Proposed Registration Decision PRD2016-09

Metofluthrin

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Overview

Proposed Registration Decision for Metofluthrin

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of SumiOne Technical Grade and OFF! Clip On Mosquito Repellent, containing the technical grade active ingredient metofluthrin, as a personal insect repellent.

SumiOne Technical Grade (Registration Number 30210) and OFF! Clip On Mosquito Repellent (Registration Number 30211) are conditionally registered in Canada. The detailed review for SumiOne Technical Grade and OFF! Clip On Mosquito Repellent can be found in Evaluation Report ERC2015-01, *Metofluthrin*. The current applications were submitted to convert SumiOne Technical Grade and OFF! Clip On Mosquito Repellent from conditional registration to full registration.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of SumiOne Technical Grade and OFF! Clip On Mosquito Repellent.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on metofluthrin, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on metofluthrin, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Metofluthrin?

Metofluthrin is an active ingredient which belongs to the pyrethroid class of insecticides and is used to repel mosquitoes. OFF! Clip On Mosquito Repellent is a battery-powered device which contains a metofluthrin-impregnated cartridge. The OFF! Clip On Mosquito Repellent device is worn on the person and functions as a personal insect repellent by vaporising metofluthrin and emitting it over an area large enough to protect the wearer from mosquitoes.

Health Considerations

Can Approved Uses of Metofluthrin Affect Human Health?

OFF! Clip On Mosquito Repellent containing metofluthrin is unlikely to affect your health when used according to label directions.

Potential exposure to metofluthrin may occur when handling or using the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

In laboratory animals, metofluthrin was of low acute toxicity by the oral and dermal routes of exposure. It was of slight acute toxicity by the inhalation route of exposure and as such the hazard statement "Caution Poison" is required on the label. Metofluthrin was minimally irritating to the eye, was nonirritating to the skin, and did not cause an allergic skin reaction. Metofluthrin does, however, belong to a class of pesticides that may cause a transient itching, tingling or burning sensation of the skin following skin contact.

OFF! Clip On Mosquito Repellent product consists primarily of metofluthrin; therefore, the toxicity profile and label statements for technical grade metofluthrin are representative of this product.

Registrant-supplied short, and long term (lifetime) animal toxicity tests, as well as information from the published scientific literature were assessed for the potential of metofluthrin to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment included neurotoxicity characterized by clinical signs. In addition, although there was no evidence of increased susceptibility of the young in the guideline toxicity studies submitted, residual uncertainty remains since young animals have differences (such as the age-dependent maturation of key metabolic processes) that may lead to increased susceptibility of the young to pyrethroid toxicity. There was also evidence of effects on the liver. Longer-term dosing with metofluthrin resulted in liver tumours in rats, but not in mice. The risk assessment protects against the effects noted above by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Risks in Residential Environments

Estimated risk for residential exposure is not of concern provided that directions specified on the label are observed.

For the original residential exposure review of metofluthrin, please see ERC2015-01. Two data requirements were identified during the original review, a new passive dosimetry study and a new in vivo dermal absorption study. The risk assessment has been updated and all data requirements have now been satisfied.

A risk assessment conducted for individuals handling, or those in the vicinity of the OFF! Clip On Mosquito Repellent device, indicated that risks to adults, youth and children are not of concern when the product is used according to label directions.

Environmental Considerations

What Happens When Metofluthrin Is Introduced Into the Environment?

OFF! Clip On Mosquito Repellent will not pose an unacceptable risk to non-target aquatic and terrestrial organisms.

Metofluthrin enters the environment when used as an insect repellent in a personal device, which allows the active ingredient to vaporize into the air. Significant deposition of metofluthrin in the environment is unlikely due to the volatile nature of the compound, rapid transformation processes in soil, and limited use pattern.

Metofluthrin is highly toxic to aquatic invertebrates, fish, and bees. But the exposure of these nontarget organisms to metofluthrin is, however, unlikely based on the use pattern.

Value Considerations

What Is the Value of OFF! Clip On Mosquito Repellent?

OFF! Clip On Mosquito Repellent is a personal insect repellent device that provides protection from mosquitoes for up to 12 hours.

Mosquitoes are an outdoor nuisance pest across all of Canada, especially in the morning and evening. Mosquito bites can cause discomfort and irritation, and can vector diseases such as West Nile Virus. In addition to health risks associated with mosquito bites, annoyance from mosquitoes can reduce the enjoyment of being outdoors and cause people to avoid outdoor activities when mosquito populations are heavy.

While no additional value data were required to convert the end-use product OFF! Clip On Mosquito Repellent from conditional to full registration, data was submitted to support an increase in the protection time from 11 to up to 12 hours.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of OFF! Clip On Mosquito Repellent to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

For OFF! Clip On Mosquito Repellent the hazard statement “Caution Poison” is required on the product label. The label states to keep out of reach of children and thus, it is considered unlikely for youth and children to replace the cartridge (refill disk); however, to exclude this activity from being considered in the risk assessment for youth, the following statement is on the label “only adults are permitted to replace the refill disk.” In addition, a statement identifying the device should not be worn while barbecuing is required.

Environment

Key risk-reduction measures for the protection of the environment include the precautionary label statement:

- Toxicity statement for aquatic organisms.

Next Steps

Before making a final registration decision on metofluthrin, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and the Agency’s response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on metofluthrin (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA’s Reading Room (located in Ottawa).

Science Evaluation

Metofluthrin

1.0 The Active Ingredient, Its Properties and Uses

Please refer to Evaluation Report ERC2015 01, *Metofluthrin* for information on the identity of the active ingredient, physical and chemical properties of the active ingredient and end-use product and mode of action.

1.1 Directions for Use

OFF! Clip On Mosquito Repellent is a personal insect repellent for use outdoors that repels mosquitoes for up to 12 hours. To use OFF! Clip On Mosquito Repellent, a mosquito repellent disk is inserted into the battery-powered device. The device is then turned on and clipped onto the user's belt, pants, shorts, waistband, or purse. OFF! Clip On Mosquito Repellent requires several minutes to provide mosquito repellency after being turned on or after moving to a new location. If the device is turned off before 12 hours have elapsed, the remainder of the repellent can be used at a future time.

2.0 Methods of Analysis

Please refer to ERC2015-01.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for metofluthrin was conducted previously and is summarized in ERC2015-01.

Results of the toxicology studies conducted on laboratory animals with metofluthrin, as well as the toxicology endpoints for use in human health risk assessment, and an overall summary of the data can be found in ERC2015-01.

Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents to the PMRA, including adverse effects to Canadian health and the environment. Incidents were searched and reviewed for the active metofluthrin. As of 4 March 2015, there were 15 human and one domestic animal incident reports as well as seven packaging failure reports involving metofluthrin in the PMRA database. All reported incidents were associated with the product OFF! Clip On Mosquito Repellent.

Of the 15 human cases, the symptoms reported in four moderate and nine minor cases were determined to have some degree of association with the reported exposure. Two of the minor cases involved children between six and 12 years of age. Exposure to metofluthrin in most cases occurred during use of the insect repellent product as per label directions. The commonly reported route of exposure was inhalation. In five cases, other exposure scenarios were noted which included deliberate inhalation of product vapor, dermal contact with the product and wearing the product on shirts or blouses. A wide range of symptoms were reported. These included dizziness, muscle tremors, muscle weakness, fainting, vomiting, nausea, erythema, skin irritation, swelling, irregular heart rate, lethargy, respiratory irritation and eye irritation.

The domestic animal incident occurred in Canada and involved a dog. The dog had no known direct exposure to the product containing metofluthrin; however, it was reported to have been in the general vicinity of the owner who was wearing the product. The animal experienced vocalization, fecal and urinary incontinence and a seizure.

There were seven packaging failure incidents involving metofluthrin. The failures in packaging in four reports were described as: the device continuing to operate in the 'OFF" position, leakage of acid from the device battery, and device malfunction resulting in damage to clothing. Human injury did occur in one case, where skin irritation and blistering were reported as a result of dermal contact with the device battery acid. In three incident reports, the failure in packaging was only described as 'container leaked'. No other details were provided in these cases.

The incidents involving metofluthrin were considered in this review. Labelling language for the OFF! Clip On Mosquito Repellent product will be strengthened regarding appropriate placement of the device on clothing, as well as mitigation of potential direct inhalation exposure. The PMRA will continue to monitor incident information associated with the active ingredient metofluthrin.

3.1.1 PCPA Hazard Characterization

Please refer to ERC2015-01.

3.2 Acute reference dose, acceptable daily intake and cancer assessment

Please refer to ERC2015-01.

3.3 Residential Risk Assessment

Residential exposure to OFF! Clip On Mosquito Repellent is considered intermediate in duration and is predominantly by the dermal, inhalation and incidental oral routes.

3.3.1 Toxicological Endpoints

Please refer to ERC2015-01.

3.3.1.1 Dermal Absorption

A suspension of methoxymethylbenzyl-α-14CS-126RTZ and methoxymethylbenzyl-α-14CS-126RTE (98:2 ratio) in carboxymethylcellulose, at doses of 2, 20, and 200µg/cm^2, was dermally applied to a 10cm^2 dorsal area on male CRL:CD(SD) rats. For each dose, four rats were used and monitored for each time period of six, 24, 48, and 168 hours post-application. After an exposure period of six hours, all rats were anesthetized, application site skin was washed (with detergent), and urine (including cage wash) and feces were collected. For rats monitored for longer intervals than six hours, the protective cover was replaced and urine, feces, and cage washes, were collected every 24 hours, until termination. The application site skin was washed again at the time of termination. At the 6-hour termination, and at each termination interval, the absorbed dose (urine, cage washing, feces, blood, gastrointestinal tract and contents, and carcass), potentially absorbable dose (stratum corneum (tape strips), and application site skin), and unabsorbed dose (absorbent cotton for washing, protective equipment, administration site bandage, abdominal bandage, plus the spatula used for administration) were measured for radioactivity and results (means and standard deviations) were presented as radioactive recovery in percentage of applied dose.

Total recoveries of the applied doses, at all the termination intervals, were between 91.1 and 100%. All total recoveries were considered within the acceptable range (90 - 110%). Results were not adjusted for incomplete recovery of the applied dose. The majority of residues were recovered from the 6-hour skin washes: at 2µg/cm^2, between 57.6% and 64.3%; at 20µg/cm^2, between 68% and 78.4%; and at 200µg/cm^2, between 80.5% and 85.4%.

In all three doses, dermal absorption values were estimated as the total of the absorbed dose and the potentially absorbable dose. The dermal absorption values decreased (21.5%, 16.9%, and 7.0%) as applied dose increased (2, 20, and 200µg/cm^2), respectively, at the 168 hour final monitoring period. However, the potentially absorbable residues did not decrease significantly after the 72 hour time period, but were accounted for as skin bound residues and final skin wash residues. The residues in the carcass, gastrointestinal tract and contents decreased to non-detectable levels by the 72 hour time period, while the urine and feces residues increased during the same time period. This indicates that no further significant systemic absorption took place 72 hours following application. Therefore, the dermal absorption for all doses was considered complete. The dermal absorption value determined to be most appropriate from this study is 22%, from the lowest dose and monitoring interval of 168 hours. This dermal absorption value is considered to be conservative as it considers the skin bound residues that may not become systematically available.

No major limitations in the study were identified.

3.4.2 Residential Exposure and Risk

Residential exposure and risk assessment was conducted for the product, OFF! Clip On Mosquito Repellent. The device is a battery powered portable device that clips onto a belt, pants, shorts, waistband or purse. The active ingredient (a.i.), metofluthrin, is located in a small capsule (cartridge) that is inserted into the device and then disposed of when empty. An electric fan drives air flow across the cartridge containing metofluthrin and vaporizes it into the air

surrounding the user, thus, repelling the insects. The active ingredient in one device cartridge (refill disk) weighs 46 mg (guarantee: 31.2%), therefore, it contains 14.35 mg active ingredient and provides up to 12 hours of protection against mosquitos with each refill. Users are unlikely to load more than one cartridge per day.

3.4.2.1 Residential Handler Exposure and Risk Assessment

Adults

There is potential for dermal exposure to (adult) homeowners inserting or replacing the cartridge containing metofluthrin in the device. This exposure is expected to be short term in duration. Since no exposure estimates were provided to quantify handler exposure, the pet collar scenario from the United States Environmental Protection Agency (USEPA) Residential SOP (2012) was used.

Table 3.4.2.1 Exposure estimates to adults loading the device

Amount of metofluthrin in cartridge (kg)	Unit of exposure (mg/kg a.i.)[1]	No. of cartridges used/day	Exposure (mg/kg bw/day)[2]	MOE[3] (Target MOE = 300)
14.35×10^{-6}	264	1	4.74×10^{-5}	6335128

1. Treated pet section in USEPA Residential SOP (2012) for pet collar (exposure data for spot-on applications were recommended as surrogate data).
2. Exposure = $\frac{\text{Unit of exposure (from spot-on scenario)} \times \text{amount handled per cartridge} \times \text{No. of cartridges used /day}}{\text{BW (80kg)}}$
3. MOE = $\frac{\text{NOAEL (300 mg/kg bw/day)}}{\text{Exposure}}$

Youth and Children

The label states to keep out of reach of children. Since it is considered unlikely for youth and children to replace the cartridge (refill disk) and in order to exclude this activity from being considered in the risk assessment for youth, the following statement will be added to the label "only adults are permitted to replace the refill disk."

3.4.2.2 Post-application Residential Exposure and Risk

Potential dermal, inhalation and oral post-application exposure are expected from the use of OFF! Clip On Mosquito Repellent. A new passive dosimetry study was submitted to estimate the dermal and inhalation exposure generated from using the OFF! Clip On Mosquito Repellent device. The study estimated the inhalation and dermal exposures of a homeowner wearing the device as well as bystander who may be in the vicinity of someone wearing the device.

Passive Dosimetry Study

This study was conducted to estimate the amount of residues generated during the use of an OFF! Clip On Mosquito Repellent. The deposition of metofluthrin residues on the skin, the air concentrations and the amount of residues left on the device were measured in the study and used for the estimation of the dermal, inhalation and incidental oral exposures of metofluthrin.

This Good Laboratory Practice (GLP) compliant chemical specific passive dosimetry exposure study was conducted in an outdoor location at the laboratory to mimic actual use conditions of the device. In this study, an adult mannequin and a child mannequin were used to simulate a device user and bystander. Two scenarios were modeled; 1) the device was placed on the waist of the adult mannequin with the child mannequin as the bystander and 2) the device was placed on the waist of the child mannequin and the adult mannequin was the bystander. Both mannequins were dressed in cotton long johns (dosimeters) and wore air sampling pumps connected to air sampling tubes placed at the breathing zone with air intake of 2L/min. The device was activated first, followed by the air pumps. Air samples were collected from 0-3 and 3-6 hours following activation of the device. At the end of the six hours, the device was switched off; the cotton dosimeters were collected and cut into six sections (Lower Arms, Upper Arms, Front Torso, Rear Torso, Lower Legs, and Upper Legs) for analysis. The hands of the mannequins were wiped with gauze wetted with isopropyl alcohol (IPA) and the gauze wipes were saved for analysis. Head, face and neck were not monitored. Additionally, at the end of the six hours, the devices were wiped with gauze wetted with dioctyl sodium sulfosuccinate (DSS) followed by gauze wetted with IPA to measure the residues that precipitated on the device and which may end up on the user's hand when touching the device.

Three trials were conducted with the adult mannequin wearing the device and three trials were conducted with the child mannequin wearing the device, resulting in a total of six trials. The study was performed starting no earlier than two hours before sunset to minimize the effect of sunlight and possible photodecomposition of the active ingredient. One trial of each scenario was conducted on three separate nights to complete the six trials. The results of the metofluthrin residues found in the breathing zone ranged from 4.64×10^{-3} mg/m^3 to 2.35×10^{-2} mg/m^3. For the three trials in which the adult mannequin was wearing the device, the average air concentration for the adult mannequin was 1.06×10^{-2} mg/m^3 and the child mannequin was 1.41×10^{-2} mg/m^3. For the three trials in which the child mannequin was wearing the device, the average air concentration for the adult mannequin was 1.29×10^{-2} mg/m^3 and the child mannequin was 1.29×10^{-2} mg/m^3.

Potential dermal exposure was calculated for adult and child separately in both scenarios (adult wearing the device and child wearing the device). Total residues of metofluthrin, corrected for field fortification, on each of the six dosimeter sections and hand wipe samples were summed. Given the nature of clothing normally worn while engaging in outdoor activities (shorts and short-sleeved shirt), total dermal exposure considered 100% of the residues for body sections that are not covered and 50% (clothing protection factor) of the residues for body sections that are covered. Total residues were normalized per hour and per amount of active ingredient in the cartridge. For the three trials in which the adult mannequin was wearing the device, the average dermal unit exposure for the adult mannequin was 332343 µg/kg active ingredient handled and for the child mannequin, standing in the vicinity of the adult mannequin, was 108169 µg/kg active ingredient handled. For the three trials in which the child mannequin was wearing the device, the average dermal unit exposure for the child mannequin was 1248474 µg/kg active ingredient handled, while for the adult mannequin, standing in the vicinity of the child mannequin, the average dermal unit exposure to the adult was 109490 µg/kg active ingredient handled.

The average dermal hand (that is, both hands) exposure for adults where the adult mannequin was wearing the device was 16102 µg/kg active ingredient handled and for the child mannequin was 1766 µg/kg active ingredient handled The average dermal hand exposure for adults where the child mannequin was wearing the device was 9746 µg/kg active ingredient handled and for the child mannequin was 9746 µg/kg active ingredient handled.

Residues of metofluthrin remaining on the device after running for six hours were wiped with DSS followed by IPA. Total mean residues deposited on the device in the two scenarios were 0.5866 µg/sample. However, when normalized for duration and amount of active ingredient in the cartridge, the unit of exposure was 82853 µg/kg active ingredient handled. Since the residues deposited on the device were believed to result from the condensation of the active ingredient vapours and are not influenced by the person wearing it, the total mean residues deposited on the device from all the trials was used to increase sample size.

Dermal units of exposure

The dermal exposure was calculated separately for adult and child by summing the mean residues of metofluthrin measured on each section of the dosimeter and the hand wipes. While a youth mannequin was not included in the study, considering the residues emitted from the device are constant, the child dermal unit of exposure will be the highest among the age groups (adult and youth) as child has the lowest surface area. Therefore, the child dermal exposure is not expected to underestimate the exposure to youth and no dermal risk assessment was conducted for youth.

The table below lists the dermal units of exposure for each subpopulation: 1) a person wearing the OFF! Clip On Mosquito Repellent device; 2) a bystander in the vicinity of someone wearing the device; and 3) a person wearing the device and in the vicinity of someone wearing the device. The child hand unit of exposure is also included below as it will be used in estimating the child exposure from incidental non-dietary oral ingestion of residues.

Table 3.4.2.2 Post-application dermal units of exposure (µg/kg a.i. handled)

Subpopulation	Unit exposure from wearing the OFF! Clip On Mosquito Repellent device	Unit of exposure from being in the vicinity of someone wearing the OFF! Clip On Mosquito Repellent device	Combined units of exposure
Adult[1]	332343	109490	441833
Child[1]	1248474	108169	1356642
Child Hand[2]	64.97	11.77	76.74

[1] Dermal exposure from the passive dosimetry study using residues from all body sections and hand wipes, and considering wearing shorts and short-sleeved shirt.

[2] Child hand unit of exposure (µg/kg a.i. handled/cm^2) = single hand residue / (6 h × 0.00000118 kg a.i. handled/day × 150 cm^2 hand surface area)

The whole active ingredient in a cartridge is 14.2×10^{-6} kg a.i. /12 hours (1.18×10^{-6}) based on a protection time of 12 hours

Inhalation units of exposure

The inhalation exposure was presented in µg/m^3. Considering the inhalation rate for an adult and a child and that one cartridge has a protection time of 12 hours, the inhalation units of exposure in µg/kg active ingredient handled are captured below for: 1) a person wearing the OFF! Clip On Mosquito Repellent device; 2) a bystander in the vicinity of someone wearing the device; and 3) a person wearing the device and in the vicinity of someone wearing the device.

The passive dosimetry study did not measure the amount of residues inhaled by youth. Although the youth inhalation rate is higher than the child, the youth body weight is much higher than the child. Therefore, the child inhalation exposure is not expected to underestimate the inhalation exposure of a youth. Hence, no inhalation risk assessment was conducted for youth population.

Table 3.4.2.3 Post-application inhalation units of exposure for people wearing the device

	Air concentrations (µg/m^3)[1]	Inhalation exposure (µg/hour) = Air conc. (µg/m^3) × inhalation rate (m^3/h)[2]	Units of exposure (µg/kg a.i. handled)[3]
Adult	10.60	6.68	5659322
Child	12.87	2.96	2508559
Post-application inhalation units of exposure for a bystander in the vicinity of someone wearing the device			
	Air concentrations (µg/m^3)[1]	**Inhalation exposure (µg/hour) = Air conc. (µg/m^3) × inhalation rate (m^3/h)[2]**	**Units of exposure (µg/kg a.i. handled)[3]**
Adult	12.90	8.13	6887288
Child	14.08	3.24	2744407
Post-application inhalation units of exposure for a person wearing the device and in the vicinity of someone wearing the device			

	Air concentration from wearing the device (µg/m^3)[1]	Air concentration from being in the vicinity of a device (µg/m^3)[1]	Total air concentration (µg/m^3)	Inhalation exposure (µg/hour) = Air conc. (µg/m^3) × inhalation rate (m^3/h)[2]	Units of exposure (µg/kg a.i. handled)[3]
Adult	10.60	12.90	23.50	14.81	12546610
Child	12.87	14.08	26.95	6.20	5252966

[1]Passive dosimetry study

[2] Inhalation rate for intermediate-term for adult is 0.63 m^3/hour and for child is 0.23 m^3/hour^3.The amount of kg a.i. in one cartridge handled per 12 hours is 1.18 × 1 0^{-6}.

Device Wipe Exposure

Metofluthrin residues may precipitate on the device when it is in use. As these residues may be transferred to both adult and child skin through touching the device, exposure to these residues is estimated in this risk assessment as incidental dermal exposure. The passive dosimetry study presented the total residues from wiping the device (by both IPA and DSS solutions) in µg/sample which were then normalized for the amount of active ingredient in one cartridge and for duration, as noted in the table below.

Moreover, the amount of residues precipitated on the device is also used when considering a child incidental non- dietary oral ingestion (hand to mouth following touching the device). For this assessment the residues were normalized per cm^2 of one child hand and estimated in µg/kg a.i. handled/cm^2.

Table 3.4.2.4 Dermal unit of exposure from residues precipitating on the device

Total wipe samples (µg/sample)[1]	Total residues in an hour of exposure (µg/hour)	Unit of exposure[3] (µg /kg a.i. handled)[2]	Amount of residues per cm^2 of one hand of a child (µg / kg a.i. handled/ cm^2)[3]
0.59	0.10	82853	552

1. Mean amount of residues on device
2. Adjusted for 0.00000118 kg a.i. handled
3. Normalized per childhand surface area (150 cm^2/hand)

3.4.2.2.1 Adult Post-application Residential Exposure and Risk

There is potential for dermal and inhalation exposure to adult consumers wearing OFF! Clip On Mosquito Repellent device while engaging in outdoor activities. The exposure duration will be considered intermediate as it is used during the four months of mosquito season according to the DEET insect repellent risk assessment from the DEET joint venture (RRD2002-01 – *Personal insect repellents containing DEET (N,N-diethyl-m-toluamide and related compounds)*.

Dermal and inhalation exposure during the use of the device

Post-application dermal exposure was estimated by coupling the dermal unit of exposure derived from the passive dosimetry study with the amount of product handled per day per kg body weight. Given the nature of clothing that is normally worn while engaging in outdoor activities (shorts and short-sleeved shirt, chosen from the USEPA Residential SOP (2012)), a protection factor of 50% (USEPA Residential SOP (2012)) was applied to the units of exposure for the sections of the body that are covered.

Although many of the dermal samples monitored in the passive dosimetry study for adults were non-quantifiable, dermal exposure was calculated using ½ level of quantitation (LOQ). For those non-detect samples it was based on ½ level of detection (LOD).

Inhalation exposure was estimated by coupling the inhalation units of exposure values derived from the passive dosimetry study with the amount of product handled per day per kg body weight.

Table 3.4.2.5 Dermal and Inhalation Exposure and Risk Estimates for Adults

Dermal Unit Exposure[1] (UE; µg/kg a.i. handled)	Inhalation Unit Exposure[1] (UE; µg/kg a.i. handled)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Dermal Exposure[2] (mg/kg bw/day)	MOE[3] (Target MOE = 300)	Inhalation Exposure [2] (mg/kg bw/day)	MOE[3] (Target MOE = 300)
332343	5659322	14.35	1	5.96×10^{-5}	5032373	1.02×10^{-3}	17140

1. Dermal and inhalation units of exposure: See Tables 3.4.2.2 and 3.4.2.3.
2. Dermal and Inhalation Exposures = $\frac{\text{UE X Amount a.i./cartridge X No.of cartridges used/day X conversion factor}}{\text{BW (80 kg)}}$

   Dermal absorption was not factored in as the endpoint used was derived from a dermal study
3. MOE = $\frac{\text{NOAEL (300 mg/kg bw/day)}}{\text{Exposure}}$

Incidental exposure to residues on the surface of a device during its use

Incidental dermal exposure, expected from touching the device, was estimated using the passive dosimetry study which measured the total amount of residues accumulating on the device. A conservative estimate was derived based on the potential that all the residues on the device may be available and incidentally transferred to the hand. The unit of exposure from the residues on the device was coupled with the amount of product handled per day per kg body weight.

Table 3.4.2.6 Incidental Dermal Exposure Estimates and Risks to Adults

Potentially transferable residue (µg/kg a.i. handled)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Exposure (mg/kg bw/day)[2]	MOE[3] (Target MOE = 300)
82853	14.35	1	1.49×10^{-5}	20186039

1. Potentially transferable residue µg/kg a.i. handled (See Table 3.4.2.4)
2. Exposure = $\frac{\text{Potentially transferable residue X Amount a.i./cartridge X No.of cartridges used/day X conversion factor}}{\text{BW (80 kg)}}$

   Dermal absorption was not factored in as the endpoint used was derived from a dermal study
3. MOE = $\frac{\text{NOAEL (300 mg/kg bw/day)}}{\text{Exposure}}$

3.4.2.2.2 Children Post-application Residential Exposure and Risk

Since the label does not prohibit the use by children, these individuals may be exposed to metofluthrin when wearing OFF! Clip On Mosquito Repellent while engaging in outdoor activities.

Similar to adults, the exposure duration was considered intermediate as the OFF! Clip On Mosquito Repellent is used during the four months of mosquito season per year according to the DEET insect repellent risk assessment from DEET joint venture (RRD 2002-01 - *Personal insect repellents containing DEET (N,N-diethyl-m-toluamide and related compounds).*

Dermal and inhalation exposure during the use of the device

Post-application dermal exposure was estimated by coupling the unit exposure values from the passive dosimetry study with the amount of product handled per day. Given the nature of clothing that is normally worn while engaging in outdoor activities (shorts and short sleeved shirt were chosen from the USEPA Residential SOP (2012). A protection factor of 50% (USEPA Residential SOP (2012)) was applied to the unit exposure.

Although many of the dermal samples monitored in the passive dosimetry study for children were non-quantifiable, dermal exposure was based on ½ LOQ. For those non-detect samples it was based on ½ LOD.

Post-application inhalation exposure was estimated by coupling the inhalation units of exposure values derived from the passive dosimetry study with the amount of product handled per day per kg body weight.

Table 3.4.2.7 Dermal and Inhalation Exposure and Risk Estimates for Children 1 to <2 years of age

Dermal Unit Exposure[1] (µg/kg a.i. handled)	Inhalation Unit Exposure[1] (µg/kg a.i. handled)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Dermal Exposure (mg/kg bw/day)[2]	MOE[3] (Target MOE = 300)	Inhalation Exposure (mg/kg bw/day)[2]	MOE[3] (Target MOE = 300)
1248474	2508559	14.35	1	1.63×10^{-3}	184197	3.27×10^{-3}	5317

1. Dermal and inhalation units of exposures: See Tables 3.4.2.2 and 3.4.2.3.
2. Dermal and Inhalation Exposures = $\frac{\text{UE X Amount a.i./cartridge X No.of cartridges used/day X conversion factor}}{\text{BW (11 kg)}}$

   Child 1 to <2 years of age

   Dermal absorption was not factored in as the endpoint used was derived from a dermal study
3. MOE = $\frac{\text{NOAEL (300 mg/kg bw/day)}}{\text{Exposure}}$

Incidental dermal exposure to residues on the surface of a device during its use

Similar to adults, the incidental dermal exposure expected from children touching the device was estimated using the passive dosimetry study which measured the total amount of residues accumulating on the device. A conservative estimate was derived based on the potential that all the residues on the device may be available and incidentally transferred to the hand. The unit of exposure from the residues on the device was coupled with the amount of product handled per day per kg body weight.

Table 3.4.2.8 Incidental Dermal Exposure Estimates and Risks to Children 1 to <2 years of age

Potentially transferable residue (µg/kg a.i. handled)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Exposure (mg/kg bw/day)[2]	MOE[3] (Target MOE = 300)
82853	14.35	1	1.08×10^{-4}	2775580

1. Potentially transferable residue (See Tables 3.4.2.4).
2. Exposure = $\frac{\text{Transferable residue X Amount a.i./cartridge X No.of cartridges used/day X conversion factor}}{\text{BW (11 kg)}}$

   Dermal absorption was not factored in as the endpoint used was derived from a dermal study
3. MOE = $\frac{\text{NOAEL (300 mg/kg bw/day)}}{\text{Exposure}}$

Incidental non-dietary oral ingestion

Incidental non-dietary oral exposure may occur when children 1 to <2 years of age touch the device that has been running all day then put their hand in their mouth and ingest the residues that were precipitated on the device. The unit of exposure, determined from the residues on the device, was adjusted for the surface area of a child's hand. Another possible route of incidental non-dietary oral exposure is hand-to-mouth considering the residues on the hand following a 12-hour use of the device. The unit of exposure per hand, determined from the mean amount of residues deposited on the hands from the passive dosimetry study, was adjusted for the surface area of a child's hand. All the residues on the device were assumed to be transferred onto the hand of a child. In addition, the residues on both hands are assumed to be all on one single hand (the study does not identify the amount of residues per hand). Exposure from hand-to-mouth activity was calculated based on the algorithm utilized in SHEDS-Multimedia presented in (USEPA Residential SOP (2012); post-application non-dietary ingestion exposure assessment: hand-to-mouth, insect repellents section).

Table 3.4.2.9 Hand-to-mouth Exposure Estimates and Risks After Touching The Device

Potentially transferable residue[1] (µg/kg a.i. handled/cm^2)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Saliva Removal Efficiency (SRE; %)	Exposure[2] (mg/kg bw/day)	MOE[3] (Target MOE = 300)
552	14.35	1	48	1.37×10^{-5}	1093448

1. Potentially transferable residue (mean amount of residues on device adjusted for kg a.i. handled and for cm^2 child hand surface area)
2. Exposure = $[HR*(F_M*SA_H)*(\#Apps)*(1-(1-SE)^{ET*Freq\_HtM/\#APPs})]/BW$
   HR = Hand Residues µg/cm^2 (Potentially transferable residues X amount handled per day)
   F_M = fraction hand surface area mouthed/event (12.7% fraction/event)
   SA_H = typical surface area of one hand (150 cm^2)
   #Apps = number of applications per day (considered one)
   SE = saliva extraction factor (0.48)
   Freq_HtM = number of hand-to-mouth contact events per hour (13.9 events/hour)
   BW = 11 kg
3. MOE = $\frac{\text{Oral NOAEL (15 mg/kg bw/day)}}{\text{Exposure}}$

Table 3.4.2.10 Hand-to-mouth Exposure Estimates and Risks After Using The Device

Hand residue[1] (µg/kg a.i. handled)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Fraction of hand surface area cm^2	Saliva Removal Efficiency (SRE; %)	Exposure[2] (mg/kg bw/day)	MOE[3] (Target MOE = 300)
64.97	14.35	1	19.20	48	1.61×10^{-6}	9290181

1. Child hand residue adjusted for child hand surface area

2. Exposure = $[HR*(F_M*SA_H)*(\#Apps)*(1-(1-SE)^{ET*Freq\_HtM/\#APPs})]/BW$
   HR = Hand Residues µg/cm^2 (Potentially transferable residues × amount handled per day)
   F_M = fraction hand surface area mouthed/event (12.7% fraction/event)
   SA_H = typical surface area of one hand (150 cm^2)
   #Apps = number of applications per day (considered one)
   SE = saliva extraction factor (0.48)
   Freq_HtM = number of hand-to-mouth contact events per hour (13.9 events/hour
   BW = 11 kg
3. MOE = Oral NOAEL (15 mg/kg bw/day) / Exposure

3.4.2.3.1 Aggregate Non Cancer Assessment

For metofluthrin, the adverse effects of tremor and mortality were considered similar regardless of exposure routes. Thus, it is appropriate to combine the route-specific MOEs into a single risk estimate. The route specific risk assessments have the same target MOE of 300, therefore, dermal, inhalation and oral MOEs were combined.

Table 3.4.2.11 Adult Aggregate Non Cancer Risk Assessment

DERMAL					INHALATION		Combined MOE
Applicator Exposure	Post-application Exposure	Incidental Exposure	Total Exposure	MOE	Post-application Exposure	MOE	
4.74×10^{-5}	5.96×10^{-5}	1.49×10^{-5}	1.22×10^{-4}	2462432	1.02×10^{-3}	17140	17022

Where: Combined MOE$= \frac{1}{\frac{1}{MOE_{\text{applicator + post-application dermal + dermal incidental}}} + \frac{1}{MOE_{\text{Inhalation}}}}$

Table 3.4.2.12 Child Aggregate Non Cancer Risk Assessment

Child Aggregate Non Cancer Risk Assessment										
DERMAL				INHALATION		INCIDENTAL ORAL				Combined MOE
Post-application Exposure	Incidental Exposure	Total Exposure	MOE	Post-application Exposure	MOE	Incidental Exposure	Hand-to-mouth	Total Exposure	MOE	
1.63×10^{-3}	1.08×10^{-4}	1.74×10^{-3}	172734	3.27×10^{-3}	5317	1.37×10^{-5}	1.61×10^{-6}	1.53×10^{-5}	978302	5131

Where: Combined MOE$= \frac{1}{\frac{1}{MOE_{\text{post-application dermal + dermal incidental}}} + \frac{1}{MOE_{\text{Inhalation}}} + \frac{1}{MOE_{\text{incidental oral ingestion}}}}$

3.4.2.3.2 Aggregate Cancer Assessment

To estimate the cancer risk, the average daily dose (ADD) from the dermal exposure (which factored in the dermal absorption) and the inhalation exposure were calculated, after which the lifetime average daily dose (LADD) was determined. Exposure frequency was considered 15 days per year, while the exposure duration was expected to be 63 years for adults, 5 years for youths and 5 years for children, with a life expectancy of 78 years. Lifetime average daily dose was multiplied by the q1* value to determine the lifetime cancer risk (LCR).

$$\textbf{LADD} = \frac{\textbf{ADD} \times \textbf{Exposure frequency (day/year)} \times \textbf{Exposure duration}}{\textbf{365 days/year} \times \textbf{Lifetime Years}}$$

Table 3.4.2.13 Estimate of Lifetime Cancer Risk

Age Category	Scenario		ADD[1]	LADD	LCR
Adult	Dermal	Applicator	1.04×10^{-5}	3.46×10^{-7}	4.0×10^{-9}
		Post-application	1.31×10^{-5}	4.35×10^{-7}	5.0×10^{-9}
		Post-application incidental	7.11×10^{-6}	2.36×10^{-7}	3.0×10^{-9}
		Total	3.06×10^{-5}	1.02×10^{-6}	1.0×10^{-8}
	Inhalation		1.02×10^{-3}	3.37×10^{-5}	4.0×10^{-7}
	Total				4.0×10^{-7}
Youth*	Dermal		3.82×10^{-4}	1.01×10^{-6}	1.0×10^{-8}
	Inhalation		3.27×10^{-3}	8.62×10^{-6}	1.0×10^{-7}
	Total				1.0×10^{-7}
children	Dermal	Post-application	3.58×10^{-4}	9.44×10^{-7}	1.0×10^{-8}
		Post-application incidental	2.38×10^{-5}	6.26×10^{-8}	7.0×10^{-10}
		Total	3.82×10^{-4}	1.01×10^{-6}	1.0×10^{-8}
	Inhalation		3.27×10^{-3}	8.62×10^{-6}	1.0×10^{-7}
	Oral	Ingestion (device residue))	1.37×10^{-5}	3.61×10^{-8}	4.0×10^{-10}
		ingestion (hand residue)	1.61×10^{-6}	4.25×10^{-9}	5.0×10^{-11}
		Total	1.53×10^{-5}	4.04×10^{-8}	5.0×10^{-10}
	Total				1.0×10^{-7}
Lifetime					6.0×10^{-7}

1. Dermal ADD = $\frac{\text{Dermal UE} \times \text{Amount a.i./cartridge} \times \text{No.of cartridges used/day} \times \text{conversion factors X DA}}{\text{BW}}$

Inhalation and Oral ADD = $\frac{\text{UE} \times \text{Amount a.i./cartridge} \times \text{No.of cartridges used/day} \times \text{conversion}}{\text{BW}}$

* While a qualitative non-cancer risk assessment was considered for youth, for the cancer risk assessment, the children post-application dermal and inhalation lifetime cancer risk values were used for youth.

3.4.2.4 Post-application exposure from wearing device and being in the vicinity of other device

Since more than one person could be wearing the OFF! Clip On Mosquito Repellent in a defined area, there is potential for dermal and inhalation exposure to consumers not only from wearing the OFF! Clip On Mosquito Repellent, but also as a bystander while someone else is also wearing the same device. Therefore the combined exposures from these two scenarios will be estimated.

3.4.2.4.1 Adult Post-application Residential Exposure and Risk

The exposure duration will be also considered intermediate as it is used during the four months of mosquito season according to the DEET insect repellent risk assessment from the DEET joint venture (RRD 2002-01, *Personal insect repellents containing DEET (N,N-diethyl-m-toluamide and related compounds)*.

Dermal and inhalation exposure during the use of the device as well as a being near someone using the device

Post-application dermal and inhalation exposures were estimated by coupling the dermal and inhalation units of exposure derived from the passive dosimetry study for both scenarios.

Table 3.4.2.14 Combined Dermal and Inhalation Exposure and Risk Estimates for Adults

Combined Dermal and Inhalation Exposure and Risk Estimates for Adults							
Dermal Unit Exposure[1] (UE; µg/kg a.i. handled)	**Inhalation Unit Exposure[1] (UE; µg/kg a.i. handled)**	**Amount of metofluthrin in cartridge (mg)**	**No. of cartridges used/day**	**Dermal Exposure[2] (mg/kg bw/day)**	**MOE[3] (Target MOE = 300)**	**Inhalation Exposure [2] (mg/kg bw/day)**	**MOE[3] (Target MOE = 300)**
441833	12546610	14.35	1	7.93×10^{-5}	3785308	2.25×10^{-3}	7731

1. Dermal and inhalation units of exposure: See Tables 3.4.2.2 and 3.4.2.3.
2. Dermal and Inhalation Exposures = $\frac{\text{UE X Amount a.i./cartridge X No.of cartridges used/day X conversion factor}}{\text{BW (80 kg)}}$

   Dermal absorption was not factored in as the endpoint used was derived from a dermal study
3. MOE = $\frac{\text{NOAEL (300 mg/kg bw/day)}}{\text{Exposure}}$

Incidental dermal exposure to residues on the surface of a device during its use

The presence of two devices is not likely to result in higher incidental dermal exposure than from a single device. Refer to the relevant section under 3.4.2.2.1.

3.4.2.4.2 Children Post-application Residential Exposure and Risk

Dermal and inhalation exposure during the use of the device as well as being near someone using the device

A post-application dermal and inhalation exposure was estimated by coupling the child dermal and inhalation units of exposure from the passive dosimetry study for both scenarios

Table 3.5.2.15 Combined Dermal and Inhalation Exposure and Risk Estimates for Children 1 to <2 years of age

Dermal Unit Exposure[1] (µg/kg a.i. handled)	Inhalation Unit Exposure[1] (µg/kg a.i. handled)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Dermal Exposure (mg/kg bw/day)[2]	MOE[3] (Target MOE = 300)	Inhalation Exposure (mg/kg bw/day)[2]	MOE[3] (Target MOE = 300)
1356642	5252966	14.35	1	1.77×10^{-3}	169511	6.85×10^{-3}	2539

1. Dermal and inhalation unit exposures: See Tables 3.4.2.2 and 3.4.2.3.
2. Dermal and Inhalation Exposures = $\frac{\text{UE X Amount a.i./cartridge X No.of cartridges used/day X conversion factor}}{\text{BW (11 kg)}}$

Dermal absorption was not factored in as the endpoint used was derived from a dermal study.

3. MOE = $\frac{\text{NOAEL (300 mg/kg bw/day)}}{\text{Exposure}}$

Incidental dermal exposure to residues on the surface of a device during its use

The presence of two devices is not likely to result in higher incidental dermal exposure than from a single device. Refer to the relevant section under 3.4.2.2.2.

Incidental non- dietary oral ingestion

Hand-to-mouth following touching the device

The presence of two devices is not likely to result in higher hand-to-mouth exposure than from a single device. Refer to the relevant section under 3.4.2.2.2.

Hand-to-mouth following using the device

The mean hand residues deposited on the hands after wearing the device combined with those deposited on the hands from another device in the vicinity was estimated from the passive dosimetry study after adjusting for children hand surface area.

Table 3.4.2.16 Hand-to-mouth Combined Exposure Estimates and Risks After Using The Device

Hand residue[1] (µg/kg a.i. handled)	Amount of metofluthrin in cartridge (mg)	No. of cartridges used/day	Fraction of hand surface area cm^2	Saliva Removal Efficiency (SRE; %)	Exposure[2] (mg/kg bw/day)	MOE[3] (Target MOE = 300)
76.74	14.35	1	19.2	48	1.91×10^{-6}	7865300

1. Hand residue adjusted for child hand surface area
2. Exposure = $[HR*(F_M*SA_H)*(\#Apps)*(1-(1-SE)^{ET*Freq\_HtM/\#APPs})]/BW$
   HR = Hand Residues µg/cm^2 (Potentially transferable residues X amount handled per day)
   F_M = fraction hand surface area mouthed/event (12.7% fraction/event)
   SA_H = typical surface area of one hand (150 cm^2)
   #Apps = number of application per day (considered one)
   SE = saliva extraction factor (0.48)
   Freq_HtM = number of hand-to-mouth contact events per hour (13.9 events/hour
   BW = 11 kg
3. MOE = Oral NOAEL (15 mg/kg bw/day) / Exposure

3.4.2.5.1 Aggregate Non Cancer Assessment

Table 3.4.2.17 Adult Aggregate Non Cancer Risk Assessment

DERMAL					INHALATION		Combined MOE
Applicator Exposure	Post-application Exposure	Incidental Exposure	Total Exposure	MOE	Post-application Exposure	MOE	
4.74×10^{-5}	7.93×10^{-5}	1.49×10^{-5}	1.41×10^{-4}	2120583	2.25×10^{-3}	7731	7703

Where: $\text{Combined MOE} = \frac{1}{\frac{1}{MOE_{\text{applicator + post-application dermal + dermal incidental}}} + \frac{1}{MOE_{\text{Inhalation}}}}$

Table 3.4.2.18 Child Aggregate Non Cancer Risk Assessment

Child Aggregate Non Cancer Risk Assessment										
DERMAL				INHALATION		INCIDENTAL ORAL				Combined MOE
Post-application Exposure	Incidental Exposure	Total Exposure	MOE	Post-application Exposure	MOE	Incidental Exposure	Hand-to-mouth	Total Exposure	MOE	
1.77×10^{-3}	1.08×10^{-4}	1.88×10^{-3}	159754	6.85×10^{-3}	2539	1.37×10^{-5}	1.91×10^{-6}	1.56×10^{-5}	959988	2493

Where: $\text{Combined MOE} = \frac{1}{\frac{1}{MOE_{\text{post-application dermal + dermal incidental}}} + \frac{1}{MOE_{\text{Inhalation}}} + \frac{1}{MOE_{\text{incidental oral ingestion}}}}$

3.4.2.5.2 Aggregate Cancer Assessment

Table 3.4.2.19 Estimate of Lifetime Cancer Risk

Estimate of Lifetime Cancer Risk					
Age Category	**Scenario**		**ADD[1]**	**LADD**	**LCR**
Adult	Dermal	Applicator	1.04×10^{-5}	3.46×10^{-7}	4.0×10^{-9}
		Post-application	1.74×10^{-5}	5.79×10^{-7}	7.0×10^{-9}
		Post-application incidental	3.26×10^{-6}	1.08×10^{-7}	1.0×10^{-9}
		Total	3.11×10^{-5}	1.03×10^{-6}	1.0×10^{-8}
	Inhalation		2.25×10^{-3}	7.47×10^{-5}	8.0×10^{-7}
	Total				9.0×10^{-7}
Youth*	Dermal		4.13×10^{-4}	1.09×10^{-6}	1.0×10^{-8}
	Inhalation		6.85×10^{-3}	1.81×10^{-5}	2.0×10^{-7}
	Total				2.0×10^{-7}
children	Dermal	Post-application	3.89×10^{-4}	1.03×10^{-6}	1.0×10^{-8}
		Post-application incidental	2.38×10^{-5}	6.26×10^{-8}	7.0×10^{-10}
		Total	4.13×10^{-4}	1.09×10^{-6}	1.0×10^{-8}
	Inhalation		6.85×10^{-3}	1.81×10^{-5}	2.0×10^{-7}
	Oral	Ingestion (device residue))	1.37×10^{-5}	3.61×10^{-8}	4.0×10^{-10}
		ingestion (hand residue)	1.91×10^{-6}	5.02×10^{-9}	6.0×10^{-11}
		Total	1.56×10^{-5}	4.12×10^{-8}	5.0×10^{-10}
	Total				2.0×10^{-7}
Lifetime					1.0×10^{-6}

1. Dermal ADD = $\frac{\text{Dermal UE X Amount a.i./cartridge X No.of cartridges used/day X conversion factors X DA}}{\text{BW}}$

Inhalation and Oral ADD = $\frac{\text{UE X Amount a.i./cartridge X No.of cartridges used/day X conversion}}{\text{BW}}$

*While a qualitative non-cancer risk assessment was considered for youth, for the cancer risk assessment, the children post-application dermal and inhalation lifetime cancer risk values were used for youth.

4.0 Impact on the Environment

Please refer to ERC2015-01 for information on the impact on the environment, specifically fate and behaviour in the environment, environmental risk characterization, risks to terrestrial organisms and risks to aquatic organisms.

5.0 Value

5.1 Consideration of Benefits

OFF! Clip On Mosquito Repellent has value as it repels mosquitoes from the person wearing the device for up to 12 hours. Mosquitoes are an outdoor nuisance pest across all of Canada, especially in the morning and evening. Mosquito bites can cause discomfort and irritation, and can vector diseases such as West Nile Virus. Protection from mosquito bites is important to prevent the possibility of contracting a mosquito-borne illness. In addition to health risks associated with mosquito bites, annoyance from mosquitoes can reduce the enjoyment of being outdoors and cause people to avoid outdoor activities when mosquito populations are heavy.

5.2 Acceptable Claims and Effectiveness Against Pests

Five studies were submitted for review. These studies included both field and laboratory studies and all were conducted on human volunteers. These studies were sufficient to demonstrate that OFF! Clip On Mosquito Repellent provided at least 95% mosquito repellency for up to 11 hours. Subsequently, two additional studies were submitted to support an increase in the claim for the duration of efficacy to 12 hours of mosquito repellency. One of the additional studies tested knock-down of mosquitoes in response to exposure to metofluthrin vapours while the second was a field trial which measured mosquito repellency using a CO_2-baited trap. These trials demonstrated that OFF! Clip On Mosquito Repellent was effective for up to 12 hours. Based on the reviewed studies, a claim that OFF! Clip On Mosquito Repellent can repel mosquitoes from the wearer for up to 12 hours is supported.

5.3 Non-Safety Adverse Effects

Please refer to ERC2015-01.

5.4 Supported Uses

A claim that OFF! Clip On Mosquito Repellent can repel mosquitoes from the wearer for up to 12 hours is supported.

6.0 Pest Control Product Policy Considerations

Please refer to ERC2015-01 for information on toxic substances management policy considerations and formulants and contaminants of health or environmental concern.

7.0 Summary

Please refer to ERC2015-01.

7.1 Value

OFF! Clip On Mosquito Repellent has value as a personal insect repellent as it repels mosquitoes from the person wearing the device for up to 12 hours. Mosquitoes are an outdoor nuisance pest across all of Canada, especially in the morning and evening. Mosquito bites can cause discomfort and irritation, and can vector diseases such as West Nile Virus. Protection from mosquito bites is important to prevent the possibility of contracting a mosquito-borne illness. In addition to health risks associated with mosquito bites, annoyance from mosquitoes can reduce the enjoyment of being outdoors and cause people to avoid outdoor activities when mosquito populations are heavy.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of SumiOne Technical Grade and OFF! Clip On Mosquito Repellent, containing the technical grade active ingredient metofluthrin, as a personal insect repellent.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

#Apps	number of applications per day
<	less than
µg	micrograms
a.i.	active ingredient
ADD	average daily dose
bw or BW	body weight
CBI	confidential business information
CD	Charles Darwin
cm^2	centimetre squared
conc.	concentration
d	day(s)
DACO	data requirement
DEET	N,N-diethyl-m-toluamide
DSS	dioctyl sodium sulfosuccinate
ERC	Evaluation Report
F_M	fraction hand surface area mouthed
Freq_HtM	number of hand-to-mouth contact events per hour
g	gram
GLP	Good Laboratory Practice
h	hour
HR	Hand Residues
IPA	isopropyl alcohol
kg	kilogram
L	litre
LADD	lifetime average daily dose
LCR	lifetime cancer risk
LOD	limit of detection
LOQ	limit of quantitation
m^3	cubed metre(s)
mg	milligram
min	minute
MOE	margin of exposure
No.	number
NOAEL	no observed adverse effect level
PCPA	*Pest Control Products Act*
PMRA	Pest Management Regulatory Agency
q_1*	cancer potency factor
RRD	Re-Evaluation Decision document
SA_H	typical surface area of one hand
SE	saliva extraction factor
SHEDS	Stochastic Human Exposure and Dose Simulation model

SOP	Standard Operating Procedure
SRE	Saliva Removal Efficiency
UE	unit exposure
USEPA	United States Environmental Protection Agency

References

A. List of Studies/Information Submitted by Registrant

1.0 Human and Animal Health

PMRA Document Number	References
2407736	2014, Exposure Summary, DACO: 5.1
2407737	2013, Final Report, Measurement of Air Concentration and Deposition on Cotton Dosimeters of Metofluthrin Generated by a Personal Outdoor Insect Repellent Device in an Outdoor Environment, DACO: 5.4 CBI
2407738	2013, Raw Data Package, Measurement of Air Concentration and Deposition on Cotton Dosimeters of Metofluthrin Generated by a Personal Outdoor Insect Repellent Device in an Outdoor Environment, Vol. 1, DACO: 5.4 CBI
2407739	2013, Raw Data Package, Measurement of Air Concentration and Deposition on Cotton Dosimeters of Metofluthrin Generated by a Personal Outdoor Insect Repellent Device in an Outdoor Environment, Vol. 2, DACO: 5.4 CBI
2407741	2014, Dermal Absorption - Bridging request (CBI removed), DACO: 5.8
2407743	2014, Dermal Absorption - Bridging request, DACO: 5.8 CBI
2407935	2013, In Vivo Dermal Absorption Study of 14C metofluthrin in Rats, DACO: 5.8
2407936	2014, Dermal Absorption (in vivo) Supporting Document: Test Substance Relevance Dermal Absorption Study of [14C]-metofluthrin in Rats, DACO: 5.8
2407938	2014, Dermal Absorption (in vivo) Supporting Document: Selection of Dose Levels and Duration of Exposure Dermal Absorption Study of [14C]-metofluthrin in Rats, DACO: 5.8

2.0 Value

2407750	2014, Value Summary, DACO: 10.2.3.1
2407752	2013, Aire II vs. Churchill SLA 360 Prototypes - Knockdown Testing in the $20m^3$ Chambers, DACO: 10.2.3.2
2407753	2013, Aire II vs Churchill 360, DACO: 10.2.3.3

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

2409268 USEPA (2012a). Standard Operating Procedures for Residential Pesticide Exposure Assessment. EPA: Washington, DC. Revised October 2012.