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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September 14, 2006

MEMORANDUM

SUBJECT: **Metofluthrin:** Exposure and Risk Assessment for Use as a Mosquito Repellent Strip and as a Personal Outdoor Insect Repellent.

PC Code:	109709
DP Barcode:	D313561
Chemical Class:	Pyrethroid Insecticide (Repellent)
Trade Names:	Sumione Technical, EPA File Symbol 10308-GN
	NORM-1 Personal Generator, EPA File symbol 4822-LUE
	Deckmate Mosquito Repellent, EPA File Symbol 10308-GN
MRID Nos.	46402004, 46406509 46406510, 46406511, 46406512

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1.0 INTRODUCTION/BACKGROUND

RRB4 has been requested to conduct an exposure and risk assessment for metofluthrin [(Cyclopropanecarboxylic acid, 2,2-dimethyl-3-(1-propenyl)-, [2,3,5,6- tetrafluoro-4-(methoxymethyl)phenyl]methyl ester]. Inhalation, dermal, incidental oral, and cancer assessments were done, where appropriate. Registration of a metofluthrin technical (Sumione Technical) and two end use products are proposed. Sumitomo is the technical producer of metofluthrin.

The first end use product containing metofluthrin, Deckmate Mosquito Repellant, proposed for use by Sumitomo, is a mosquito repellent used as a paper strip hung at outdoor sites and in companion animal premises. The repellant strips are claimed to last one week. The second end use product, proposed for registration by S. C. Johnson, is NORM1, a personal outdoor insect repellent device attached to the users clothing. The latter product is activated by turning on a small battery operated fan and is claimed to be effective for 12 hours.

The exposure/risk assessment for the Deckmate Mosquito Repellant strip product will address inhalation exposure only. Dermal and oral exposures are considered to be negligible. The assessment for the NORM-1 personal insect repellent will consider dermal, inhalation exposures, and incidental oral exposures to children.

The registrants submitted 6 studies to be used for the ORE assessment for these metofluthrin products. Three were contractor prepared risk assessments, one studied the evolution rate from DeckMate Mosquito Repellant, one was a study on an esbiothrin mosquito coil, and one studied inhalation and deposition from the use of NORM-1, using manikins.

2.0 CONCLUSIONS

Applicator Exposure to metofluthrin from both of the proposed end use registrations is considered negligible and has not been assessed.

Post-application exposure by inhalation only to metofluthrin from use of the DeckMate repellant strip was assessed. Dermal exposure is considered negligible and has not been assessed. The submitted study on the esbiothrin mosquito coil was not considered applicable to the post application exposure assessment for metofluthrin, because the coil is combusted to release the esbiothrin insecticide, and DeckMate is not.

The Agency has used a different approach for the post-application inhalation exposure assessment to metofluthrin from the use of the DeckMate repellant strips. This bounding estimate is **HIGHLY CONSERVATIVE**, based in the Ideal Gas Law. If the air were saturated with metofluthrin, which will never occur in the outdoor environment, the concentration of metofluthrin would be 0.28 mg/m^3. Assuming that an individual spends 12 hours per day in the proximity of the pest strip and with a NOAEL of 100 mg/m^3 (16 mg/kg/day), the resulting MOE would be approximately 400 (target MOE = 100). This is a short-term exposure scenario.

The NORM-1 personal repellent contains a battery powered fan attached to the individuals clothing to blow air through a cartridge containing metofluthrin. The product is not to be used indoors or in enclosed spaces. One refill for the product will last up to 12 hours, according to the label.

For post-application exposure to NORM-1 personal insect repellant, first a bounding assessment for inhalation and dermal exposure to children was conducted. The amount of metofluthrin in the repellant device would have to be distributed over such a large volume of air that the metofluthrin could not all be inhaled. Thus, the high end inhalation exposure assessment for the

DeckMate repellant strips would be applicable to the high end exposure assessment of the NORM-1 personal insect repellant, with an MOE of 400 (target MOE = 100). For post-application dermal exposure, HED did two high end assessments, 1) assuming that the entire cartridge of 20 mg metofluthrin was available for dermal absorption, which resulted in a dermal MOE of 66 (target MOE = 100); and 2) assuming that the claimed emission rate of 0.75 mg/hr was available for dermal exposure. This resulted in a dermal MOE of 150 (target MOE = 100). This is considered to be a short term scenario.

The registrant conducted a monitoring study to be used to assess exposure to the personal outdoor insect repellent (NORM 1). HED has used the results of this study as a lower estimate of exposure to metofluthrin. Two manikins were used as surrogates for actual human beings, one representing an adult and the other a child. The generating device was located on a belt at the adult manikin's waist with the material generated in a downward direction. Air monitoring was conducted for the "breathing zone" for each adult manikin. No material was detected in any of the air samples. Half of the LOQ of 42.8 ng was used for inhalation calculations. Dermal exposure was monitored for the adult only using patches (25 cm^2) cut from a whole body dosimeter. Total potential dermal exposure for adults was 0.00057 mg/kg/day (12 hours). The manikin representing a child was not sampled for dermal exposure. HED used adjustments from the Exposure Factors Handbook to assess dermal exposure to children. Clothing penetration was not monitored and no adjustment was made for that factor. There were a large number of patches with non-quantifiable metofluthrin residues in the study, adding to potential uncertainty. The short term inhalation MOEs for adults and children were 1.9×10^6 and 9.4×10^5, respectively (target MOE = 100). The short term dermal MOE for adults was 44000, and for children was 15000 (target MOE = 100).

To measure incidental oral exposure, assuming that children could mouth the entire surface of the device, the device was wiped with dioctyl sodium sulfosuccinate (DSS), which simulates saliva extraction. The daily oral exposure was determined to be 2.3×10^{-5} mg/kg/day, which resulted in an MOE of 6.5×10^5 (target MOE = 100).

Cancer risk was estimated using the total adult exposure per use and assuming the product is used 12 times per year over 50 years, based on a use survey conducted by REJV (3). Estimated cancer risk was 6.5×10^{-9}. An upper bounding estimate was also conducted using the Ideal Gas Law. This estimate, which can never occur in reality, yielded a cancer risk of 1.5×10^{-5}.

The toxicological endpoints and studies are presented in Tables 1 and 2. A more detailed summary of the exposure assessment for the NORM-1 Personal Insect Repellant is found in Table 3.

Table 1. Toxicity Categories and Results of Toxicity Studies for Metofluthrin.			
Guideline No./ Study Type	MRID No.	**Results**	**Toxicity Category**
870.1100 Acute oral toxicity	46406719	LD50 > 2000 mg/kg	III
870.1200 Acute dermal toxicity	46406721	LD50 >= 2000 mg/kg	III
870.1300 Acute inhalation toxicity	46406723	LC50 > 1.08 and < 1.96 mg/L	III
870.2400 Acute eye irritation	46406724	Not an eye irritant	IV
870.2500 Acute dermal irritation	46406724	Mildly irritating to the skin (PDI = 0.8)	IV
870.2600 Skin sensitization	46406726	Not a dermal sensitizer	-

Table 2. Summary of Toxicological Doses and Endpoints for Metofluthrin for Use in Non-Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Incidental Oral Short-Term (1-30 days)	NOAEL = 15 mg/kg/day	UF_A = 10x UF_H=10x	Residential LOC for MOE = 100	Developmental Rat Study LOAEL = 30 mg/kg/day based on increased incidence of tremor in maternal animals
Dermal Short-Term (1-30 days)	NOAEL= 300 mg/kg/day	UF_A = 10x UF_H= 10x	Residential LOC for MOE = 100	Developmental Rat Study LOAEL = 1000 mg/kg/day based on mortality and clinical signs
Inhalation Short-Term (ALL DURATIONS)	NOAEL = 16 mg/kg/day	UF_A = 10x UF_H =10x	Residential LOC for MOE = 100	28-Day Inhalation Study in Rats LOAEL = 32 mg/kg/day based on mortality and clinical signs including tremors, ataxia, hypersensitivity, ataxic gait, tiptoe gait, lateral position, clonic convulsion, and hypothermia in both sexes
Cancer (oral, dermal, *inhalation*)	Likely to be a human carcinogen	Q1* = $1.62x10^{-2}$ $(mg/kg/day)^{-1}$		Based on female rat liver combined adenoma and carcinoma tumor rates

NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (intraspecies). UF_H = potential variation in sensitivity among members of the human population (interspecies). UF_{DB} = to account for the absence of key date (i.e., lack of a critical study). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Table 3. Short to Intermediate Term Exposures and Risk to Metofluthrin Used as a Personal Insect Repellent based on the Manikin Study Using the NORM 1 Generator.

Exposure Scenario	NOAEL	Total Exposure (Adult)	Total Exposure (Child)	MOE (Adult)	MOE (Child)	Level of Concern (LOC)
Incidental Oral, Short Term (1-30 days), based on DSS wipes[1]	15 mg/kg/day	NA	2.3×10^{-5} mg/kg/day	NA	6.5×10^{5}	100
Incidental Oral, Short Term (1-30 days), based on isopropanol wipes	15 mg/kg/day	NA	7.33×10^{-5} mg/kg/day	NA	2.1×10^{5}	100
Dermal Short Term (1-30 days)	300 mg/kg/day	0.0069 mg/kg/day	0.020 mg/kg/day	44000	15000	100
Inhalation	16 mg/kg/day	8.5×10^{-6} mg/kg/day	1.7×10^{-5} mg/kg/day	1.9×10^{6}	9.4×10^{5}	100

[1] DSS simulation extraction of saliva.

3.0 PROPOSED END-USE PRODUCTS/PATTERNS

The proposed label for the use of DeckMate Mosquito repellant was contained in MRID 46406504. The proposed label for the use of NORM-1 Personal Insect Repellant was contained in MRID 46406505.

3.1 DeckMate Mosquito Repellent Strip

Deckmate ™ Mosquito Repellent Strip is an impregnated paper strip (~3,528 cm^2) containing 1.82 percent metofluthrin as the active ingredient, and a total of 200 mg metofluthrin in the strip. The product also contains Bitrex ™ to discourage oral exposure to children or animals. The product may be used outdoors, and in barns/stables and kennels to protect companion non-food animals, such as horses, ponies, and dogs. The product cannot be used in milk barns, milk rooms, milk parlors, dairies, poultry houses, or swine or livestock houses. The product is for use on patios, campsites, decks, cabanas, and other outdoor areas. One strip is applied per 10 ft × 10 ft outdoor area. Indoors the application rate is two strips per 50 m^3. The strips can provide up to one week of protection. The product contains an indicator which tells when the product is used up. The product expires 30 days after opening the package. The label contained a number of optional statements which are not reiterated here. A schematic of the DeckMate Mosquito Repellent Strip is presented in Appendix A.

3.2 NORM-1 Personal Insect Repellant

The NORM-1 personal repellent consists of a holder with a battery powered fan, which is attached to the individuals clothing (such as a belt). A cartridge coated with 15-20 mg metofluthrin is inserted into the holder. The product is activated by turning on a battery powered fan to release the metofluthrin into the air surrounding the individual. The product is to be used outdoors, and is not to be used indoors or in enclosed spaces. One refill for the product will last up to 12 hours, according to the label. The cartridges contain Bitrex, to discourage children and pets from ingesting the product. The label contained a number of optional statements which are not reiterated here.

4.0 Residential Exposure Assessment

4.1 Residential Applicator Exposure Assessment

Applicator Exposure to metofluthrin from both of the proposed end use registrations, DeckMate Mosquito Repellant and NORM-1 Personal Insect Repellant, is considered negligible and has not been assessed.

4.2 Residential Post-application Exposure Assessment

4.2.1 Post application exposure from DeckMate Mosquito Repellent Strip

To assess the post-application exposure to metofluthrin from the use of DeckMate Mosquito Repellant strips, the registrant has proposed the use of a study using a surrogate compound, Esbiothrin, generated by combustion of a mosquito coil attached to cardboard to estimate the air concentration of metofluthrin. This was considered to be conservative by the registrant. The registrant also submitted evolution data for the DeckMate product. The submitted study on the esbiothrin mosquito coil was not considered applicable to the post application exposure assessment for metofluthrin, because the coil is combusted to release the esbiothrin insecticide, and DeckMate is not. The evolution rate study did not measure air concentrations and was not used to estimate exposure.

Post-application exposure by inhalation only to metofluthrin from use of the DeckMate repellant strip was assessed. Dermal exposure is considered negligible and has not been assessed.

HED used a different approach to provide a **BOUNDING** estimate of air concentrations using the Ideal Gas Law. Metofluthrin has a vapor pressure of 1.47×10^{-5} mm Hg (1.9×10^{-8} atm) at 25°C (298° K) and has a Molecular Weight of 360.36 g/mole. Using the Ideal Gas Law of the form:

$$PV = nRT$$

$$n = \frac{PV}{RT}$$

Where:
n = number of moles
P = 1.47×10^{-5} mm Hg (1.9×10^{-8} atm)
V = volume (1 liter is assumed)
R = the Ideal Gas Constant = 0.0821 L atm per mole ° K
T = temperature = 298 ° K

$$n = \frac{(1.9 \times 10^{-8} \text{ atm}) \times (1 \text{ liter})}{0.0821 \text{ L atm/mole} \circ \text{K} \times 298 \circ \text{K}} = 7.8 \times 10^{-10} \text{ moles}$$

The concentration would be:

Concentration (µg/L) = 7.8×10^{-10} moles × 360.36 g/mole × 106 µg/g = 0.28 µg/L

$\times 10^{-3}$ mg/µg $\times 10^{3}$ L/m^3 = 0.28 mg/m^3

If an individual (adult or child) is exposed to areas around the strip for 12 hours per day, the air concentration in 24 hour equivalents is

0.28 mg/m^3 x 12 hours/24 hour = 0.14 mg/m^3

An inhalation NOAEL of 100 mg/m^3 has been reported based on a 28-day rat study. The rats were exposed 4 hours per day, so the Human Equivalent Concentration would be 17 mg/m^3. In terms of mg/kg/day the exposure is: 0.14 mg/m^3 × 20 m^3/day ÷ 70 kg, = 0.04 mg/kg/day, assuming a 70 kg adult breathes 20 m^3 per day.

[Memorandum from K. Bailey (RAB2) to R. Gebken (RD), titled "Metofluthrin (S-1264): New Chemical Screen of Submitted Toxicology Studies. PC Code 109709, DP Barcode: D313560"].

The MOE is calculated in the following equation

$$\text{MOE} = \frac{16 \text{ mg/kg/day}}{0.04 \text{ mg/kg/day}} = 400$$

The target MOE is 100.

This estimate is considered to be very conservative, as the air concentration calculated by the ideal gas law (saturation) would never be fully achieved by the pest strip under real conditions. However, since this high end estimate does not exceed HED's level of concern, further refinement is not necessary.

4.2.2 Post-Application Exposure from NORM-1 Personal Insect Repellant

NORM 1 is a generator attached to the worn on an item of clothing, such as a belt. The product consists of a battery powered fan into which is inserted a cartridge coated on the inside with 15 to 20 mg of 100% technical metofluthrin. No photo or diagram of the device was included. The device can be worn for 12 hours and is intended for outdoor use (patios, campsites decks, etc.). According to a registrant submitted summary, the emission rate data indicate that approximately 0.75 mg/hour of the chemical will be emitted. The raw data supporting this emission rate were not provided. An exposure time of 12 hours was used in the exposure study and was used by the Agency in this risk assessment.

For post-application exposure to NORM-1 personal insect repellant, first a high end assessment for inhalation and dermal exposure was conducted. Then an assessment based on the data provided was conducted.

Bounding exposure assessment:

The amount of metofluthrin in the repellant device would have to be distributed over such a large volume of air that the metofluthrin could not all be inhaled. Thus, the high end inhalation exposure assessment for the DeckMate repellant strips would be applicable to the high end exposure assessment of the NORM-1 personal insect repellant, with an MOE of 400 (target MOE = 100). For post-application dermal exposure to children (which would be a worst case), HED did two high end assessments, 1) assuming that the entire cartridge of 20 mg metofluthrin was available for dermal absorption, which resulted in a dermal MOE of 225 (target MOE =

100); and 2) assuming that the claimed emission rate of 0.75 mg/hr was available for dermal exposure. This resulted in a dermal MOE of 500 (target MOE = 100). This is considered to be a short term scenario.

Amount available for dermal exposure	Wt. of Child	NOAEL	MOE
20 mg/day	15 kg	300 mg/kg/day	225 (Target 100)
0.75 mg/hr × 12 hr/15 kg	15 kg	300 mg/kg/day	500 (Target 100)

$$\text{MOE} = \frac{\text{NOAEL}}{\text{Exposure/wt of child}} = \frac{\text{NOAEL}}{\text{Amount Available x Dermal absorption / wt of child}}$$

$$= \frac{300 \text{ mg/kg/day}}{20 \text{ mg/day} / 15 \text{ kg}} = 225$$

Data based exposure assessment. Exposure of adults and children was estimated using manikins, one representing adults and the other representing a child. Only a summary report of the study was provided. Three separate 6 hour runs, each beginning close to 6 PM and ending around midnight, were conducted. The device was attached at the right waist of the adult manikin with the material generated in a downward direction (directionality is not specified on the label, although the label specifies that the switch is to be on the upper side). A distance of 0.4 m separated the manikins. Two 3-hour air samples were collected were collected from the breathing zone of both the adult and child manikin during each run.

Dermal exposure was assessed in the study using the adult manikin, and was measured using a whole body dosimeter (union suit). Patches (25 cm^2) were cut out of the dosimeter on the chest, upper torso, lower torso, upper right leg, lower right leg, lower right arm, and upper left leg. No dermal measurements were conducted on the "child" manikin. A diagram showing the locations of the device, manikins, and dermal dosimeters is presented in Appendix B. The environmental conditions during the study are presented in Appendix C.

In order to address incidental oral exposure, following each run the generating device was wiped twice with a gauze pad moistened with dioctyl sodium sulfosuccinate (DSS), which simulates saliva extraction. This was repeated with isopropyl alcohol (IPA).

All samples were frozen at <-5° C until analysis. Analysis was by gas chromatography. No detector was specified. No copy of the analytical method was included. A few sample chromatograms were included. The LOQs were stated to be 42.8 ng/sample, 0.535 ng/sample, and 1.07 ng/sample for air monitoring samples, dosimeter samples, and DSS samples, respectively.

Air samples were collected at heights of 1.0 and 1.6 m from the ground through OVS tubes, containing XAD-2 as the trapping agent, using calibrated personal sampling pumps operating at a rate of 2 liters per minute for 3 hours. Two sets of samples were collected for each run, at intervals of 1-3 hours and 3-6 hours. The estimated respiratory exposures and Margins of Exposure (MOEs) are presented in Table 4. Estimated dermal exposures are presented in Table

5. Incidental oral exposure of children simulating mouthing of the entire metofluthrin cartridge, and measured by wiping the cartridge with one of two solutions are presented in Table 6.

In order to estimate exposure and risk for individuals using this product a number of assumptions were required:

1) An average adult weighs 70 kg and a child weighs 15 kg.
2) The material is used 12 times during a year, based on the median number of applications for DEET products (3).
3) The dermal estimates are not corrected for clothing penetration (naked person scenario).
4) Since no dermal data were provided for the child, dermal exposure was estimated for children using adult values ($\mu g/cm^2$) and adjusting for total body surface area of 7640 cm^2 from the EPA Exposure Factors Handbook. (2) The Agency considers this to be conservative in that the NORM 1 study did not monitor all surface areas and the handbook considers all body locations.

Table 4. Air concentrations and Respiratory Risk to Adults and Children Using a NORM 1 Generator Containing Metofluthrin.

Description	Inhalation Residue (ng)			MEAN (ng)	Flow Rate (L/min)	Duration (min)	Total Volume (m^3)	Conc. ($\mu g/m^3$)	MOE (based on a NOAEL of 16 mg/kg/day)
	Run 1	Run 2	Run 3						
Child 1-3 hrs	21.41	21.4	21.4	21.4	2	180	0.36	0.059	9.4×10^5
Adult 1-3 hrs	21.4	21.4	21.4	21.4	2	180	0.36	0.059	1.9×10^6
Child 3-6 hrs	21.4	21.4	21.4	21.4	2	180	0.36	0.059	9.4×10^5
Adult 3-6 hrs	21.4	21.4	21.4	21.4	2	180	0.36	0.059	1.9×10^6

1 None detected in any of the samples, half of the LOQ of 42.8 ng/sample was used for calculations.

Volume = 2 L/min x 180 min x 10^{-3} m^3/L = 0.36 m^3

$$21.4 \text{ ng} / 0.36 \text{ m}^3 = 59 \text{ ng/ m}^3 = 0.0059 \text{ } \mu\text{g/ m}^3 = 0.000059 \text{ mg/ m}^3$$

Converting to mg/kg/day units:

Adult:

$$0.000059 \text{ mg/ m}^3 \text{ x } 20 \text{ m}^3\text{/day} \times 0.5 \text{ days} \times 1/70 \text{ kg} = 8.5 \times 10^{-6} \text{ mg/kg/day}$$

$$\text{MOE} = \frac{16 \text{ mg/kg/day}}{8.5 \times 10^{-6} \text{ mg/kg/day}} = 1.9 \times 10^6$$

Child:

$$0.000059 \text{ mg/ m}^3 \text{ x } 8.7 \text{m}^3\text{/day} \times 0.5 \text{ days} \times 1/15 \text{ kg} = 1.7 \times 10^{-5} \text{ mg/kg/day}$$

$$\text{MOE} = = \frac{16 \text{ mg/kg/day}}{1.7 \times 10^{-5} \text{ mg/kg/day}} = 9.4 \times 10^5$$

Table 5. Metofluthrin Residues and Dermal Exposures from the Use of a Generator Attached at the Waist for Six Hours.

Body Area	Residue (µg)			Adjusted Residue (µg) (Adjusted for low field fortification recovery of 71.3%)			MEAN (µg)	MEAN (µg/ per cm²)	Surface Area (cm²)	Total Potential Dermal Exposure (µg)	Total Potential Dermal Exposure of Child (mg/kg/ day)	Total Potential Dermal Exposure of Adult (mg/kg/day)
	Run 1	Run 2	Run 3	Run 1	Run 2	Run 3						
Lower Right Leg	0.268	0.268	0.268	0.268	0.268	0.268	0.268	0.011	1190	13.1	0.00175	0.00037
Upper Right Leg	0.268	1.15	0.536	0.268	1.62	0.75	0.880	0.035	1910	66.9	0.00892	0.00191
Lower Torso	0.268	0.841	1.43	0.268	1.18	2.01	1.150	0.046	1775	81.7	0.01089	0.00233
Upper Torso	0.268	0.268	0.268	0.268	0.268	0.268	0.268	0.011	1775	19.5	0.0026	0.00056
Chest	0.268	0.268	0.268	0.268	0.268	0.268	0.268	0.011	3550	39.1	0.00521	0.00112
Lower Right Arm	0.268	0.268	0.268	0.268	0.268	0.268	0.268	0.011	605	6.7	0.00089	0.00019
Upper Left Leg	0.268	0.268	0.268	0.268	0.268	0.268	0.268	0.011	1190	13.1	0.00175	0.00037
								TOTAL	**11995**	**240.1**	**0.020**	**0.0069**
									7640	**152.9**		

Exposure Factors:

Body Weight (kg)	Surface Area (cm²)
Adult = 70	11995 (from Study)
Child = 15	7640 (from Reference 2)

Note: Total exposures for children were calculated by adjusting the adult total exposures by the surface in the study to that of a 3 year old child from the Exposure Factors Handbook (95 percentile, Reference 2). This is considered conservative because the study did not monitor the entire body and the Handbook considers all of the body areas. The adult value was further adjusted by the ratio of the body weights.

Formulas:

$\mu g/cm^2$ = residues (μg)/Patch Area (25 cm^2)

Total Exposure (μg) = Sum of exposure to individual body parts

Daily Exposure (mg/kg/day) = Total Exposure (μg/6 hr run) × 1 mg/1000 μg × 2 runs/day × 1/BW (kg)

NOTE: Exposure run was 6 hours, 12 hours are assumed per day = 2 runs/day

Table 6. Residues and Resulting Exposure to Children from Incidental Oral Ingestion from Mouthing a Metofluthrin Generator.

Sample Type	Metofluthrin Residue (μg)			MEAN (μg)	MEAN (mg)	Cumulative Residue (mg)[1]	Daily Oral Exposure (mg/kg/day)[2,3]
	Run 1	Run 2	Run 3				
Dioctyl sodium sulfosuccinate (DSS)	0.54	0.54	0.54	0.54	0.00054	0.00108	2.3×10^{-5}
Isopropanol (IPA)	1.52	1.73	1.86	1.70	0.0017	0.0034	7.3×10^{-5}

The resulting MOEs (short term scenario) were 6.0×10^5 for the DSS extraction and 2.1 × 105 for the estimate based on isopropanol extraction.

1 Cumulative Residue (12 exposure) = Mean Residue (6 hour) x 2

2 Daily Oral Exposure = cumulative residue (mg) x 0.32 (Saliva Efficiency)/15 kg (BW)

3 A child's body weight is assumed to be 15 kg

4.3 Estimated Cancer Risk

The Q1* for metofluthrin was based on female hepatocellular adenomas, carcinomas, and combined adenomas/carcinomas in rats. The Q1* is 1.62 x 10^{-2} (mg/kg/day) $^{-1}$.

A bounding worst (and unrealistic) case inhalation cancer assessment was done for the metofluthrin products (DeckMate and NORM-1). The saturation concentration of 0.28 mg/ m^3 was used, with a 12 hour / day exposure time (half a day). An adult breathes 20 m^3 of air per day. The use frequency was 12 applications per year from the use survey conducted by REJV. The users are expected to use the products over a 50 year period in their 70 year lifetime. This results in a Lifetime Average Daily Dose (LADD) of 0.000939 mg/kg/day. The LADD is multiplied by the Q1*, which results in an estimated cancer risk of 1.5 x 10^{-5}.

$$\text{LADD} = \frac{\text{air concentration x respiratory volume x time exposed}}{\text{Lifetime x wt of individual}}$$

$$= \frac{0.28\ \text{mg/m}^3 \times 20\ \text{m}^3\text{/day} \times 0.5\ \text{day} \times 12\ \text{days/yr} \times 50\ \text{years}}{365\ \text{days} \times 70\ \text{years} \times 70\ \text{kg}} = 0.000939\ \text{mg/kg/day}$$

Estimated Cancer Risk = LADD x Q1* = 0.000939 mg/kg/day x 0.0162 $(\text{mg/kg/day})^{-1}$

$$= 1.5 \times 10^{-5}$$

It must be emphasized that this scenario cannot possibly occur in reality and provides an extreme upper bound and this estimated cancer risk is based on the saturation concentration.

A more realistic approximation can be derived from the NORM 1 exposure study. In the monitoring study for the NORM-1 product, no metofluthrin was quantifiable in the air samples taken (< 0.000059 mg/m³, LOQ = 0.00012 mg/m³). At the level of quantification (LOQ), which is still conservative, the cancer risk would be:

$$\text{LADD} = \frac{\text{air concentration x respiratory volume x time exposed}}{\text{Lifetime x wt of individual}}$$

$$= \frac{0.00012\ \text{mg/m}^3 \times 20\ \text{m}^3\text{/day} \times 0.5\ \text{day} \times 12\ \text{days/yr} \times 50\ \text{years}}{365\ \text{days} \times 70\ \text{years} \times 70\ \text{kg}} = 4.0 \times 10^{-7}\ \text{mg/kg/day}$$

Estimated Cancer Risk = LADD × Q1* = 4.0×10^{-7} mg/kg/day × 0.0162 $(\text{mg/kg/day})^{-1}$

$$= 6.5 \times 10^{-9}$$

Assumptions used in the dermal cancer assessment included a daily dermal exposure of 0.0008 mg/kg/day, from the dermal exposure from the NORM-1 product. The use frequency was 12 applications per year from the use survey conducted by REJV. The user is expected to use the product over a 50 year period over a 70 year lifetime.

Estimated Cancer Risk = 1.62 x 10^{-2} (mg/kg/day) -^{1}(Q*) × Exposure (0.0008 mg/kg/day) ×12 applic./yr ÷ 365 days/yr × 50yrs/70 yrs = 3.0×10^{-7}

Because of the conservatism in the inhalation cancer estimate, it is inappropriate to add the estimated risks for inhalation and dermal exposure.

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2) EPA (1997 Exposure Factors Handbook Volume 1. EPA/600P-95/002Fa
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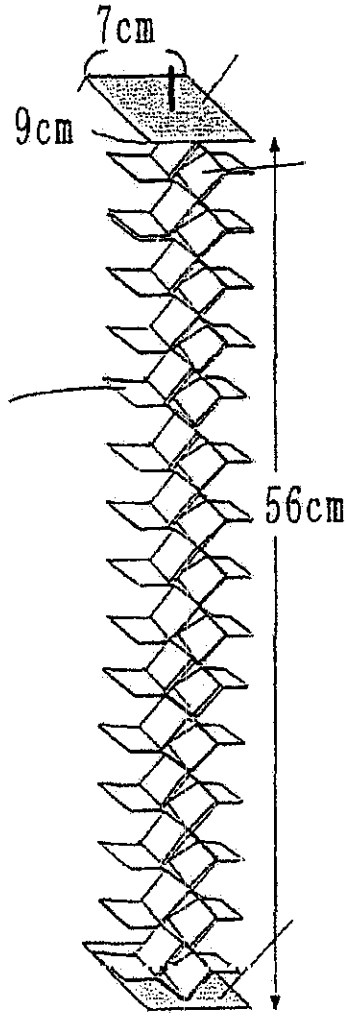
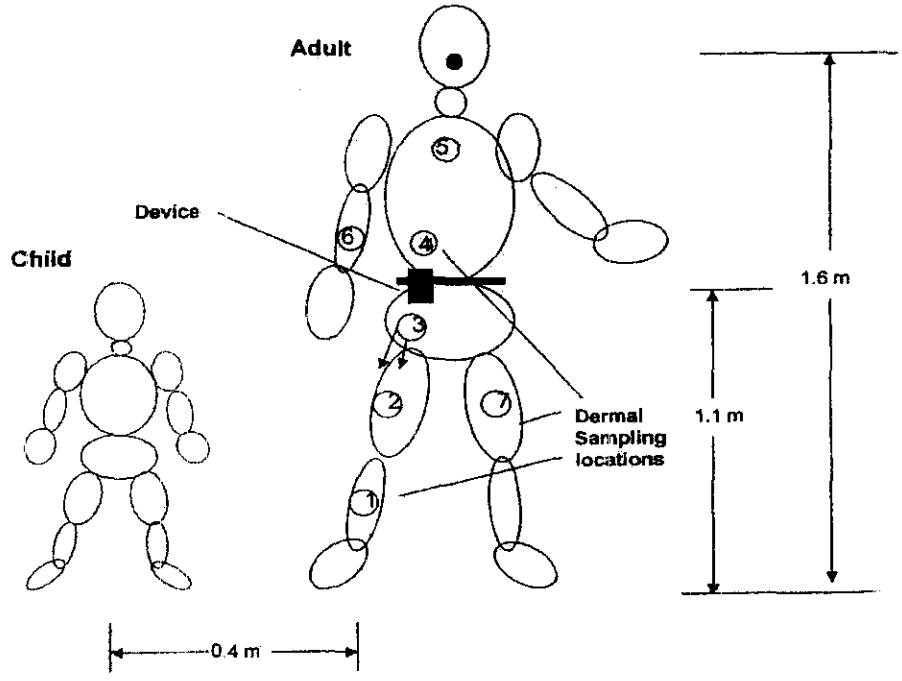
APPENDIX A. SCHEMATIC OF DECKMATE MOSQUITO REPELLENT STRIPS



APPENDIX B. LOCATION OF DEVICE, MANIKINS AND DERMAL DOSIMETER SAMPLES

Location of Device, Manikins and Dermal Dosimeter Samples



APPENDIX C. Environmental Conditions During Exposure Study with NORM 1 Generator.

Day	Temp °F	Humidity (%)	Wind Speed (MPH)	Light Conditions
1	84.5	31.6	None	Shaded, Sun at horizon
1	81.4	35.9	None	Dark
1	75.6	44.2	None	Dark
1	73.7	44.9	None	Dark
1	71.4	49.9	None	Dark
1	68.6	55.7	None	Dark
1	65.9	61.5	None	Dark
2	84.8	35.5	None	Shaded, Sun at horizon
2	81.0	39.6	None	Dark
2	77.9	42.2	None	Dark
2	72.9	47.9	None	Dark
2	69.8	55.9	None	Dark
2	67.3	73.5	None	Dark
2	66.0	73.4	None	Dark
3	87.0	41.8	None	Shaded
3	81.7	46.7	None	Sun at horizon
3	77.7	53.7	None	Dark
3	76.3	58.3	None	Dark
3	73.2	56.8	None	Dark
3	71.1	69.5	None	Dark
3	71.9	65.7	None	Dark
3	71.1	65.6	None	Dark

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R132945

Chemical: Metofluthrin

PC Code:
109709
HED File Code: 12000 Exposure Reviews
Memo Date: 9/14/2006
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