Proposition 65

Interpretive Guideline No. 2018-01

Residential exposure to methyleugenol in bait stations and lures during invasive pest eradication program activities

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A. Summary

Anticipated lifetime exposure to methyleugenol when used in either bait stations or lures by the California Department of Food and Agriculture's (CDFA) invasive pest eradication programs does not pose a significant cancer risk to the average resident near treated areas for purposes of Proposition 65. The estimated lifetime cancer risk is calculated to be well below one excess cancer case in an exposed population of 100,000, the risk level that represents no significant cancer risk[1].

B. Scope of Interpretive Guideline

The Office of Environmental Hazard Assessment (OEHHA) may issue an Interpretive Guideline that interprets Proposition 65 and its implementing regulations, as applied to specific facts. The Interpretive Guideline reflects OEHHA's scientific interpretation of the available information as the lead agency for implementation of the Act.[2]

Methyleugenol was listed as a chemical known to cause cancer under Proposition 65 on November 16, 2001 based on its identification as a carcinogen by the US National Toxicology Program (NTP).[3] This Interpretive Guideline only applies to methyleugenol in bait stations and lures when used by CDFA in their invasive pest eradication programs. This guideline calculates the cancer risk using a cancer slope factor derived from a laboratory animal study and an average resident's lifetime exposure to methyleugenol from living near treated area. Risk at or below 10^{-5} is considered insignificant and is exempt from the warning requirements of Proposition 65.

Methyleugenol is a naturally occurring compound, that is a colorless to yellow liquid with a clove smell and bitter taste; it is highly volatile and has very low solubility in water. It is found in many plants and essential oils, most notably cloves, basil, nutmeg, and orange peel, many of which are used as flavoring agents. Methyleugenol is also used as a component in perfumes, soaps, and lotions. This report focuses on the exposure of residents who may be repeatedly exposed to methyleugenol from CDFA's use of the chemical in bait stations and lure traps.

C. Methyleugenol in Bait Stations and Lures

Bait stations and lure traps are two of the methods used by CDFA in its invasive pest eradication programs to control and manage fruit flies. Both devices use methyleugenol as an insect attractant.

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[1] Title 27, California Code of Regulations, Section 25703(b). All further references are to Title 27, Cal. Code of Regs., unless indicated otherwise.
[2] Health and Safety Code section 25249.12
[3] California Proposition 65 list of chemicals known to cause cancer and reproductive toxicity. Most recent list is available at http://oehha.ca.gov/proposition-65/chemicals

Bait stations: STATIC Spinosad ME™ is a bait station used by CDFA that contains two active ingredients – spinosad and methyleugenol. The inert carrier consists mainly of waxes and oils and serves as a matrix to control the release of the active ingredients. Spinosad is the insecticide while methyleugenol acts as an insect attractant. During application, a small amount of the STATIC-spinosad formulation, in the form of a viscous liquid, is applied through a high-pressure nozzle onto a light pole or tree trunk, 6 to 12 feet above the ground in a public place (i.e., street easement or parks, not private properties). The formulation sticks to a hard surface and forms a disc of about 6 inches in diameter; this is referred to as a STATIC bait station. It gradually releases methyleugenol into the surrounding air and attracts fruit flies to the bait station. The flies are then killed when they come into contact with the insecticide on the bait station.

Lure traps: The type of lure trap used by CDFA to detect and control invasive fruit fly pests is a small tent-like device with a sticky surface on the inside; it also contains a cotton wick impregnated with up to approximately 5mL of lure. The lure is a mixture of a pesticide, such as naled in Dibrom 8 Emulsive®, and an insect attractant, such as methyleugenol. The trap is hung in fruit and ornamental trees 6 to 8 feet above the ground. In areas with low-growing host plants and a lack of trees, traps may be hung on poles 3 to 5 feet above the ground. Male fruit flies are attracted to the lure and killed by the pesticide when they land on the wick, and are retained in the trap by the sticky surfaces. The trap also functions to suppress the breeding of fruit flies by removing males from the population.

D. Development of Cancer Potency for Methyleugenol

To develop the cancer potency for methyleugenol, OEHHA relied on the 2000 NTP report entitled "Toxicology and Carcinogenesis Studies of Methyleugenol (CAS No. 93-15-2) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies)"[4]. This document summarizes the available data from rodent carcinogenicity studies of methyleugenol, as well as other information relevant to the carcinogenic activity of the chemical.

D.1. Selection of Studies Used to Determine Cancer Potency

OEHHA reviewed the available data from the rodent carcinogenicity studies of methyleugenol discussed by NTP[5], and determined that the two-year gavage studies

[4] National Toxicology Program (NTP, 2000). Toxicology and Carcinogenesis Studies of Methyleugenol in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP Technical Report Series No. 491. US Department of Health and Human Services, NTP, Research Triangle Park, NC.

[5] National Toxicology Program (NTP, 2000). Toxicology and Carcinogenesis Studies of Methyleugenol in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP Technical Report Series No. 491. US Department of Health and Human Services, NTP, Research Triangle Park, NC.

conducted by NTP in male and female F344/N rats and B6C3F$_1$ mice met the criterion in Section 25703 as being sensitive studies of sufficient quality.

In the NTP rat studies, groups of 50 male and female rats were exposed to methyleugenol in 0.5% methylcellulose by gavage at doses of 37, 75, or 150 milligrams per kilogram of body weight (mg/kg), 5 days per week for up to 105 weeks. Groups of 60 male and female rats received the 0.5% methylcellulose vehicle only. The lifetime average daily doses of methyleugenol administered in the studies were calculated by OEHHA to be 0, 26.4, 53.6, and 107.4 mg/kg-day. Stop-exposure groups of 60 male and 60 female rats received 300 mg/kg in 0.5% methylcellulose by gavage for 52 weeks followed by just the 0.5% methylcellulose vehicle for the remaining 53 weeks of the study.

Survival rates of male rats in the 150 and 300 mg/kg dose groups were reduced compared to controls, and survival rates of female rats in the 300 mg/kg dose group was reduced compared to controls. However, both male and female deaths occurred late in the studies, and were due to liver and glandular stomach tumors.

Statistically significant increases in incidences of hepatocellular adenomas and carcinomas, benign and malignant neuroendocrine tumors of the glandular stomach, renal tubule adenomas of the kidney, malignant mesothelioma, fibroadenoma of the mammary gland, and fibroma or fibrosarcoma of the skin were observed elevated in methyleugenol treated male rats. These tumor types, with the exception of skin tumors, exhibited statistically significant positive trends. In female rats, a statistically significant increase in the incidence of hepatocellular adenomas and carcinomas and benign and malignant neuroendocrine tumors of the glandular stomach were observed, with statistically significant positive dose-related trends. The incidences of treatment-related tumors included in the dose-response analysis from both of the rat studies are presented in Table 1.

In the NTP mouse studies[6], groups of 50 male and female mice were exposed to methyleugenol in 0.5% methylcellulose by gavage at doses of 0, 37, 75, or 150 mg/kg, 5 days per week for up to 105 weeks. The lifetime average daily doses of methyleugenol administered in the studies were calculated by OEHHA to be 0, 26.4, 53.6, and 107.4 mg/kg-day. Survival was not affected by treatment with methyleugenol at any dose in the male mouse study. Survival of all treated female mice was significantly less than that of the control group. The majority of female mice in these groups died with hepatocellular adenomas or carcinomas: 76% (38/50) in the 37 mg/kg group, 98% (48/49) in the 75 mg/kg group, and 98% (49/50) in the 150 mg/kg group, compared to

[6] National Toxicology Program (NTP, 2000). Toxicology and Carcinogenesis Studies of Methyleugenol in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP Technical Report Series No. 491. US Department of Health and Human Services, NTP, Research Triangle Park, NC.

14% (7/50) in the control group. Tumor-related mortality predominantly occurred late in the study (between weeks 85 and 105).

Statistically significant increases in incidences of hepatocellular adenomas, carcinomas, or hepatoblastomas were observed in both male and female rats, with statistically significant positive trends. The incidences of treatment-related tumors included in the dose-response analysis from both of the mouse studies are presented in Table 2.

Table 1. Tumor incidences[a] of treatment-related lesions in F344/N rats administered methyleugenol by gavage (NTP, 2000)

Organ	Tumor type	Methyleugenol administered concentrations (mg/kg-day)				Trend test p-value[b]
		0	37	75	150	
Male Rats						
Liver	Hepatocellular adenoma or carcinoma[c] (day 431)[d]	7/49	14/48	28/49***	43/48***	$p < 0.001$
Glandular stomach	Benign or malignant neuroendocrine tumors[c] (day 642)[d]	0/37	0/33	0/33	7/26**	$p < 0.001$
Kidney	Renal tubule adenoma[c] (day 575)[d]	4/45	6/44	17/42***	13/40**	$p < 0.01$
Multiple organs	Malignant mesothelioma (day 409)[d]	1/49	3/48	5/49	12/49***	$p < 0.001$
Mammary gland	Fibroadenoma (day 546)[d]	5/47	5/45	15/44**	13/43*	$p < 0.05$
Skin	Fibroma or fibrosarcoma (day 535)[d]	1/47	12/47***	8/44*	8/43*	NS
Female Rats						
Liver	Hepatocellular adenoma or carcinoma[c] (day 508)[d]	1/45	8/47*	14/48***	34/48***	$p < 0.001$
Glandular stomach	Benign or malignant neuroendocrine tumorsc (day 548)[d]	0/45	1/46	25/45***	34/44***	$p < 0.001$

[a] The numerator represents the number of tumor-bearing animals and the denominator represents the number of animals alive at the time of first occurrence of tumor.

[b] p-values for exact trend test conducted by OEHHA.

[c] Treatment group tumor incidences with asterisks indicate significant results from Fisher pairwise comparison with controls (performed by OEHHA): * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[d] First occurrence of tumor.

Table 2. Tumor incidences[a] of treatment-related lesions in B6C3F$_1$ mice administered methyleugenol by gavage (NTP, 2000)

Organ	Tumor type	Methyleugenol administered concentrations (mg/kg-day)				Trend test p-value[b]
		0	37	75	150	
Male Mice						
Liver	Hepatocellular adenoma, carcinoma, or hepatoblastoma[c] (day 430)[d]	31/47	47/48***	46/48***	41/47*	$p < 0.05$
Female Mice						
Liver	Hepatocellular adenoma, carcinoma, or hepatoblastoma[c] (day 450)[d]	25/49	50/50***	49/49***	49/49***	$p < 0.001$

[a] The numerator represents the number of tumor-bearing animals. For male mice the demoninator has been adjusted with the poly-3 method. For female mice the denominator represents the number of animals alive at the time of first occurrence of tumor.

[b] p-values for exact trend test conducted by OEHHA.

[c] Treatment group tumor incidences with asterisks indicate significant results from Fisher pairwise comparison with controls (performed by OEHHA): * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[d] First occurrence of tumor.

D.2. Estimation of Cancer Potency Using the Multistage Model

The mechanisms by which methyleugenol induces tumors are not known. Several genotoxicity studies provide information relevant to a genotoxic mechanism of action. The International Agency for Research on Cancer (IARC) notes that "methyleugenol induces chromosomal aberrations in vitro and DNA adducts in the liver of rodents in vivo" and that "there is moderate evidence that a mutational mechanism underlies the induction of tumours by methyleugenol in rodents."[7] Therefore, the approach using a linearized multistage model is applied to derive a cancer potency estimate for each of the four NTP studies. There are not principles or assumptions scientifically more appropriate, based on the available data, than this approach.

The lifetime probability of a tumor at a specific site given exposure to the chemical at dose d is modeled using the multistage polynomial model:

$$p(d) = \beta_0 + (1 - \beta_0)\left(1 - exp\left[-\left(\beta_1 d + \beta_2 d^2 + \ldots + \beta_j d^j\right)\right]\right)$$

[7] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 101, Some Chemicals Present in Industrial and Consumer Products, Food and Drinking-water, International Agency for Research on Cancer, World Health Organization, Lyon, France, 2013.

where the background probability of tumor, β_0, is between 0 and 1 and the coefficients β_i, $i = 1, \ldots, j$, are positive. The β_i are parameters of the model, which are taken to be constants and are estimated from the data. The parameter β_0 provides the basis for estimating the background lifetime probability of the tumor.

The multistage polynomial model is used to describe the probability of tumor at a single site. To derive a measure of the cancer response to methyleugenol (per mg/kg-day) in the study in male mice, where increases in treatment-related tumors were observed at a single site, the dose associated with a 5% increased risk of developing a tumor was calculated and the lower bound for this dose was estimated using the multistage polynomial model for cancer in US Environmental Protection Agency's (US EPA) Benchmark Dose Software (BMDS)[8]. The ratio of the 5% risk level to that lower bound on dose is known as the "animal cancer slope factor (CSF_{animal})," or the "animal cancer potency."

In the study in female mice, the tumor incidence was 51% in the control group compared to 100% in all three dose groups. The cancer potency cannot be estimated in BMDS because the 100% tumor incidence in all dosed animals leads to an infinite maximum likelihood estimate (MLE) for β_1 in the multistage polynomial; this in turn generates an infinite potency estimate. However a lower 5% confidence bound on cancer potency can be obtained, providing a range of potency estimates from that lower bound to infinity. This can be derived from the lower bound estimate of the probability of tumor in all animals in the low-dose group. To estimate a lower bound on the cancer potency, first a simplified version of the multistage polynomial model is used:

$$p(d) = 1 - exp\left(-\left[\beta_0 + \beta_1 d\right]\right),$$

where β_0 is derived from the incidence in the control group (exposed to a dose of zero; $p(d=0) = 1 - exp\left(-\left[\beta_0\right]\right)$.

Thus β_1 is given by:

$$\beta_1 = -\frac{\ln\left[\frac{1-p(d)}{1-p(0)}\right]}{d}$$

[8] US EPA Benchmark Dose Software (BMDS) Version 2.6.0.1 (Build 88, 6/25/2015). National Center for Environmental Assessment. Available from: http://www.epa.gov/bmds

Then the values for $p(d)$ (the lower 5% confidence bound for the probability that all animals in the low-dose group are tumor-bearing: $0.05 = p(d)^n \rightarrow \sqrt[n]{0.05} = p(d)$) and $p(0)$ (the probability of tumor in the control group: 51%) are substituted into the equation above and the resulting finite estimate for β_1 is taken as the lower 5% confidence bound on CSF_{animal}, based on the study in female mice.

For carcinogens that induce tumors at multiple sites and/or in different cell types at the same site in a particular species and sex, US EPA's BMDS[9] can be used to derive the potency representing the cumulative risk of all treatment-related tumors. In order to derive a measure of the total cancer response to methyleugenol (per mg/kg-day) in a given study, the dose associated with a 5% increased risk of developing a tumor at one or more of the sites of interest was calculated and the lower bound for this dose was estimated using the multisite model in BMDS. The ratio of the 5% risk level to that lower bound on dose is known as the multisite "animal cancer slope factor (CSF_{animal})," or "animal cancer potency." Animal cancer potencies were estimated using this approach for the male and female rat incidence data provided in Table 1.

D.3. Calculation of Average Daily Doses

The lifetime average dose in units of mg/kg-day of methyleugenol was calculated for each of the relevant dose groups, based on the dose level and exposure regimen. Administered dose was calculated by multiplying the gavage dose by 5 days exposed per week divided by 7 days per week.

D.4. Estimation of Human Cancer Potency

Human cancer potency is estimated by an interspecies scaling procedure. According to Section 25703(a)(6), dose in units of mg per kg body weight scaled to the three-quarters power is assumed to produce the same degree of effect in different species in the absence of information indicating otherwise. Thus, for each of the studies described above, scaling to the estimated human potency (CSF_{human}) is achieved by multiplying the animal potency (CSF_{animal}) by the ratio of human to animal body weights

[9] US EPA Benchmark Dose Software (BMDS) Version 2.6.0.1 (Build 88, 6/25/2015). National Center for Environmental Assessment. Available from: http://www.epa.gov/bmds

(bw_{human}/bw_{animal}) raised to the one-fourth power when CSF_{animal} is expressed in units $(mg/kg\text{-}day)^{-1}$:

$$CSF_{human} = CSF_{animal} \times (bw_{human} / bw_{animal})^{1/4}$$

The default human body weight is 70 kg. The average body weights for male and female rats were calculated to be 0.4119 kg and 0.2760 kg, respectively, and the average body weights for male and female mice were calculated to be 0.0480 kg and 0.0495 kg, respectively. The derivation of the human cancer slope factors using these body weights are summarized below in Table 3.

As shown in Table 3, of the experiments for which a finite estimate of potency could be calculated, male mice were the most sensitive to the carcinogenic effects of methyleugenol with the human cancer slope factor of 0.53 $(mg/kg\text{-}day)^{-1}$. This value falls within the range of potency estimates that could be derived for the female mice.

Table 3. Derivation of CSF_{human} using mean animal body weights for the studies and data presented in Tables 1 and 2

Sex/strain/ species	Type of neoplasm	Body Weight (kg)	CSF_{animal} $(mg/kg\text{-}day)^{-1}$	CSF_{human} $(mg/kg\text{-}day)^{-1}$
Male F344/N rats	Hepatocellular adenoma or carcinoma	0.4119	0.0125	
	Benign or malignant neuroendocrine tumors of the glandular stomach		0.00238	
	Renal tubule adenoma of the kidney[a]		0.00941	
	Malignant mesothelioma		0.00312	
	Fibroadenoma of the mammary gland		0.00469	
	Fibroma or fibrosarcoma of the skin[b]		0.0162	
	Multisite:		0.0374	0.14
Female F344/N rats	Hepatocellular adenoma or carcinoma	0.2760	0.00795	
	Hepatocholangiocarcinoma		0.000787	
	Benign or malignant neuroendocrine tumors[b]		0.00296	

	Multisite:		0.00936	0.037
Male $B6C3F_1$ mice	Hepatocellular adenoma, carcinoma, or hepatoblastoma[a]	0.0480	0.085	**0.53**
Female $B6C3F_1$ mice	Hepatocellular adenoma, carcinoma, or hepatoblastoma[c]	0.0495	0.0807	0.49

[a] The top dose was removed for benchmark dose modeling.

[b] The top two doses were removed for benchmark dose modeling.

[c] A lower bound on potency was derived due to 100% tumor incidence in low-dose group.

E. Inhalation Exposure to Methyleugenol

Inhalation is the most relevant route for human exposure to methyleugenol released from bait stations and lure traps. Since bait stations and lure traps are typically placed 6 to 12 feet off the ground, oral or dermal exposures are not expected.

To estimate inhalation exposure of released methyleugenol, data for STATIC bait stations were used in a screening-level analysis. For STATIC bait stations, the maximum application rate is 5.16 grams of methyleugenol per station. For Dibrom 8 lures, the maximum application rate is 3.2 grams of methyleugenol per lure. Since bait stations and lure traps are used in similar fashions and a larger amount of methyleugenol is usually used in a bait station, for the purpose of this assessment, exposure levels and cancer risk determined for STATIC bait stations will be used to cover both devices.

As there are no measured methyleugenol air concentrations available for the type of exposure scenarios we are interested in, a screening-level air dispersion model, AERSCREEN (Version 15181),[10] was used to estimate the air concentration that the average resident living near the treated area is likely to be exposed to.

E.1. Air Concentration

Methyleugenol slowly evaporates from bait stations over the course of the treatment period. The release rate of methyleugenol is dependent on temperature and wind speed, so bait stations are generally effective for 2 to 6 weeks. Once in the air, methyleugenol degrades in sunlight within a few hours. Treatment periods can last 3 to 4 months per year for several years within a particular area and frequent re-application of bait stations is often required.

According to the manufacturer, the station is composed of 51.6% methyleugenol and up to 69 percent of the chemical can evaporate during the first four weeks under normal weather conditions in California.[11]

Assuming a high-end application amount of 10 milliliters (equivalent to 10 grams (g) of STATIC formulation per bait station, including methyleugenol, inert carrier, and active ingredient), no degradation of methyleugenol, and a constant release of methyleugenol in the first four weeks, an average release rate can be calculated by the following:

Amount of methyleugenol released over four weeks: $10\ g \times 0.516 \times 0.69 = 3.56\ g$

[10] AERSCREEN downloaded from https://www3.epa.gov/scram001/dispersion_screening.htm
[11] Gomez, L. E., Boucher, R.E., Crouse, C.K., Racke, K.D. (2008). SPLAT-MAT Spinosad ME: Efficacy and methyl eugenol loss, Dow AgroSciences LLC

Average release rate over the first four weeks:

$$= 3.56\ g \times 1/(4\ weeks \times 7\ days/week \times 24\ hours/day) \times 1\ hour/3600\ seconds$$

$$= 1.47 \times 10^{-6}\ g/second$$

For modeling the air concentration, OEHHA assumed that the bait station is 2 meters (6.5 feet) above the ground, has a diameter of 0.15 meters (6 inches), and releases methyleugenol passively. The average resident was assumed to be at ground level and 5 m (16 feet) from the nearest bait station. Table 4 shows the input parameters used for the AERSCREEN model.

Table 4. AERSCREEN Modeling Inputs

Parameter	Value	Description
Source type	P	Point source
Emission Rate (g/s)	0.00000147	Four week release rate
Stack Height (m)	2	2m (6ft) high
Stack Diameter (m)	0.15	~6inch splat
Stack Temperature (ºK)	0	Enter 0 for ambient temperature
Exit Velocity (m/s)	0.001	Passive release
Rural or Urban	U	Urban setting
Population of Urban Area	3000	62m between bait stations, area is 3.844 km^2 at 750 ppl/km^2, value is rounded[12]
Min distance to ambient air	1	Default of 1m
NO_2 chemistry	1	No need to model NO_2 or NOx
Building downwash	N	Not included
Terrain Height	N	Not included
Max distance to probe	62	62m between bait stations
Discrete distances	Y	Used 1.0, 2.0, 3.0, 5.0, 10.0, 15.0, and 20.0 meters
Flagpole Receptor	N	Not included
Source elevation (m)	0	Default of 0m
Ambient temperature	Default	Ambient temp, 250 - 310ºK
Wind Speed	0.5	Default of 0.5m/s
Anenometer Height	10	Default of 10m
Surface Characteristics	2	AERMET seasonal tables
Dominant Surface profile	7	Urban
Dominant Climate Profile	1	Average moisture

[12] OEHHA Air Toxics Hot Spots Program Risk Assessment Guidelines (2015) Chapter 4

Parameter	Value	Description
Debug option	Y	Enable debug option

Abbreviations: ft = feet, km = kilometers, m = meters, ppl = people, s = second.

During the first four weeks, a maximum one-hour screening concentration of 0.052 $\mu g/m^3$ was estimated for a distance of five meters from the source. The maximum one hour screening concentration is the highest modeled concentration (on an hourly basis in a given day) accounting for factors such as emission rate, wind speed, average temperature, location, and other parameters shown in Table 4.

E.2. Exposure Level

Proposition 65 regulations address how to calculate the exposure to chemicals listed as known to cause cancer:

> "For purposes of Section 25249.10(c) of the Act, the level of exposure to a chemical listed as causing cancer, assuming lifetime exposure at the level in question, shall be determined by multiplying the level in question (stated in terms of a concentration of a chemical in a given medium) times *the reasonably anticipated rate of exposure* for an individual to the given medium of exposure measured over a lifetime of seventy years…"[13] (emphasis added)

By this provision, the reasonably anticipated rate and frequency of exposure to a chemical for the average resident was used in the exposure calculations. The amount of methyleugenol the average resident might be exposed to during a lifetime from living near a STATIC bait station was calculated using the modeled maximum air concentration (C_{air}), and an average adult breathing rate of 20 cubic meters of air per day (m^3/day) (Table 5). The resident was assumed to be outdoors, 5 meters from the source, for an average time of 4.7 hours per day[14] for 3 months (90 days) each year[15]. CDFA eradication efforts in a particular area are assumed at maximum to be 10 years.

[13] Section 25721(c).
[14] US EPA Exposure Factors Handbook: 2011 Edition, Table 16-22. Value of 281 minutes/day (= 4.7 hours/day) is for mean total time outdoors for 18-64 year-old adults.
[15] https://www.cdfa.ca.gov/plant/PDEP/treatment/oriental_ff.html

Table 5. Parameter values used to calculate the average resident's inhalation exposure to methyleugenol.

Parameters	Value
Adult breathing rate	20 m^3/day
Modeled maximum air concentration at an average distance of 5 meters from nearest bait station	0.052 µg/m^3
Time spent outdoors, at the average distance from bait station[a]	4.7 hrs/day
Treatment duration in a year	90 days/year
Length of eradication efforts in a particular area	10 years
Average adult life span	70 years
Average adult bodyweight	70 kg

[a] US EPA Exposure Factors Handbook (2011). Abbreviation: hrs = hours, kg = kilogram, m = meters.

The estimated lifetime average daily inhalation dose (LADID) was calculated as:

$$\text{LADID} = \frac{C_{air} \times \text{Breathing Rate} \times \text{Frequency of Exposure}}{\text{Body Weight}}$$

Therefore,

$$\text{LADID} = \frac{\frac{0.05175\ \mu g}{m^3} \times \frac{20\ m^3}{day} \times \left(\frac{4.7\ hours}{24\ hours} \times \frac{90\ days}{365\ days} \times \frac{10\ years}{70\ years} \right)}{70\ kg}$$

Thus, the LADID estimated for residents exposed methyleugenol from STATIC bait stations is 0.0001 µg/kg-day (or $1x10^{-6}$ mg/kg-day). The LADID is considered a high-end exposure estimate for the following reasons:

- The amount of methyleugenol actually used for each application may be lower than the maximum application rate that was assumed.
- The modeled air concentration from AERSCREEN may be lower than that assumed using fixed distance and weather condition assumptions. In reality, the average resident is likely much further away from the nearest bait station at least some of the time and thus exposed to a much lower concentration. Changes in wind direction and decreased ambient temperature could also reduce the air concentration.
- The average resident may not be outdoors 4.7 hours per day for 90 days each year and for 10 years, and at ground level to a bait station. Furthermore, a different treatment method may be used in the same area during the 10-year

time period. The location of the nearest STATIC bait station could vary from application to application and from year to year.

- This exposure estimate is health protective for exposure from lures containing methyleugenol since a higher amount of methyleugenol is contained in bait stations relative to lures.

F. Cancer Risk from Methyleugenol Exposure of the Average Resident

OEHHA calculated a range of human cancer slope factors from 0.037 to 0.53 $(\text{mg/kg-day})^{-1}$ for methyleugenol based on the results of scientific studies deemed to be of sufficient quality (Table 3). OEHHA then conducted a screening analysis to determine the level of exposure of residents to methyleugenol in bait stations and lure traps used in CDFA's invasive pest eradication program. The estimated high-end lifetime average exposure to methyleugenol via inhalation is 0.001 μg/kg-day (or $1\text{x}10^{-6}$ mg/kg-day). The cancer risk from exposure to methyleugenol can be calculated as:

$$\text{Risk} = \text{CSF}_{\text{human}} \times \text{Exposure}$$

Using the highest slope factor, OEHHA concludes that an average resident's cancer risk from exposure to methyleugenol from a bait station or lure trap when used by CDFA in fruit fly eradication programs is:

$$\text{Risk} = 0.53\ (\text{mg/kg-day})^{-1} \times 1 \times 10^{-6}\ \text{mg/kg-day} = 5.3 \times 10^{-7}$$

This risk, 5.3×10^{-7}, is well below the established no significant risk level under Proposition 65[16] of 10^{-5}. Therefore, no warning is required[17] for either the bait stations or lure traps for exposures to methyleugenol.

This interpretive guideline is intended to provide information for the general public. It is limited to the facts and assumptions contained herein. Further information can be obtained from the OEHHA website at: http://oehha.ca.gov/proposition-65/interpretive-guidelines-proposition-65.

[16] Section 25703(b)

[17] Note: Proposition 65 does not apply to government entities, but does apply to any business with 10 or more employees that causes an exposure to a listed chemical. See Health and Safety Code sections 25249.6 and 25249.11(b).