well as through dietary routes of exposure (at least four chronic toxicity studies in rats, mice, and dogs). Chronic toxicity and oncogenicity of methyl bromide were discussed in volume I (pages 55 to 64).

There was no clear evidence of oncogenicity in the currently available studies. This is puzzling because methyl bromide is a direct-acting mutagen, especially in *in vitro* systems (see volume I pages 65 to 69). It was found positive in *Salmonella typhimurium* strains TA 100 and TA 1535, *Escherichia coli* strains Sd-4 and WP2hcr, and in *Saccharomyces cerevisiae*. It also produced a dose-dependent induction of sex-linked recessive lethality in *Drosophila melanogaster*. In *in vivo* assays methyl bromide was found to cause dominant lethal mutations, an increase of micronuclei, and a dose-related increase in the frequency of sister chromatid exchanges in bone marrow. DNA adducts were detected in liver, lung, stomach, and forestomach of rats exposed to high concentration of methyl bromide by inhalation.

We recommend that a discussion of the lack of correlation between strong mutagenic activity and no clear evidence of carcinogenicity be included in volume III.

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Department of Pesticide Regulation

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M E M O R A N D U M

TO: Gary Patterson, Ph.D., Chief
Medical Toxicology

FROM: Lori O. Lim, Ph.D., Staff Toxicologist

DATE: September 21, 2001

SUBJECT: RESPONSE TO COMMENTS FROM OEHHA ON DRAFT METHYL BROMIDE RCD FOR DIETARY EXPOSURE

The following is my response to comments (in the Attachment) from the Office of Environmental Health Hazard Assessment (July 27, 2001) on the Department's draft Methyl Bromide Risk Characterization Document for Dietary Exposure (February 15, 2001):

Page 1, last ¶: "We recommend...a comparison of the pharmacokinetics, toxicity, and the lowest levels...via inhalation or in the diet...discussion more appropriate for volume III"

Response: A discussion will be provided in Volume III.

Page 2, 2nd ¶: "We recommend that the...RCD provide the range of...concentrations for particular commodities...Such ranges could serve as a reference source...to...proposed or approved tolerance values..."

Response: It is not possible to provide a useful range of methyl bromide concentrations for particular commodities because there are many commodities involved. The range of reference concentrations depends on the consumption amount and pattern for each commodity relative to other commodities. For each commodity, this range can be anywhere between 0 to 100% of the reference dose depending on the contributions from the other commodities to the total exposure.

Page 2, 3rd ¶: "...Dietary exposure analyses...showed that children...had the highest potential acute and chronic dietary exposure...Although the risks...were still within the acceptable range, we recommend...discussion of the issue be included in the dietary RCD.

Response: There was a discussion on this issue under **V.E.**

Pages 2-3, 1st ¶: "...these differences in metabolism may be a factor in identifying susceptible subpopulations...we recommend that such a discussion be included in volume III."

Page 3, 3rd ¶: "We recommend that a discussion of the lack of correlation between strong mutagenic activity and no clear evidence of carcinogenicity be included in volume III."

Response: For both comments, discussion in Volume I will be cited.

cc. Keith Pfeifer