

Transfluthrin indoor air concentration and inhalation exposure during application of electric vaporizers

Aude Vesin, Philippe Glorennec, Barbara Le Bot, Henri Wortham, Nathalie Bonvallot, Etienne Quivet

► **To cite this version:**

Aude Vesin, Philippe Glorennec, Barbara Le Bot, Henri Wortham, Nathalie Bonvallot, et al.. Transfluthrin indoor air concentration and inhalation exposure during application of electric vaporizers. Environment International, Elsevier, 2013, 60C, pp.1-6. 10.1016/j.envint.2013.07.011 . hal-00875320

HAL Id: hal-00875320

<https://hal-univ-rennes1.archives-ouvertes.fr/hal-00875320>

Submitted on 21 Oct 2013

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Transfluthrin indoor air concentration and inhalation exposure during application of electric vaporizers

Aude Vesin^a, Philippe Glorennec^{b,c}, Barbara Le Bot^{b,c}, Henri Wortham^a, Nathalie Bonvallot^{b,c}, Etienne Quivet^{a,*}

^a Aix Marseille Université, CNRS, LCE, FRE 3416, 13331 Marseille, France

^b EHESP Rennes, Sorbonne Paris Cité, France

^c Inserm UMR1085 Institut de Recherche sur la Santé, l'Environnement et le Travail, Rennes, France

Corresponding author: etienne.quivet@univ-amu.fr

Abstract

Different household insecticide applications via two electric vaporizers emitting transfluthrin were realized in a full-scale experimental room under controlled air exchange rate conditions. On-line high-time resolved measurements of the gas-phase concentrations of the active substance during and immediately after the spreading periods were performed with a High Sensitivity Proton-Transfer-Reaction Mass Spectrometer (HS-PTR-MS). Experimental and modelled data from the ConsExpo 4.0 software were also compared to evaluate the sources of differences. Different application scenarios were also compared. Averaged inhaled concentrations over 1 h, 1 week, and 5 months were estimated to be 8.3, 1.8, and 1.8 $\mu\text{g}\cdot\text{m}^{-3}$, respectively. Corresponding margins of exposures range from 1000 to 10,000, claiming for the absence of effect. Dermal and dust ingestion pathways, although roughly estimated, seems being non-negligible. This claims for a more in-depth integrated risk assessment.

Keywords: Exposure, Pyrethroid, Pesticide, Indoor, HS-PTR-MS

1. Introduction

The evaluation of indoor air contamination to environmentally-significant and health-relevant chemicals becomes a growing issue of concern, due to the current way of living that makes people spending more than 80% of their time in indoor environments (Schweizer et al., 2007). In this context, the increasing application of commercial household insecticides in indoor atmospheres is raising questions due to the potential hazardous properties of the active substances, since both exposure level and duration to those chemicals are likely to be significant.

Among the existing active substances present in household insecticides, synthetic pyrethroids belong to the insecticide family most frequently applied today (Bekarian et al., 2006; Hahn et al., 2010) due

to their low toxicity for mammals, compared to organochlorine or organophosphate analogues (CDC, 2009). The use of pyrethroid insecticides is actually increasing for about ten years now (Horton et al., 2010), especially via the application of electric vaporizers in France (Bouvier et al., 2006). Human toxicity of pyrethroid is considered as limited (Soderlund et al., 2002) due to rapid metabolic degradation of these compounds by hydrolysis, oxidation and conjugation reactions leading to water-soluble metabolites that undergo urinary and biliary excretion (Leng et al., 1999). At levels below those inducing obvious signs of neurotoxicity (T-syndrome or CS-syndrome, Coats, 1990), several studies on animals however, show potential effects on neurodevelopment, reproduction and immune system after the exposure to some pyrethroids (ATSDR, 2003). Pyrethroid long-term effects on human health also still remain unclear (Feo et al., 2010; Kolaczinski and Curtis, 2004) but exposure to these compounds has nevertheless been shown to cause some adverse effects, especially for children and pregnant women (ATSDR, 2003). Pyrethroid exposure thus appears to cause neurotoxicity and developmental neurotoxicity (Shafer et al., 2005), as well as adverse effects on the immune system (Rosenberg et al., 1999). Besides, many studies reveal an increased risk of cancer due to pyrethroid exposure (Ila et al., 2008; Kocaman and Topaktaş, 2009; Shukla et al., 2002). More specifically, some pyrethroids were classified by the US EPA as possible human carcinogens (US EPA (2006a,b) RED reports for permethrin and cypermethrin). Finally, these molecules are suspected to be endocrine

disruptors (European Commission, 2004). Despite very frequent use of these insecticides in western countries (Bouvier et al., 2006; Grey et al., 2006), only very few studies deal with the concentration of insecticidal substances during and immediately after commercial household insecticide application (Berger-Preiss et al., 2009; Leva et al., 2009; Matoba et al., 2004; Nazimek et al., 2011; Pentamwa et al., 2011).

Consequently, this study intends to evaluate the exposure to transfluthrin during the application of two electric vaporizers in a full-scale environmental test room. Few studies (Hahn et al., 2010; Whyatt et al., 2007) demonstrated that inhalation is one of the primary routes for residential pesticide exposure. For this reason a particular attention is given to the measurements of the concentrations of the gas-phase and particulate phase in the indoor environment. An evaluation of the gas-phase concentration is also performed with the ConsExpo software in order to compare both experimental and modelling approach. Due to the suspected health effects of these molecules as well as the potential frequencies, levels and durations of exposure, the evaluation of the average inhaled concentrations for different durations during the application of household insecticide via electric vaporizers have been estimated to supplement existing long-term exposure data.

2. Materials and methods

2.1. Insecticide electric vaporizers

Two commercial electric vaporizers (5 Welectric heating units) used for household treatment against mosquitoes were considered: “Raid® Electric — Fly & Mosquito Protector” and “Baygon® Genius Protector — Electric Liquid”. The active substance transfluthrin (CAS# 118712-89-3), a type I pyrethroid, is used in both commercial refills, under different formulations: solid pad refill or liquid mix refill. The active substance content (% w/w) and formulation are detailed in Table 1.

2.2. Test room description and conditions of application

Different application scenarios of the electric vaporizers (Table 1) were realized in the “Mechanised house for Advanced Research on Indoor Air” (MARIA) experimental house, at the Scientific and Technical Centre of Building (CSTB), Marne-la-Vallée, France (Ribéron and O’Kelly, 2002). The electric vaporizers were mounted on the supports and applied in an empty room ($V = 32.3 \text{ m}^3$) of MARIA house. The ceiling is concrete painted and walls are covered with patches of painted plaster. The temperature and relative humidity were continuously measured during the experiments. Air exchange rates (AERs) were kept constant, at 0.35 h^{-1} for experiments A and C and at 0.14 h^{-1} for experiment B (Table 1).

Concerning the ventilation, the experimental air exchange rates (0.14 and 0.35 h^{-1}) correspond to realistic worst-case conditions compared to residential ventilation conditions that typically range from 1 to 0.5 h^{-1} for existing and new housing, respectively (Spengler et al., 2001). However, such ventilation conditions can be found in dwellings (Frederiksen et al., 2011) with defective mechanical ventilation systems (Lucas et al., 2009). More importantly, such low ventilation conditions especially occur during the night (Lucas et al., 2009) when electric vaporizers are supposed to be applied.

The vaporizers were plugged in the centre of the room at a height of about 1 m above the floor level. The application lasted 8 h according to typical night duration. The concentration of the pesticide was monitored 1 h before the beginning of the spreading period (so-called “reference situation”), during the application (increase of concentration) and once the vaporiser was unplugged, until the concentration level becomes stable and close to the initial background level (elimination phase). The vaporizers were weighted before and after their application (Table 1), in order to determine the quantity of active substance emitted, accounting for the active ingredient mass content provided by the manufacturer (Table 1). For more details about the experimental conditions the readers are referred to Vesin et al. (2013).

2.3. Gas-phase transfluthrin measurements

The household insecticide treatment exhibits high emission variability. Therefore, the measurements of the gaseous transfluthrin emitted by the electric vaporizer refills was performed with a High Sensitivity Proton-Transfer-Reaction Mass Spectrometer (HS-PTR-MS) (Ionicon Analytik), which provided on-line and high time-resolved measurements (Vesin et al., 2012). The HS-PTR-MS technique is based on chemical ionization of the molecules under study through H_3O^+ transfer reactions, combined with subsequent mass spectrometric ion detection (Lindinger et al., 1998). The instrument is composed of an ion source in which H_3O^+ are produced from pure water vapour with a hollow cathode, a drift tube where the proton transfer reactions between H_3O^+ and the molecules under study occur, and a quadrupole mass spectrometer, which differentiates the ions, according to their m/z , downstream coupled to a secondary electron multiplier detector for selective and sensitive detection.

HS-PTR-MS calibration was realized through the generation of a standard gaseous flux of transfluthrin at constant temperature under continuous controlled nitrogen flow. During the room experiments, the HS-PTR-MS was operated under the experimental conditions adjusted during the calibration step (Vesin et al., 2012).

2.4. Modelling of transfluthrin gas-particle partitioning

Due to the relatively low vapour pressure of transfluthrin (4.12×10^{-4} Pa at 25 °C), this Semi-Volatile Organic Compound (SVOC) is likely to be distributed between the gas-phase and the different surfaces present in the indoor environment (i.e., airborne particles, settled dust, indoor surfaces). In order to evaluate the inhalation exposure following insecticide household application, the concentrations of transfluthrin in both the gas-phase and particulate phase ought to be considered. Particles of transfluthrin may actually arise due to nucleation or condensation processes that occur only if the saturated gas-phase concentration of transfluthrin ($62 \mu\text{g}\cdot\text{m}^{-3}$ at 25 °C) is reached. A SMPS (Scanning Mobility Particle Sizer) (Grimm Technik) device scanning particles ranging from 11.1 to 1083.3 nm in diameter was used to observe eventual particle formation.

Transfluthrin is likely to be adsorbed on airborne particles (suspended matter) being already present in the room. Transfluthrin equilibrium partitioning in the air compartment between the gas-phase and airborne particles was evaluated with the model developed by Weschler and Nazaroff (2008) that has been extended in Weschler and Nazaroff (2010) and Little et al. (2012) (details are provided in supplemental material).

A modelling of the gas-phase concentration via the ConsExpo 4.0 software was also realized to enable a comparison with the experimental data. The model was run as a standard user would do it, only having basic information about electric vaporizer application, viz. the application duration (8 h), the volume of the room (32.3 m^3), the commercial product amount spread in the room (μg), the weight fraction of active substance in the commercial product and the air exchange rate (% w/w) (Table 1). It was supposed that the pesticide is released with a constant rate during the application duration.

Table 1: Characteristics of the vaporizers refills and conditions of application

Exp.	Active substance	Commercial formulation	Commercial brand	Content (% w/w)	AER (h^{-1})	Mass of commercial product emitted during the 8h application (mg)
A	Transfluthrin	Solid	Raid®	13.4	0.35	18.44
B	Transfluthrin	Solid	Raid®	13.4	0.14	18.56
C	Transfluthrin	Liquid	Baygon®	0.88	0.35	463.06

2.5. Exposure assessment

As suggested by the [US EPA \(1992\)](#), the exposure over a period of time is assessed according to the Eq. (1):

$$E_i = \int_{t_1}^{t_2} C(t) dt \quad (1)$$

where E_i is the magnitude of the exposure during the application i ($\mu\text{g}\cdot\text{m}^{-3}$), $C(t)$ is the concentration as a function of time ($\mu\text{g}\cdot\text{m}^{-3}$), t is time (h), $t_2 - t_1$ being the exposure duration (h).

The exposure duration depends on the simulated exposure. However, there is currently a significant lack with respect the usage scenarios of household insecticides in Europe. Consumer habits and behaviours are actually most of the time unknown and are likely to vary a lot from a country to another. In the context of the Directive 98/8/EC, (1998, 2010) concerning the placing of biocidal products on the market, the dossier of evaluation of transfluthrin as product-type 18 assumes a 5 months per year daily exposure to evaluate the exposure arising from the application of electric vaporizers ([CAR, 2010](#)). The ConsExpo factsheet ([Bremmer et al., 2006](#)) as well as the study of [Hahn et al. \(2010\)](#) assumed the same frequency of application for electric vaporizers. Their working time is assumed to be of 8 h per day of application, in bedrooms when people are asleep ([Bremmer et al., 2006](#)). During the other period of time it was considered that people are not present in the room and thus not exposed. Accordingly we chose 5 months per year of 8 h daily exposure.

The exposure durations were set to 1 h and 1 week for acute exposures and 5 months for subchronic exposures.

3. Results and discussion

3.1. Concentrations of transfluthrin in the gas-phase

The transfluthrin gas-phase concentration profiles for the different experiments ([Fig. 1](#) for experiment C) show a rapid increase as soon as the electric vaporizer is plugged in and reach a peak a few minutes after unplugging. The active ingredient concentration then starts decreasing, to finally reach a concentration close to the initial background level in several hours.

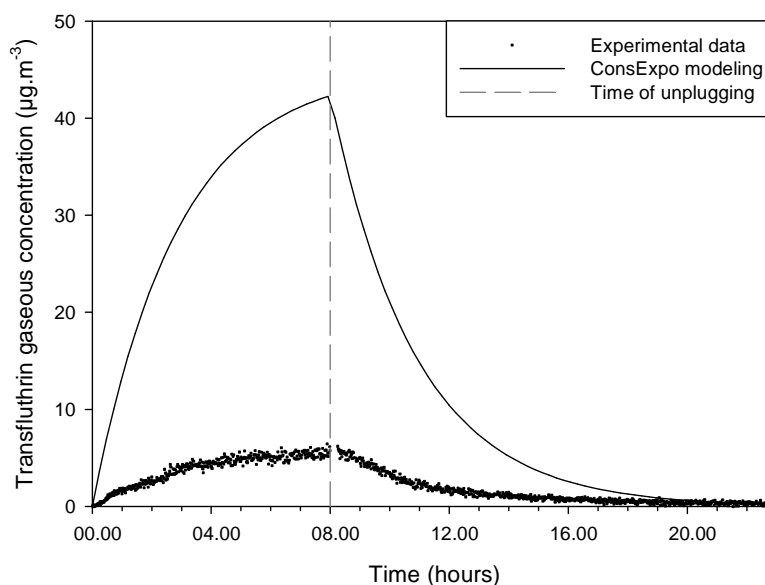


Figure 1: Concentration time profile of gaseous transfluthrin during and after vaporizer application for Experiment C.

Transfluthrin peak concentrations range from $4.9(\pm 0.8) \mu\text{g}\cdot\text{m}^{-3}$ for the solid refill of transfluthrin with an AER of 0.35 h^{-1} (Exp. A) to $8.5(\pm 0.6) \mu\text{g}\cdot\text{m}^{-3}$ for the same refill with an AER of 0.14 h^{-1} (Exp. B) (Table 2). For comparison, the background pyrethroid concentrations found in homes sometimes reach several dozens of $\text{ng}\cdot\text{m}^{-3}$ with very diverse values depending on the homes and the pesticide substances (Clayton et al., 2003; Morgan et al., 2007; Pang et al., 2002; Wilson et al., 2010). Thus, trans-permethrin is often found to have the highest indoor air concentration (gas-phase + airborne particles), with maximums ranging from several $\text{ng}\cdot\text{m}^{-3}$ ($6.8 \text{ ng}\cdot\text{m}^{-3}$ for Morgan et al., 2007, $11 \text{ ng}\cdot\text{m}^{-3}$ for Bradman et al., 2007) to more than one hundred of $\text{ng}\cdot\text{m}^{-3}$ ($130 \text{ ng}\cdot\text{m}^{-3}$ for Tulse et al., 2008 and $164 \text{ ng}\cdot\text{m}^{-3}$ for Whyatt et al., 2007). In some homes, the background trans-permethrin concentration is on the contrary very low, below the limit of quantification, ranging from 0.1 to $0.8 \text{ ng}\cdot\text{m}^{-3}$ (Morgan et al., 2007; Whyatt et al., 2002). Cypermethrin is found to have maximum indoor air background concentrations (gas-phase + airborne particles) ranging between 100 and $380 \text{ ng}\cdot\text{m}^{-3}$ (Bradman and Whyatt, 2005; Tulse et al., 2008). Compared to these concentrations typically found in indoor air, the pyrethroid exposure peak levels measured in the gas-phase during the spreading periods therefore turn out to be from 10 to 1000 time higher. Moreover, compared to the present measurements, the few literature data (Berger-Preiss et al., 2009; Class and Kintrup, 1991; Nazimek et al., 2011) concerning pyrethroid concentrations during application of electric vaporizers in indoor environments show similar concentrations, ranging from 0.4 to $12 \mu\text{g}\cdot\text{m}^{-3}$.

Table 2: Peak concentrations determined via the HS-PTR-MS experimental measurements (gaseous phase) and the ConsExpo model

Exp.	Measured peak concentration ($\mu\text{g}\cdot\text{m}^{-3}$)	ConsExpo peak concentration ($\mu\text{g}\cdot\text{m}^{-3}$)
A	4.9 ± 0.8	25.6
B	8.5 ± 0.6	45.7
C	5.6 ± 0.5	42.2

No significant formation of particles was observed with the SMPS device during the application of the electric vaporizers. However, the background concentration of PM1 airborne particles was detected around $10(\pm 2) \mu\text{g}\cdot\text{m}^{-3}$. As a result, these particles can serve as a support for adsorption of transfluthrin and become another exposure medium in the air compartment in addition to gaseous transfluthrin. According to Eq. (S3), the transfluthrin proportion being absorbed on PM1 airborne particles is found to be around 0.11% relative to the quantity present in the gas-phase. Consequently, nearly the totality of transfluthrin being present in the air compartment is found in the gas-phase.

In addition, we compared the experimental data to those modeled with the ConsExpo 4.0 software (Fig. 1), largely used for exposure evaluations to consumer products (Hahn et al., 2010). This comparison shows that the peak concentrations evaluated by ConsExpo (Table 2) are much higher than the measured concentrations. The ConsExpo modelling of concentration therefore proves not to be in compliance with the concentration which is actually present in the room. This difference between experimental and modelled data can be explained by the fact that a large proportion of emitted transfluthrin is directly adsorbed on the different surfaces (walls, soil, ceiling, dust, suspended particles). According to the model of Weschler and Nazaroff (2008, 2010) and considering the available surfaces of the test room, the proportion of transfluthrin assumed to be adsorbed on those indoor surfaces is actually evaluated to be around 90% (Details for the partition modelling are provided in supplemental information). This large proportion of transfluthrin being adsorbed on room surfaces is moreover confirmed by a mass balance calculation realized in Vesin et al. (2013). This mass balance evaluation on the present dataset actually showed an 81% - to 86% - deviation between the concentration that should have theoretically been present in the room considering the quantity that was spread by the electric vaporizers, and the transfluthrin gas-phase concentration that was actually measured by the HS-PTR-MS. The theoretical transfluthrin concentration was calculated on the basis

of the weighing of the refills before and after the experiments. Finally, several authors find agreeing results about deposition of household pyrethroids on various indoor surfaces (Classand Kintrup, 1991; Matoba et al., 2004; Pentamwa et al., 2011). The differences observed between the experimental data and the ConsExpo modelling are therefore due to the large proportion of transfluthrin being adsorbed on surfaces, since the ConsExpo model does not take into account these sorption effects (Delmaar et al., 2005), which can however considerably lower the gas-phase transfluthrin concentration, due to its semi volatile nature.

Based on the mass emission rates (E_R , $\mu\text{g}\cdot\text{h}^{-1}$) determined in Vesin et al. (2013) for the three experiments (Table 1), different application scenarios are then built to evaluate the influence of emission conditions on the gas-phase transfluthrin concentration. Assuming that ventilation is the only elimination mechanism occurring in the air compartment, the increasing gas-phase concentration profile during the spreading of pesticide is governed by the following Eq. (2):

$$C_g(t) = \frac{E_R}{k_{AER} \cdot V} + (1 - e^{-k_{AER} \cdot t}) \tag{2}$$

where t is the time (h), $C_g(t)$ is the gas-phase concentration of transfluthrin in the room ($\mu\text{g}\cdot\text{m}^{-3}$), k_{AER} is the air exchange rate constant (h^{-1}), E_R is the mass emission rate of the vaporizer ($\mu\text{g}\cdot\text{h}^{-1}$) and V is the volume of the chamber and of the sampling tubing (m^3) ($V = 32.3 \text{ m}^3 + 0.35 \text{ m}^3$).

The influence of ventilation is tested by applying different air exchange rates, of 0.14 h^{-1} , 0.35 h^{-1} , 0.5 h^{-1} and 1.0 h^{-1} respectively. Thus, the realistic worst-case conditions applied during experiments to simulate poor aeration during the night ($k_{AER} = 0.14 \text{ h}^{-1}$ and 0.35 h^{-1}) are compared to the typical residential ventilation conditions ranging from 0.5 h^{-1} to 1.0 h^{-1} . In addition, the influence of the spreading duration is investigated by modelling the gas-phase concentrations for an 8-hour emission to simulate the case of a normal and recommended application. Finally, a 24-hour emission was tested to model the case of longer application periods such as forgotten electric vaporizers plugged in all day long (Fig. 2).

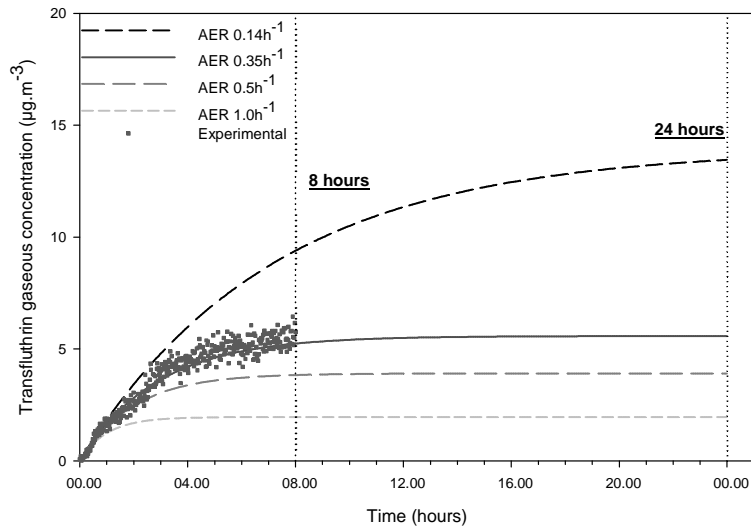


Figure 2: Modelled gaseous concentration profiles of transfluthrin for different application scenarios based on Experiment C.

The resulting peak concentration ranges for the different experiments after 8-hour and 24-hour emissions respectively, are displayed in Table 3, as well as the steady-state concentrations and the emission duration needed to reach the steady-state maximum concentrations.

According to Table 3 and Fig. 2, the lower is the AER, the higher are the concentrations at the end of pesticide application (8-hour and 24-hour emissions). A similar trend is also observed for the steady-state maximum concentrations. Moreover, these modelled data show that in the case of an overdose application (24-hour spreading), low AER values (here 0.14 h^{-1}) lead to significantly higher

concentrations compared to an 8-hour emission. In the case the electric vaporizer has been forgotten to plug into a poorly ventilated room, the resulting exposure concentrations are therefore higher. On the contrary, the data reveal that in the case of a correct ventilation (AER of 0.5 and 1.0 h⁻¹, and even for an AER of 0.35 h⁻¹), the gas-phase concentrations are similar for an 8-hour and a 24-hour emission. In other words, a correct AER prevents a significant increase of pesticide concentration in indoor atmosphere. Therefore, the air exchange rate appears to be a crucial parameter controlling the concentrations levels of the pesticide indoors. In the case of insufficient ventilation, the spreading duration also plays a significant role regarding the gas-phase exposure concentrations that can be increase of 40% for the 0.14 h⁻¹ AER condition between an 8-hour and a 24-hour application.

Table 3: Modelled gaseous concentration ranges for different application scenarios (AER and emission duration)

AER (h ⁻¹)	Concentration after 8 h emission (µg.m ⁻³)	Concentration after 24 h emission (µg.m ⁻³)	Steady-state concentration (µg.m ⁻³)	Time to reach steady-state concentration (within 1%) (h)
0.14	8.1-11.0	11.5-15.7	11.9-16.4	32.9
0.35	4.5-6.1	4.8-6.5	4.8-6.5	13.2
0.5	3.3-4.5	3.3-4.6	3.3-4.6	9.2
1	1.7-2.3	1.7-2.3	1.7-2.3	4.6

3.2. Exposure assessment

The inhalation exposure to transfluthrin corresponds to the inhaled concentration (µg.m⁻³) and depends on its concentration in all the media that are in contact with the lung. This is the case for both the gas-phase and the particulate phase (for the smaller particles). Because of the very small proportion of transfluthrin being present under the particulate phase (<0.11%, see Section 3.1), the exposure via the inhalation of particles was neglected.

The inhaled concentrations averaged over 1 h, 1 week and 5 months are presented in Table 4 for the lowest AER (0.14 h⁻¹). The mean inhaled concentrations integrated over 1 h of vaporizer use (in the area of the maximal concentration measured), 1 week and 5 months with an 8 h per day use of the vaporizer (during the plugging), are 8.3, 1.8 and 1.8 µg.m⁻³, respectively. These integrated inhaled concentrations correspond to a realistic exposure scenario (1 h of exposure around the peak during the night, 1 week of exposure or several months during the blood-feeding period of mosquitoes). These inhaled concentrations could be directly compared with toxicity indicators obtained in toxicological studies (no observed adverse effect levels, NOAELs) in order to determine a margin of exposure (i.e., the ratio between human exposure and NOAELs obtained in animal toxicity testing). For inhalation exposures, the respiratory and central nervous systems appear to be the main targets of transfluthrin. Mice were exposed by inhalation during 45 min to an aerosol (94.5% pure) of transfluthrin. A respiratory rate reduction was observed at 46 mg.m⁻³ leading to define a NOAEL at 11 mg.m⁻³ (ACP, 1997). In the first public version of Competent Authority Report for transfluthrin (CAR, 2010), a NOAEL of 15 mg.m⁻³ was identified after a daily inhalation exposure (6.5 h per day) of pups from postnatal days 10 to 16 (6 days) in mammals, based on an increase in muscarinic receptor levels in the brain cortex at day 17. Thus the lowest NOAEL at 11 mg.m⁻³ could be used for acute (1 h) to subacute (several days, 1 week) exposure duration. In subchronic toxicity studies (28 and 90 days), NOAELs between 36 and 46 mg.m⁻³ were identified after daily inhalation exposures (6 h per day, 5 days per week) of rats, based on minor clinical chemistry changes at 168 mg.m⁻³ and tremors, increased motility and bristling or ungroomed coats at 220 mg.m⁻³ (ACP, 1997). The lowest NOAEL at 36 mg.m⁻³ could be used for a 5-month exposure duration in human. After a temporal adjustment (×6 h/8 h and ×5 days/7 days), the NOAEL becomes 19 mg.m⁻³. There are no chronic toxicological studies.

Table 4: 1-hour, 1-week and 5-month inhalation exposure to transfluthrin and corresponding margins of exposure, during the use 8 h per day of an electric vaporizer with low (0.14 h^{-1}) air exchange rate.

Exposure duration	Average inhaled concentration ($\mu\text{g}\cdot\text{m}^{-3}$)	NOAEL ($\mu\text{g}\cdot\text{m}^{-3}$)	Margin of exposure
1 h	8.3	11 000	1 300
1 week	1.8	11 000	6 100
5 months	1.8	19 000	10 500

As indicated in Table 4, margins of exposure range from 1300 to 10,500, indicating that adverse effects are not likely to occur (the decision threshold could vary from 100 to 1000 according to the availability of toxicity data) (US EPA, 1993). No margin of exposure could be calculated for chronic exposures in the absence of NOAEL. In the case of the 1 h exposure duration, the margin of exposure is close to the decision threshold (1300 versus 1000) derived from the NOAEL obtained in the sensory irritation study. If no adverse effects are theoretically expected, it would probably be relevant to consider a more-in-depth evaluation. These should include multipathways and multi compounds approach.

Although other exposure pathways can occur, as published for other pyrethroid, for instance permethrin (Zartarian et al., 2012), this first tier evaluation was limited to inhalation. Regarding their specific time–activity pattern, including crawling on the floor and hand-to-mouth contact, children are likely to be exposed to the active substance through other exposure routes such as dermal contact with air and surfaces (floor especially) and ingestion of settled dust. Due to the high concentrations that are likely to be present on the room surfaces (Vesin et al., 2013) and in dust, the evaluation of the ingestion and dermal intakes (in μg of substance per day) could therefore be relevant to get evaluation of the total exposure.

Considering the ingestion route, on the basis of a $\log_{(K_{OA})}$ for transfluthrin equal to 8.43 (Vesin et al., 2012) and of a transfluthrin concentration in the gas-phase of $1.8 \mu\text{g}\cdot\text{m}^{-3}$ (averaged inhaled concentration for 8 h), the mass fraction of transfluthrin in dust can be estimated to $48.4 \mu\text{g}\cdot\text{g}^{-1}$ according to the SVOC partitioning model between the gas-phase and the settled dust (Weschler and Nazaroff, 2010). Using a mean dust intake rate of $60 \text{ mg}\cdot\text{day}^{-1}$ for a child (US EPA, 2011), we can calculate that mean intake via dust ingestion would be equal to $2.9 \mu\text{g}\cdot\text{day}^{-1}$. Breathing $8.9 \text{ m}^3\cdot\text{day}^{-1}$ (for a 2–3 years child) of air containing $1.8 \mu\text{g}\cdot\text{m}^{-3}$ of transfluthrin leads to an inhalation intake of $16 \mu\text{g}\cdot\text{day}^{-1}$. Inhalation intake is thus expected to be more than 5 times higher than ingestion one (details of ingestion exposure are provided in supplemental material).

Dermal intake is difficult to assess due to methodological difficulties and would fall beyond the scope of this paper. However it seems possible to assess relative importance of inhalation and dermal pathway to exposure, based on the framework recently proposed by Weschler and Nazaroff (2012), on the basis of chemical properties of SVOCs. Considering the chemical characteristics of transfluthrin (Vesin et al., 2012), application of this model leads to expect a dermal intake of the same order of magnitude than inhalation one (details of dermal route intake comparison with inhalation one are provided in supplemental material).

To sum up, dermal pathway is expected to double inhalation exposure whereas ingestion is expected to add 20%. This reinforces the need for a more in-depth integrated risk assessment. This work moreover shows the necessity of carefully evaluating chronic exposure to those types of chemicals that may cause health effects on the long term. Moreover, due to the significant proportion of transfluthrin being adsorbed on indoor surfaces, they can act as a secondary source of emission, because of the reversible nature of the adsorption mechanism and generate long-term and low pollution source of insecticide.

Finally, a cumulative approach considering other substances with similar mode of action and similar properties to transfluthrin (sensory irritations, neurodevelopmental effects) would be a perspective to this first tier of risk assessment of transfluthrin electric vaporization.

Acknowledgements

This project has been supported by the French Agency for Food, Environmental and Occupational Health Safety (ANSES, project EST- 2008/1/37). Aude Vesin received a doctoral grant from the French Environment and Energy Management Agency (ADEME) and the French National Centre for Scientific Research (CNRS).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.envint.2013.07.011>.

References

- ACP. Advisory Committee on Pesticides. Transfluthrin use as a public hygiene insecticide. Available from www.pesticides.gov.uk/Resources/CRD/ACP/165_transfluthrin.pdf. 1997. [United Kingdom, 74 pp.].
- ATSDR. Agency for Toxic Substances and Disease Registry. Toxicological profile for pyrethrins and pyrethroids. Available from: www.atsdr.cdc.gov/toxprofiles/tp155.pdf US Department of Health and Human Services, Public Health Service; 2003 [328 pp.].
- Bekarian N, Payne-Sturges D, Edmondson S, Chism B, Woodruff TJ. Use of point-of-sale data to track usage patterns of residential pesticides: methodology development. *Environ Health* 2006;5:1–15.
- Berger-Preiss E, Koch W, Gerling S, Kock H, Appel KE. Use of biocidal products (insect sprays and electro-vaporizer) in indoor areas — exposure scenarios and exposure modelling. *Int J Hyg Environ Health* 2009;212:505–18.
- Bouvier G, Blanchard O, Momas I, Seta N. Pesticide exposure of non-occupationally exposed subjects compared to some occupational exposure: a French pilot study. *Sci Total Environ* 2006;366:74–91.
- Bradman A, Whyatt RM. Characterizing exposures to nonpersistent pesticides during pregnancy and early childhood in the National Children's Study: a review of monitoring and measurement methodologies. *Environ Health Perspect* 2005;113:1092–9.
- Bradman A, Whitaker D, Quirós L, Castorina R, Henn BC, Nishioka M, Morgan J, Barr DB, Harnly M, Brisbin JA, Sheldon LS, Mckone TE, Eskenazi B. Pesticides and their Metabolites in the Homes and Urine of Farmworker Children Living in the Salinas Valley, CA. *J Expo Sci Environ Epidemiol* 2007;17:331–49.
- Bremmer HJ, Blom WM, van Hoesven-Arentzen PH, Prud'homme de Lodder LCH, van Raaij MTM, Straetmans EHF, et al. Pest control products fact sheet to assess the risks for the consumer. Available from www.rivm.nl/bibliotheek/rapporten/320005002.pdf. 2006. [Updated version for ConsExpo 4. RIVM Report 320005002/2006. 80 pp.].
- CAR. Competent authority report. Transfluthrin product-type 18 (insecticides, acaricides and products to control other arthropods). Available from circabc.europa.eu/sd/d/57db8369-fc84-4e2f-b3ee-c876fd434ee5/Transfluthrin_Doc%20I_public%20version_first%20draft-JUL2010.pdf, 2010.
- CDC. Center for Disease Control and Prevention. Fourth national report on human exposure to environmental chemicals. Available from: www.cdc.gov/exposurereport/pdf/fourthreport.pdf Department of Health and Human Services, Center for Disease Control and Prevention, National Center of Environmental Health; 2009 [529 pp.].
- Class TJ, Kintrop J. Pyrethroids as household insecticides: analysis, indoor exposure and persistence. *Fresenius J Anal Chem* 1991;340:446–53.
- Clayton CA, Pellizzari ED, Whitmore RW, Quackenboss JJ, Adgate J, Sefton K. Distributions, associations, and partial aggregate exposure of pesticides and polynuclear aromatic hydrocarbons in the Minnesota Children's Pesticide Exposure Study (MNCPEs). *J Expo Anal Environ Epidemiol* 2003;13:100–11.
- Coats JR. Mechanisms of toxic action and structure–activity relationships for organochlorine and synthetic pyrethroid insecticides. *Environ Health Perspect* 1990;87:255–62.
- Delmaar JE, Park MVDZ, van Engelen JGM. ConsExpo 4.0, consumer exposure and uptake models. Program Manual. Bilthoven, the Netherlands: National Institute for Public Health and the Environment (RIVM); 2005. [Report 320104004. 2005. 72 pp.].
- Directive 98/8/EC of the European parliament and of the council of 16 February 1998 concerning the placing of biocidal products on the market. *Off J Eur Communities* 1998;L 123/1.
- Directive 98/8/EC concerning the placing biocidal products on the market inclusion of active substances in annex I to directive 98/8/EC. The Netherlands; 2010 [35 pp.].
- European Commission. Commission staff working document on implementation of the community for endocrine disruptors — a range of substances suspected of interfering with the hormone systems of humans and wildlife. Brussels, Belgium: SEC; 2004:1372.
- Feo ML, Eljarrat E, Barcelo D. Determination of pyrethroid insecticides in environmental samples. *Trends Anal Chem* 2010;29:692–705.
- Frederiksen M, Bergsøe NC, Kolarik B, Spilak M, Beko G, Gustavsen S, et al. Seasonal variation in monthly average air change rates using passive tracer gas measurements. Proceedings of the Twelfth International Conference on Indoor Air Quality and Climate. Austin, TX; 2011. [Abstract No. 317. 6 pp.].
- Grey CNB, Nieuwenhuijsen MJ, Golding J. Use and storage of domestic pesticides in the UK. *Sci Total Environ* 2006;368:465–70.
- Hahn S, Schneider K, Gartiser S, Heger W, Manglesdorf I. Consumer exposure to biocide — identification of relevant sources and evaluation of possible health effects. *Environ Health* 2010;9:1–7.
- Horton MK, Jacobson JB, McKelvey W, Holmes D, Fincher B, Quantano A, et al. Characterization of residential pest control products used in inner city communities in New York City. *J Expo Sci Environ Epidemiol* 2010;21(3):291–301.
- Ila HB, Topaktas M, Rencuzogullari E, Kayraldiz A, Donbak L, Daglioglu YK. Genotoxic potential of cyfluthrin. *Mutat Res* 2008;656:49–54.
- Kocaman AY, Topaktas M. The in vitro genotoxic effects of a commercial formulation of alpha-cypermethrin in human peripheral blood lymphocytes. *Environ Mol Mutagen* 2009;50:27–36.
- Kolaczinski JH, Curtis CF. Chronic illness as a result of low-level exposure to synthetic pyrethroid insecticides: a review of the debate. *Food Chem Toxicol* 2004;42: 697–706.
- Leng G, Kühn KH, Wieseler B, Idel H. Metabolism of (S)-bioallethrin and related compounds in humans. *Toxicol Lett* 1999;107:109–21.
- Leva P, Katsoyiannis A, Barrero-Morero J, Kephelopoulou S, Kotzias D. Evaluation of fate of the active ingredients of insecticides sprays used indoors. *J Environ Sci Health B* 2009;44:51–7.
- Lindinger W, Hansel A, Jordan A. On-line monitoring of volatile organic compounds at pptv levels by means of proton-transfer-reaction mass spectrometer (PTR-MS) — medical applications, food control and environmental research. *Int J Mass Spectrom* 1998;173:191–241.

- Little JC, Weschler CJ, Nazaroff WW, Liu Z, Cohen Hubal EA. Rapid methods to estimate potential exposure to semivolatile organic compounds in the indoor environment. *Environ Sci Technol* 2012;46(20):11171–8.
- Lucas JP, Ramalho O, Kirchner S, Ribéron J. *Etat de la ventilation dans le parc de logements français*. CSTB Division Santé, Pôle Expologie des Environnements Intérieurs. Report DESE/SB-2009-37; 2009. [84 pp.].
- Matoba Y, Inoue A, Takimoto Y. Clarifying behavior of prallehrin evaporated from an electric vaporizer on the floor and estimating associated dermal exposure. *J Pest Sci* 2004;29:313–21.
- Morgan MK, Sheldon LS, Croghan CW, Jones PA, Chuang JC, Wilson NK. An observational study of 127 preschool children at their homes and day care centers in Ohio: environmental pathways to cis- and trans-permethrin exposure. *Environ Res* 2007;104: 266–74.
- Nazimek T, Wasak M, Zgrajka W, Turski WA. Content of transfluthrin in indoor air during the use of electro-vaporizers. *Ann Agric Environ Med* 2011;18:85–8.
- Pang Y, MacIntosh DL, Camann DE, Ryan PB. Analysis of aggregate exposure to chlorpyrifos in the NHEXAS-Maryland investigation. *Environ Health Perspect* 2002;110: 235–40.
- Pankow JF. Further discussion of the octanol/air partition coefficient K_{oa} as a correlating parameter for gas/particle partitioning coefficient. *Atmos Environ* 1998;32: 1493–7.
- Pentamwa P, Kanaratanadilok N, Oanh NTK. Indoor pesticide application practices and levels in homes of Bangkok Metropolitan Region. *Environ Monitor Assess* 2011;181: 363–72.
- Ribéron J, O'Kelly P. MARIA: an experimental tool at the service of indoor air quality in housing sector. Proceedings of the Ninth International Conference on Indoor Air Quality and Climate. Monterey, CA, 3.; 2002. p. 191–5.
- Rosenberg AM, Semchuk KM, McDuffie HH, Ledingham DL, Cordeiro DM, Cessna AJ, et al. Prevalence of antinuclear antibodies in a rural population. *J Toxicol Environ Health A* 1999;57:225–36.
- Schweizer C, Edwards RD, Bayer-Oglesby L, Gauderman WJ, Ilacqua V, Jantunen MJ, et al. Indoor time–microenvironment-activity patterns in seven regions of Europe. *Expo Sci Environ* 2007;17(2):170–81.
- Shafer TJ, Meyer DA, Crofton KM. Developmental neurotoxicity of pyrethroid insecticides: critical review and future research needs. *Environ Health Perspect* 2005;113:123–36.
- Shukla Y, Yadav A, Arora A. Carcinogenic and cocarcinogenic potential of cypermethrin on mouse skin. *Cancer Lett* 2002;182:33–41.
- Soderlund DM, Clark JM, Sheets LP, Mullin LS, Piccirillo VJ, Sargent D. Mechanisms of pyrethroid neurotoxicity: implications for cumulative risk assessment. *Toxicology* 2002;171:3–59.
- Spengler JD, Samet JM, McCarthy JF. *Indoor air quality handbook*. New York: McGraw-Hill Professional, Inc. 978-0-07-445549-4; 2001 [1488 pp.].
- Tulve NS, Egeghy PP, Fortmann RC, Whitaker DA, Nishioka MG, Naeher LP, et al. Multimedia measurements and activity patterns in an observational pilot study of nine young children. *J Expo Sci Environ Epidemiol* 2008;18(1):31–44.
- US EPA. Guidelines for exposure assessment. Risk Assessment Forum. Report EPA/600/Z-92/001. Federal Register, 57(104). Washington, DC: United States Environmental Protection Agency; 1992. p. 22888–938.
- US EPA. Reference dose (RfD): description and use in health risk assessments. Available from <http://www.epa.gov/iris/rfd.htm#1.1>, 1993.
- US EPA. Reregistration eligibility decision (RED) for cypermethrin — case no. 2130. Prevention, pesticides and toxic substances. Available from: www.epa.gov/oppsrrd1/REDs/cypermethrin_red.pdf Report EPA-HQ-OPP-2005-0293-0036. Washington, DC: United States Environmental Protection Agency; 2006a. [117 pp.].
- US EPA. Reregistration eligibility decision (RED) for permethrin — case no. 2510. Prevention, pesticides and toxic substances. Available from: www.epa.gov/oppsrrd1/REDs/permethrin_red.pdf Report EPA 738-R-06-017. Washington, DC: United States Environmental Protection Agency; 2006b. [195 pp.].
- US EPA. Exposure factors handbook: 2011 edition. Available from: <http://www.epa.gov/ncea/efh/pdfs/efh-complete.pdf> Report EPA/600/R-09/052F. Washington, DC: United States Environmental Protection Agency; 2011. [1435 pp.].
- Vesin A, Bouchoux G, Quivet E, Temime-Roussel B, Wortham H. Use of the HS-PTR-MS for on-line measurements of pyrethroids during indoor insecticide treatments. *Anal Bioanal Chem* 2012;403:1907–21.
- Vesin A, Quivet E, Temime-Roussel B, Wortham H. Indoor transfluthrin concentration levels during the application of electric vaporisers using a proton-transfer-reaction mass spectrometer. *Atmos Environ* 2013;65:123–8.
- Weschler CJ, Nazaroff WW. Semivolatile organic compounds in indoor environments. *Atmos Environ* 2008;42:9018–40.
- Weschler CJ, Nazaroff WW. SVOC partitioning between the gas phase and settled dust indoors. *Atmos Environ* 2010;44:3609–20.
- Weschler CJ, Nazaroff WW. SVOC exposure indoors: fresh look at dermal pathways. *Indoor Air* 2012;22(5):356–77.
- Whyatt RM, Camann DE, Kinney PL, Reyes A, Ramirez J, Dietrich J, et al. Residential pesticide use during pregnancy among a cohort of urban minority women. *Environ Health Perspect* 2002;110(5):507–14.
- Whyatt RM, Garfinkel R, Hoepner LA, Holmes D, Borjas M, Williams MK, et al. Within and between-home variability in indoor air insecticide levels during pregnancy among an inner-city cohort from New York City. *Environ Health Perspect* 2007;115(3):383–9.
- Wilson NK, Strauss WJ, Iroz-Elardo N, Chuang JC. Exposures of preschool children to chlorpyrifos, diazinon, pentachlorophenol, and 2,4-dichlorophenoxyacetic acid over 3 years from 2003 to 2005: a longitudinal model. *J Expo Sci Environ Epidemiol* 2010;20:546–58.
- Zartarian V, Xue J, Glen G, Smith L, Tulve N, Tornero-Velez R. Quantifying children's aggregate (dietary and residential) exposure and dose to permethrin: application and evaluation of EPA's probabilistic SHEDS-multimedia model. *J Expo Sci Environ Epidemiol* 2012;22(3):267–73.