Exposure and health risk assessment of applicators to DDT during indoor residual spraying in malaria vector control programme

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Abstract

We assessed exposure of applicators, health risk of DDT to the applicators and evaluated the applicability of existing pesticide exposure models for Indoor Residual Spraying (IRS). Patch sampling for dermal and personal air sampler for inhalation exposure were used in monitoring 57 applicators on the exposure assessment to DDT. The exposure of the applicators was also estimated using three exposure models. The mean actual dermal exposure was 449 mg total DDT per applicator per one house treatment. The applicators were exposed to DDT much beyond the estimated AOEL (Acceptable Operator Exposure Level) of DDT. The exposure estimated with ConsExpo 5.0 b01 model is situated between the median and the 75^{th} percentile of the experimental data. On the other hand, Spraying Model 1 and Spraying Model 10 overestimate the exposure. Thus, these three models can not be directly used for the particular circumstances of IRS as a tool for risk assessment. In general, use of DDT in IRS as a control method for malaria mosquitoes holds a high health risk for the applicators. Strict implementation of spraying procedures stated in IRS manual of World Health Organization (WHO) is necessary to reduce the exposure level and health risk of applicators to DDT.

Key words: applicators, DDT, exposure assessment, health risk assessment, indoor residual spraying

Introduction

Malaria is a very important disease in tropical regions such as Africa. Ethiopia is one of the African countries in which malaria is a leading public health problem. The number of people estimated to be residing in malarious areas of Ethiopia has shown a dramatic increase from 17.7 million in 1965 to more than 52.6 million in 2005 (Deressa et al., 2006). In the country, about 70,000 people are dying of malaria each year (President's malaria initiative, 2009).

Indoor residual praying (IRS) of pesticides is one of the malaria vector control methods which are being used in Ethiopia (Balkew et al., 2010). In the country, DDT has been on use for IRS since 1950s (President's malaria initiative, 2008). The coverage of DDT sprayed households was increased from 20% in 2006 to 65% in 2009 (unpublished data). However, IRS of DDT does not fulfill its intended use as malaria mosquitoes are becoming resistant (Balkew et al., 2003; Balkew et al., 2010; Yewhalaw et al., 2011). Instead, the possible human health risk of DDT especially to the applicators could outweigh its use. Applicators/operators (persons who mix, load and apply pesticides) have the greatest exposure because of the very nature of the work.

Exposure databases have been developed both in North America and Europe to better understand the extent and variability of exposure of applicators (Garreyn et al., 2008). These research databases have helped to evaluate the human health risk of pesticide uses. In Ethiopia, there are no exposure data available. This resulted in lack of knowledge about human exposure and health risks of DDT similar to other countries where DDT is still being used in malaria control (Eskenazi et al., 2009). Likewise, the need for additional work particularly to better characterize and understand the extent of exposure of people to DDT during IRS was also highlighted (WHO, 2009). Currently, pesticide exposure predictive models are being used in

developed nations for estimating the risk of pesticide spraying as a first tier "worst case" approach. However these models are simulating treatment conditions for agricultural use or for treatments with biocides in conditions which are not similar to the situations of IRS in malaria control. May be, it is for this reason that World Health Organization (WHO) pesticide evaluation scheme has indicated the need to develop a generic model for risk assessment of chemicals/pesticides used in IRS (WHO, 2009).

Exposure of applicators to DDT during IRS was noted in the 1950s and 1960s (Wolf et al. 1959, Durham and Wolf 1962). On the other hand, in Ethiopia, exposure of applicators to DDT has never been done since the introduction of its use in agriculture and public health sectors though the applicators are inevitably exposed. Therefore, it is the intention of this study to monitor the real exposure of applicators to DDT during IRS under the local working conditions, to assess the health risk of DDT to the applicators, and to evaluate the applicability of existing pesticide exposure models for IRS. For this purpose, we monitored 57 applicators using a patch sampling method for dermal and a personal air sampler for inhalation exposures. The acute exposure of the applicators was estimated and the health risk of DDT to the applicators was assessed in relation to the derived Acceptable Operator Exposure Level (AOEL) of DDT and other health-based exposure guidance values. AOEL is the maximum amount of active substance to which the operator/applicator may be exposed without any adverse health effects, and it is expressed as milligrams of the chemical per kilogram body weight of the operator per day (Council Directive 97/57/EC, 1997).The exposure assessment results were also compared with outputs of ConsExpo 5.0 b01 (consumer exposure model), Spraying Model 1 and Spraying Model 10 which can be possibly used for estimating exposure

during IRS. Moreover, the practice of the applicators in using personal protective equipments (PPE) was evaluated against the stated procedures for IRS (WHO, 2007).

Materials and Methods

Ethical statement

The methodology of this research is not ethically sensitive because it does not have any possible harm on the participants. However, we followed the usual appropriate procedure before the start of the research and ethical approval was obtained from Jimma University. Besides, a letter was written to all heads of health bureau of the study areas from Jimma University and their verbal consent was obtained. The purpose of the study was well explained to the applicators and their verbal informed consent was obtained.

Study area

Monitoring of exposure of applicators to DDT was conducted from June to August 2009 in rural areas of five districts (Kersa, Seka, Omo-nada, Mana and Tiro-afeta) of Jimma Zone, southwestern Ethiopia. Jimma zone has relative high annual rainfall (1,3000 - 1,800 mm) and it is malarious. It has a sub-humid, warm to hot climate with a mean annual temperature of 19°C. The altitude of the study areas is in the range of 1,580-1,975 meter above sea level.

Description of the houses in the study areas

The houses in the study areas are two kinds. These are thatched roofed houses (roof covered with grass), and CIS (corrugated iron sheet) roofed houses. Thatched roofed houses are circular in shape with a cone shaped roofs whereas CIS roofed houses are mostly rectangular and few of them are L-shaped. The CIS roofed houses have gable roofs and the roofs do not have ceilings which is alike for the roof of thatched roofed houses. All the houses have partition walls lower than the main walls and the walls are plastered with mud. The thatched roofed

houses are without windows whereas the CIS roofed houses have at least two windows. Most of the houses do not have electricity.

Study population, sample size, and demography data

The applicators of IRS of DDT involved in the five districts were local residents recruited by the health offices of the districts and all are males. They were given one week training session before the start of the spraying programme by the health offices. Half of the applicators in each district were selected at random resulting in a total of 57 applicators to be monitored in this study. A questionnaire was prepared to register the age, sex, weight, habits of Khat leaves chewing, experience and personal hygiene practice of applicators. Each applicator was weighed onsite.

Preparation and application of spray, and use of PPE

The spray solution preparation and way of spraying is according to the WHO manual for IRS (WHO, 2002; WHO, 2007). A DDT formulation (75% WDP) with content of 540 g active ingredient (a.i.), p,p´-DDT, per kg was used. The spray solution was prepared by mixing 535 g DDT formulation, in one unit-dose package, with 8 liters of water in a bucket, and then poured into the hand-operated compression sprayer. The spray tank was pumped until the pressure gauge showed 55 psi (3.8 bar) which was supposed to give the specified nozzle discharge rate of 760 ml spray per minute. The final concentration is 0.05 g total DDT (0.036 g a.i)/ml spray solution. This results in a target application dose rate of 2 g total DDT (1.44 g a.i)/m^2 surface area. The application rate was 40 ml/m^2 with a nozzle type of 8002E flat fan and 80° spray angle. The spray was applied in vertical swathes of each 75 cm wide and the swathes overlapped by 5 cm. The applicators sprayed from roof to floor, using a downward motion, and then step sideways and sprayed upwards from floor to roof though they did not cover the full

size of the roof. As a result, the remaining part of the roof was sprayed at last. They position themselves at about the middle of the house and sprayed the highest parts of the roofs (2.5 to 4 meter and 1 to 1.5 meter high up from the top end of the wall for thatched roofed and CIS roofed houses respectively). They did not use extended lance. The Length of the lance is about 60 to 70 cm. While they were spraying, they tried to keep the tip of the lance (nozzle) at about 45 cm away from the wall which helps to have a uniform deposit of DDT on wall surfaces. During spraying, the use of PPE was evaluated by using a checklist prepared according to the manual of WHO. All the applicators spray 6 days per week for 6 weeks.

Exposure assessment

We assessed dermal and inhalational exposure of applicators to DDT with a passive dosimetry (patch) and a personal air sampler method (OECD, 1997). The choice of the patch method for evaluation of the dermal exposure was already discussed in literature (Soutar et al., 2000). The main disadvantage is considered to be a possible over or under estimation of the real exposure because the placing of the patches can not compensate the heterogeneity of the pesticide deposits on the particular body part. Inspite of this, studies indicate that the patch method is still a valid method to estimate the exposure. A strong correlation was demonstrated between passive dosimetry including patch method and biomonitoring exposure assessment, and thus passive dosimetry does not tend to over or underestimate exposure (Ross et al., 2008). Similarly, a review of concurrent passive dosimetry and biomonitoring exposure monitoring studies showed that the internal exposure estimated from the passive dosimetry were often similar or at least correlated to the biomonitoring results (USEPA, 2007). However, the reason for choosing the patch method than the whole body dosimeter was mainly because of its

practicability under the local conditions and affordability (high costs of whole body monitoring).

Dermal exposure: preparation of sampling patches

The patches were prepared from 100% cotton gauze and cellulose paper (OECD, 1997). The gauze was bought from Kombolcha textile Share Company (Ethiopia) and the cellulose paper from Macherery-Nagel, Germany. The patch is composed of an impermeable polyethylene at the bottom, a single cellulose paper sheet on top of it, and four layers of gauze on top of them, and then stapled together with a final recommended size of 10 cm by 10 cm (OECD, 1997). The cellulose paper and gauze layers are the collection media whereas the polyethylene was used as a support, and preventing the contamination of the patches by DDT residues that might be deposited on the coverall during preceding sprayings. It also prevents seepage through the gauze and cellulose paper onto the clothing underneath.

Inhalation exposure: preparation of air sampling tubes

A polyethylene tube (length of 14 cm and internal diameter of 0.6 cm) was selected in such a way that it can be inserted tightly to the inlet side of the main sampling tube of the pump (internal diameter of 0.65 cm) and rolled up with plaster at the joint. The collection material was 100% cotton (absorbent type). The cotton was put in the polyethylene tube separated at three segments. The length of the first and second cotton segments of the inserted tube is 4 cm each, whereas the third is 2 cm long. The empty tube space between each cotton segment is 1 cm and both ends of the tube have 1 cm empty space. The purpose of the empty tube space is to facilitate pumping so that it may not be blocked. The first and second cotton segments were used to collect DDT, whereas the third was to check whether there is breakthrough because of

saturation and serve as a control. The pumps were calibrated with the collection media before every sampling.

Monitoring of exposure and handling of samples

Monitoring of the dermal and inhalation exposure assessment was done when an applicator sprays only one house chosen at random during their daily working scheme and the normal working procedure was followed. The exposure assessment was done during spraying of only one house because we chose to know the exposure pattern among the 57 applicators instead of the exposure pattern of an applicator while is spraying more than one house and also to avoid possible intentional care during spraying of second or third houses. The patches, 100% cotton gloves (bought from Carl Roth GmbH+Co.KG, Germany), and the personal air sampler were placed on the applicator before mixing and loading. Therefore, the dermal exposure assessment included mixing, loading and spraying activities whereas the inhalation exposure assessment was done only during spraying of the inside part of the house as it is much less significant during spraying of the outside part of the house, and mixing and loading (WHO, 2010).

The patch sampling was used to estimate the external exposure. Eleven patches and two cotton gloves were used. Ten patches were attached to the coverall with safety pins (one patch at about the middle and to the front side of each upper arm, each lower arm, each upper leg, each lower leg, chest, and one at the back), one patch (attached on a round hat) was put on the head, and two absorbent cotton gloves were used for the hands. Non-reusable latex powdered medical examination gloves were worn under the cotton gloves. The purpose of these latex gloves was to protect the contamination of the cotton gloves from the hands of the applicator, and to prevent possible pass through of DDT in case the cotton gloves are saturated. The inhalation exposure assessment was monitored by GilAir3 portable personal air sampler

attached to the applicator´s waist with a belt and the sampling tube was clipped on the right lapel pointing downward in the breathing zone of the applicator (OECD, 1997). The flow rate of the pump was 2.41 L/min.

After spraying, each patch was removed, folded with the gauze part inside, wrapped with plastic sheet, sealed, and then placed in a plastic bag. Similarly, the gloves were removed from the wrist to the fingers so that the outside part of the gloves would be inside minimizing the loss of DDT during removal of the gloves. It was also wrapped with plastic sheet and sealed. The 14 cm sampling tube was dislodged from the main sampling tube along with the adsorbent cottons and both ends of the tube were closed with aluminium foil, wrapped with plastic sheet and sealed. Then, all the labelled patches, gloves, and sampling tube from one applicator were placed in one bag and put in a cooling box. The samples were transported to Jimma University within about 5 to 7 hours and put into a deep-freezer (-20°C) until all the samples were further transported to Belgium for analysis at the Department of Crop Protection Chemistry, Faculty of Bioscience Engineering, Gent University. The storage of the samples in Gent University was also in a deep freezer. The transportation to Belgium was not with cold box but took only one day period. It can be supposed that there might be loss of DDT residues though it is one of the persistent compounds.

Residue determination of DDT

Total DDT residue was determined as the sum of p,p'-DDT and its formulation impurities and metabolites (o,p´-DDT, p,p´-DDE and p,p´-DDD). As a result, the corresponding analytical standards of p,p´-DDT, o,p´-DDT, p,p´-DDE and p,p´-DDD with 99.2%, 97.2%, 99.9%, and 99.2% purity respectively were obtained from Supelco (USA) delivered by Sigma-Aldrich logistic Gmbh, Germany. DDT residues were extracted with analytical grade n-hexane (95%

purity). Following the addition of n-hexane, samples were shaken at a speed of 170 cycles per minute for 2 hours and sonicated for 30 minutes in ultrasonic bath. Analysis was done by gas-liquid chromatography with electron capture detector (Agilent Technologies 6890N). The column was HP-5 MS 5% phenyl Methyl Siloxane coated capillary column (30 meter length and 250 µm internal diameter). The inlet temperature was set at 280°C and the detector at 320°C. Helium and nitrogen were used as a carrier and make up gas, respectively. The limit of detection and limit of quantification of the instrument was 0.036 ng/ml and 0.120 ng/ml, respectively. The analytical standard solutions of p,p´-DDT, o,p´-DDT, p,p´-DDD, and p,p´-DDE all together made with n-hexane in the range of 0.1-1 ppm (0.1, 0.2, 0.4, 0.8 and 1 ppm). The calibration curves were generated by plotting detector response (chromatographic peak) versus concentration. Analytes (DDT residues) were identified based on their respective retention time and quantified on the basis of respective peak area by using equation of the calibration curve. The squared correlation coefficient of the calibration curves produced on different days along with the analysis of the samples was > 0.997.

Analytical method validation and quality control

The recovery of the method was evaluated by spiking each sampling media (patches, cotton, and cotton gloves) with 200 µl, 400 µl, and 800 µl of 10 ppm stock solution produced from the analytical standards. The average recovery of three triplicate analysis of each spiked concentration for all the sampling media was in the range of 100-111%, 91-97%, 100-104%, and 92-98% for p,p´-DDT, o,p´-DDT, p,p´-DDD, and p,p´-DDE respectively. The relative standard deviation of all the recoveries was less than 15%. Average recover of 70-120% and relative standard deviation value ≤ 20% is stated as good standard value for accurate and precise analysis (OECD 1997). Triplicate unspiked patches, gloves, and absorbent cotton were also analysed as a blank. The consistency of the detector was evaluated by putting a blank (n-hexane), DDT standard and n-

hexane sequentially after every 10 samples. The standard was quantified as the samples and the recovery was calculated. The purpose of the two n-hexane vials is to clean the column after and before the injection of the standard. The possible loss of DDT residues during transportation and storage was not evaluated with field spiking.

Clothing penetration factor used

The actual dermal exposure (ADE) was calculated as the sum of the amount of DDT deposited on the head patch and cotton gloves, and the amount deposited on the clothing (potential dermal exposure) that is multiplied by the penetration factors (OECD, 1997). The penetration factor was not derived directly from our study because inner patches were not used. Hence, ADE was derived taking into account a protection factor of 0.1(10%) for a coverall, shirt and trousers based on previous studies (Thongsinthusak et al., 1993; Driver et al., 2007; Ross et al. 2008). In this study, the applicators wore the coverall above their normal clothing resulting in a total protection factor of 0.01(0.1*0.1) for body, arms, and legs. However, this protection factor was not used for the head and hands as the applicators were not normally using hat and gloves during spraying.

Dermal and inhalation absorption factors used

Quantification of absorption is vital in the assessment of internal exposure of pesticide applicators. In an in vitro study done on human skin, the dermal absorption rate of DDT dissolved in acetone was 18.18% (Wester et al., 1990) and 28% (Moody et al., 1994). However, for the same dose, the dermal absorption rate for an application of 40 mg soil/cm^2 human skin (with a concentration of 10 ppm DDT) resulted in a maximum dermal absorption rate of 1.8% (Wester et al., 1990). OECD guidance notes on dermal absorption (OECD, 2011) indicated that Bronaugh and Stewart (1986) reported 1.8% in vitro percutaneous absorption of

DDT when the receptor fluid was normal saline and 60.6% when oleyl ether was added in the receptor fluid. This indicates that the dermal absorption rate of DDT applied in organic solvents is very high. It is also recommended to use default values of 100% for inhalation and ingestion, and 10% for the dermal route when there is no data (WHO, 2010). Moreover, it was suggested to assume 25% dermal absorption for concentrate greater than 5% a.i when there are no data on the actual formulation (Dewhurst et al., 2010). To the best of our knowledge, there are no data on the dermal absorption rate of DDT formulations which was used in the IRS programme. Therefore, we used the dermal absorption rates of 1.8%, 10% and 25%.

Calculation methods

Total DDT residue (p,p´-DDT, o,p´-DDT, p,p´-DDE and p,p´-DDD) detected in mg/patch were added together and extrapolated to the defined surface areas (cm^2) of the body regions where the patches were attached on. Surface areas for regions of the body of adults (25^{th} percentile body weight) were used (Bremmer et al., 2006). Accordingly, surface area of 1160 cm^2 for the head and face, 3150 cm^2 for the chest, 3150 cm^2 for the back, 1730 cm^2 for both upper arms, 720 cm^2 for both lower arms, 4046 cm^2 for both upper legs, and 1554 cm^2 for both lower legs were used. No surface area extrapolation was done for the hands as absorbent cotton gloves were covering the whole surface of the hands. The dermal and inhalational exposure values were normalized in proportion to the average time spent to spray 15 houses per day by one applicator (25 minutes for dermal exposure assessment, and 12 minutes for inhalation exposure assessment). This helps to account for differences in spraying practice between applicators, and for the variation in an applicator practices during a full work day (OECD, 1997).

In the inhalation exposure assessment, the amount of DDT (mg/cotton segments) is equal to the amount of available DDT in the total volume of air (0.0289 m^3) sucked in by the personal

air sampler at the flow rate of 2.41 L/min in 12 minutes. Therefore, this has to be extrapolated to the inhalation rate of the workers. The work was assumed to be in the category of light work and the inhalation rate in relation to this work category is 32.9 m^3/day for 60 kg body weight as it used in ConsExpo model (Bremmer et al., 2006). Therefore, the calculated volume of air that is inhaled by an applicator, in 12 minutes, is 0.274 m^3. The amount of DDT calculated in 0.274 m^3 is expressed as mg per person.

The internal dose was estimated by combining the ADE with data on the dermal absorption rate (Van de Sandt et al., 2007). Accordingly, we adopted the following equations (Ross et al., 2008). Equation (1) for estimating absorbed dermal dose from the patches and gloves data, equation (2) to estimate inhalation dose, and equation (3) is to estimate total absorbed dosage from both routes of exposure.

$ADD = (PDE \times CPF_1 \times CPF_2 \times DA) + (ADE \times DA)$. …. (1)

$AID = (IE \times IA)$…….. (2)

$TAD = ADD + AID$……. (3)

Where: ADD is absorbed dermal dose, PDE is potential dermal exposure, CPF_1 and CPF_2 are the clothing penetration factors (default 10%) for coverall and clothing under the coverall respectively, DA is dermal absorption (1.8%, 10% and 25%), ADE is actual dermal exposure (for hands and head), AID is the absorbed inhalation dose, IE is inhalation exposure, IA is inhalation absorption (default 100%), and TAD is total absorbed dose.

Statistical analysis

Statistical procedures and descriptive statistics were conducted using SPSS version 17 and Statistica version 8 softwares. IE, PDE, ADE and internal dose were calculated as arithmetic mean, median and different percentile values.

Health risk assessment

Health risk assessment is a scientific procedure that compares determined or estimated exposure with health-based endpoints. The estimated total absorbed dose from both dermal and inhalation rout of exposures was divided by the average body of applicators to compare with the derived AOEL and other existing health-based noncaner endpoints of DDT. The estimated total absorbed DDT (mg/kg bw) is calculated for exposures during spraying of one house, and also during spraying of 15 houses per day. A ratio of an internal exposure to the AOEL or other endpoints greater than 1 can be considered as unacceptable risk (Machera et al., 2003). The AOEL of DDT is not available in literature. Hence, a value of 0.01 mg/kg bw/day is derived based on the guidelines for AOEL derivation and recommendations given in reviews (Council Directive, 97/57/EC 1997; ECHCPDG, 2006; EFSA, 2006).

In deriving AOEL, it is recommended to use the adverse effect exhibiting the lowest No Observed Adverse Effect Level (NOAEL) as the relevant critical effect (CEC, 2001). The lowest relevant NOAEL of DDT for developmental effects was reported 1 mg/kg bw/day (oral toxicity value) in rats (Solecki, 2000; FAO/WHO, 2002). It is stated that relevant NOAEL for developmental toxicity even in short-term exposure should be considered for AOEL setting (CEC, 2001). Although a developmental endpoint is relevant in women of child-bearing age, it is assumed that the health of all the other population sub-groups can be protected for endpoints that may occur at higher dosages above the margin of safety set on the basis of this endpoint (Krieger, 2001). Therefore, we derived the AOEL of DDT by dividing 1 mg/kg bw/day by a safety factor of 100 (10-flod factor for interspecies variability and 10-flold for intra-individual variability) as recommended in CEC (2001) and it is being applied in the European Union (EU) for crop protection products to derive AOEL (Bosman and Falke, 2006). Therefore, the derived

AOEL of DDT is 0.01mg/kg bw/day. In EU, the dermal risk assessment approach is also based on the use of NOAEL from an oral dosing toxicity study in animals (Van de Sandt, 2007). Toxicity adjustment factor for oral-to-dermal extrapolation was not considered as it was not suggested for DDT in the oral-to-dermal extrapolation paradigm developed by USEPA (2004).

This derived AOEL is the same as a Provisional Tolerable Daily Intake (PTDI) of DDT set in FAO/WHO joint meeting of 2000 after assessing new studies and reviews (Solecki, 2000). The PTDI value is used to compare exposure levels of people to DDT (WHO, 2003; EFSA, 2006; Chung et al., 2008; Rajaei et al., 2010). On the other hand, the AOEL is greater than the endpoints indicated in ATSDR (2002), RIVM (2001), and USEPA (1996). RIVM (2001), after reviewing the available data, derived a Tolerable Daily Intake (TDI) of 0.0005 mg/kg bw/day from a NOEL of 0.05 mg/kg bw/day for hepatictoxic effects observed in rats from a study of Laug et al. (1950). Reference dose (RfD) of 0.0005 mg/kg bw/day was also set from the same study (USEPA, 1996). Similarly, an acute oral Minimal Risk Level (MRL) of 0.0005 mg/kg bw/day was derived based on neurodevelopment effects in mice reported in a series of studies (ATSDR, 2002).

Exposure assessment with models

In literature several models are described for the exposure assessment of pesticide applicators. In the framework of this study, a selection was made on the basis of their possible applicability to the particular conditions of IRS of pesticides. For this reason ConsExpo 5.0 b01 and Spraying Model 1 and Spraying Model 10 were selected because the operational underlying conditions of these models are the closest as compared to IRS (Bremmer et al., 2006; EC, 2007).

Results

Demography, experience and personal hygiene practice

The age of the 57 applicators was in the range of 20 to 52 years with a mean age of 35 years, and their weight was in the range of 43 to 76 kg with a mean weight of 57 kg. Applicators with 1 year of experience in the IRS programme were the majority (60%), whereas the rest had different years of experience [12% (2-3 years), 19 % (5-10 years), and 9% (14-30 years)]. The applicators wore 100% cotton coverall over their normal clothing. They used only one coverall for all the days of the spraying campaign, and they did not use gloves and hat. They also did not take shower throughout the 36 days of spraying, and they did not wash their hands thoroughly before eating food or chewing Khat leaves. All of them chew Khat leaves. Generally, the use of PPE was not according to the WHO manual for IRS (WHO, 2007).

Potential exposure of applicators to DDT

The dermal route of exposure was the most important route of exposure to DDT as compared to inhalation exposure. In the inhalational exposure, DDT residues were not detected on the third cotton segment. This shows that there was no pass through of DDT from the first two segments of cotton and thus all the DDT was retained. Comparing the exposure of the different parts of the body indicated that the deposits of DDT are all over the body with high variability (Table 1).

The deposition of DDT on the upper body parts (hands, chest, back and head) is greater than the lower body parts (legs). The hands and head of applicators were highly exposed than the rest of the body parts (Figure 1). Linear regression of the sum of DDT deposition on the hands and head against the total potential dermal exposure indicates a positive association explaining 95.6% of the variability in the assessment of dermal exposure. Statistical evaluation of the

exposure distribution of the different sprayers split up by sampled parts of the body shows that there is log normal distribution pattern of exposures. The age, experience of the applicators, room temperatures, and volume of the houses did not have linear relationship with dermal and inhalation exposures. However, the exposure of applicators to DDT during spraying of thatched roofed houses and CIS roofed houses has different relationship to sizes of houses. The PDE of applicators tend to decrease as the volume/size of the thatched roofed houses increases (Pearson Correlation, r = -0.11). On the other hand, the PDE of applicators positively correlated to the volume of CIS roofed houses (Pearson Correlation, r = 0.31).

Estimated ADE of the applicators to DDT

The ADE of applicators is more attributed to the hands and head (Table 2). The rate of ADE (mg/min, and mg/m^3 volume of a house) was higher in thatched roofed houses than CIS roofed houses (Table 3). Linear regression of the sum of DDT deposition on the hands and head against the total actual dermal exposure indicates a positive association explaining 100% of the variability in the assessment of dermal exposure.

Health risk of DDT for the applicators

The estimated internal exposure of applicators, at all dermal absorption rates, is greater than the AOEL and other health-based endpoints even during spraying of one house (Table 4). As a result, all the ratios of the internal exposure of applicators to these endpoints are greater than 1 which is unacceptable risk. For example, the median absorbed dose at 1.8% dermal absorption is 10 times of the AOEL or PTDI and 200 times of the RfD, TDI and the MRL during spraying of only one house.

Exposure monitoring data versus model estimated results

The estimated acute and chronic internal DDT level in the applicators was compared with those estimated by ConsExpo model. ConsExpo model calculated the acute internal dose per one house spraying exposure and the chronic exposure for the 36 days of spraying at rate of 15 houses per day at steady state. We also calculated the acute and chronic exposure accordingly for the sake of comparison. The chronic internal dose is calculated as [ADE (mg/kg bw) x dermal absorption factor x 15 (number of houses sprayed/day) x 36 (total number of spraying days/year)] ÷ 365 days/year. The internal exposure obtained with ConsExpo 5.0 b01 is situated between the median and the 75^{th} percentile of the experimental data for the dermal exposure and less than mean for the inhalation exposure (Tables 5 and 6). Whereas, Spraying Model 1 and Spraying model 10 overestimates exposure of applicators by a factor of about 2 to 10. Spraying Model 1 also overestimate the inhalatory exposure but Spraying Model 10 underestimates the inhalatory exposure (Table 6).

Discussion

In order to conduct occupational health risk assessment, knowledge of the exposure levels (dermal and inhalation) are very important (Berger-Preib et al., 2005). In this study, the dermal route of exposure to DDT was a significant route of exposure during IRS of DDT. This might be because of inappropriate practice of spraying that could lead to frequent spills, and due to the low vapour pressure of DDT as it is indicated in previous similar studies. Handling of pesticides with low to moderate vapor pressure has resulted in higher dermal exposure of pesticides compared to inhalation exposure (Geer et al., 2004). In the same study, higher dermal exposures were also attributed to frequent spills on the body.

The exposures of the applicators are considerably variable, both between individuals and anatomical regions as it can be seen from the standard deviation (Table 1). The distribution of these exposures was lognormal which is in agreement to studies done elsewhere (Kromhout and Vermeulen, 2001). The variability of the individual dermal exposure, regardless of the size of the house, could be due to differing degrees of speed, care and skill in performing the mixing and spraying activities, and to the inherent characteristics of field studies where conditions are less controlled (Machera et al., 2003; USEPA, 2007). In such variation of exposure of anatomical regions, the linear relationship between the direct exposure of hands and head against the total dermal exposure shows that protection of these body regions can considerably reduce the exposure of the applicators during IRS.

The exposure of applicators tend to decrease as the size of thatched roofed houses increases whereas the exposure of applicators tend to increase as the size of CIS roofed house increases. The reason might be related to ventilation, non-adherence to the spraying procedure and other factors. This observation needs further study and may contribute to the improvement of spraying practices. Moreover, the rate of exposure of applicators per volume of house and per time is higher during spraying of thatched roofed houses than CIS roofed houses. The probable reason for such rate of exposure difference might be attributed to the shape of the house, height of the roof, and visibility for the sprayer in the house. The visibility was better in CIS roofed houses than thatched roofed houses. The height of the roof of thatched roofed house is greater than the height of the roof of CIS roofed houses. As a result, the spray released did not reach to the top parts of the roofs of thatched roofed houses because the applicators did not use extended lance. Instead, the spray could probably fall down onto the applicators. Spraying above the head has resulted in higher exposures (Wolfe et al., 1959).

The estimated internal (systemic) exposure of the applicators is greater than the health-based end points. The minimum, median, and 95th percentile exposure of the applicators at the lowest dermal absorption rate (1.8%) is two times, 10 times, and 54 times greater than the AOEL or PTDI (Table 4). In an exposure assessment study done on field crop sprayers to 13 pesticides by Ramwell et al. (2005), some applicators were exposed to a level equal to the AOEL of each pesticide in 12 hours of exposure and others in greater than 12 hours of exposure. In this study, the exposure level of applicators exceeds the AOEL or PTDI within 25 minutes of spraying (during spraying of one house). This indicates how much the exposure can be during spraying of 15 houses per day for 36 days of spraying programme. For example, in an experimental study done on volunteers by Chen et al. (2009), at lower dosage, 0.4% of the administered DDT dose was recovered as DDA from urine. The calculated 75th percentile total absorbed dose at 1.8% dermal absorption rate during spraying of 36 days is 75.6 mg/kg bw at steady state. Based on the 0.4% recovery/excretion, 99.6% of this total absorbed dose (75.298 mg/kg bw) remains in the body of the applicators. It was also noted that the excretion of DDA in urine was reduced during post application time (Chen et al., 2009). This shows that high amount of DDT remains in the body of applicators resulting in unacceptable health risk level.

Moreover, the applicators are possibly exposed to DDT through ingestion of DDT and contact of applicators with treated surfaces. There could be ingestion of DDT during hand-to-mouth contact that might result from chewing of Khat leaves without washing their hands. The role of hand-to-mouth contact in the ingestion of pesticides is highlighted elsewhere (Ross et al., 2008). The applicators´ houses were also treated with DDT which can expose them to the residue of DDT through inhalation and contact with treated surfaces and floor dust (Van Dyk et al., 2010; Ritter et al., 2011). The half-life time of indoor used pesticides tend to be longer than

those used in an outdoor environment (Bouviera et al., 2006). DDT has also bioaccumulative characteristics and more persistent in human body than animals (OECD, 2011). The half-lives for DDT and DDE in humans were reported to be 4.2–5.6 years (Smith, 1999), the median half-life 8.6 years (Wolff et al., 2000). They are still detectable in human tissues in the population of USA though the use of DDT in USA was banned three decades ago (Kirman et al., 2011). Perhaps, the dermal and inhalation exposure level can also be affected by the sampling materials used as DDT might be adsorbed to the polyethylene sheet fixed at the back of the patch and to the polyethylene pipe of the air sampling. Further validation may be necessary on the possible loss of samples in using these materials for exposure monitoring of organochlorine pesticides.

Therefore, taking into account the higher persistence of DDT in the indoor environment, the possible ingestion of DDT, the bioaccumulation of DDT in the human body, contact with treated surfaces and the prevailing inappropriate practice of IRS, the estimated internal dose of DDT from spraying exposure is not most likely overestimated. Data on the systemic concentration of DDT and its metabolites in men and women from studies done in South Africa and in other countries suggest that IRS can result in high DDT exposure in humans (Eskenazi et al., 2009; Chen et al, 2009). Consequently, the applicators of IRS might be experiencing or may experience in the future the health risks of DDT (Aneck-Hahn et al., 2007; Rignell-Hydbom et al., 2009; Van den Berg, 2009).

However, the real amount of absorbed DDT may not be exactly as it is estimated. The dermal absorption rate may be affected by the adherence rate of the applicators to the safety precautions that must be followed during IRS. The applicators were not taking shower at the end of every day of spraying and they were using one coverall throughout the spraying days

without washing it. These practices can increase the loading of DDT on the coverall and their skin. In 87 dermal absorption rate experimental studies (including pesticides), 63% of the experiment showed an inverse relationship between relative dermal absorption and dermal loading (Buist et al., 2009). This shows that the proportion penetrating the skin appears to increase at decreasing the external dose. It was also noted that higher proportion of pesticides deposited on the outer dosimeters appeared on the inner dosimeters as the outer loading/amount of pesticide decreases (Driver et al., 2007). Nevertheless, these do not mean that the amount of DDT passing through the coverall or absorbed at lower exposure is greater than at higher exposure but the coverall pass-through or absorbed proportion against the actual exposure is higher during lower dosing. Otherwise, the total amount of pesticides absorbed is higher for high amount of ADE than less amount of ADE. Moreover, more contact time of skin with pesticides can increase the amount of absorbed pesticides (Durkin et al., 1995). Human exposure to DDT during IRS is foreseeable but the result of analysis of health risk versus benefit of using DDT should determine whether or not to continue using DDT in the IRS.

In the 1940s to 1960s, IRS with DDT as the main method of malaria eradication programme has resulted in the eradication or great reduction of malaria in many countries worldwide (Rogan and Chen, 2005). This is a historical convincing evidence that DDT is very effective against the malaria vector mosquito. IRS of DDT can reduce mortality and morbidity attributed from malaria particularly maternal and infant mortality rate in Africa (Rogan and Chen, 2005). On the other hand, evidence is growing that indicates DDT may have adverse effects on human health (WHO, 2011; ATSDR, 2002). IRS of DDT also inevitably exposes women of child-bearing age and breast feeding women to DDT that may increase infant mortality. Reproductive hazardous effects of DDT are the major concern (Rogan and Chen,

2005). Under normal circumstances, we think that the high mortality and morbidity from malaria outweighs all the probable health effects of DDT that likely results from long term exposure. It is possible to reduce human exposure of DDT by proper management of DDT use and particularly the exposure of applicators can be reduced effectively by adhering to the appropriate spraying procedure. However, when the effectiveness of DDT in the control of malaria vector is compromised by DDT resistance development in mosquito species, *Anopheles* arabiensis, which is the major vector in Ethiopia (Balkew et al., 2003), the benefit of DDT is questionable. In recent study, *An.* Arabiensis is 100% resistant to DDT (Yewhalaw et al., 2011). This shows that the use of DDT in the IRS has hardly contributed in the reduction of malaria incidence since the malaria vector became resistant. This shows that the hazardous health effects of DDT outweigh its use.

The comparison of the results of this study with ConsExpo 5.0 b01, Spraying Model 1, and Spraying Model 10 showed that these models can not be directly used as a "realistic worst case" scenario for pesticide exposure assessment of applicators during IRS of DDT. However, the comparison also indicated the possibility of developing correction factors. The correction factors can be applied on the model estimated results so that it may be possible to estimate the real exposure of applicators. This shows that the study has generated an important exposure database that may be used as a bench mark for further studies and to adopt these models or develop new models. Based on the existing high prevalence of malaria, the use of pesticides in the IRS will continue unless other alternative methods of malaria mosquitoes control are made available in the future. Therefore, the adoption of such models or development of new models is important for the risk assessment scheme in the regulatory processes of pesticide use for IRS

and other uses of pesticides. This is because modeling saves time, money and other resources to be invested on field risk assessment researches.

In general, all the existing scenarios and the determined exposure level depict that the applicators are highly exposed to DDT. IRS with DDT as control method for malaria mosquitoes holds a health risk for the applicators. ConsExpo 5.0 b01, Spraying Model 1, and Spraying Model 10 can not be directly used for the particular circumstances of IRS as a tool for risk assessment. Thus, the default imput parameters of these models shall be adopted with experimental results. Strict implementation of spraying procedures stated in the manual of WHO (2007) is necessary to reduce the exposure level and health risk of applicators to DDT or other insecticides. Such as, wearing a protective hat and face-shield or goggles; washing hands and face with soap and water after spraying and before eating, chewing Khat leaves or smoking or drinking; taking shower at the end of every day's spraying and change into clean clothes; washing overalls at the end of every spraying day in soap and water; washing off immediately with soap and water when DDT or other insecticides touches the skin of the applicator while he is spraying; and changing clothes immediately if they become contaminated with DDT or other insecticides.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Table 1. Potential dermal and inhalation exposures (mg) of different body regions of 57 DDT applicators during spraying of one house for an average of 25 minutes and 12 minutes for dermal and inhalation exposures respectively.

Body parts	Minimum	Mean	Median	Percentiles 75th	90th	95th	Maximum
Head	0.78	136.29 ± 318	39.37	105.82	2240.46	728.07	1793.35
Chest	3.03	54.62± 98	19.76	64.32	121.18	206.20	665.92
Back	0.79	32.11 ± 67	10.92	35.77	69.02	132.87	463.11
URA	0.45	63.49 ± 129	19.50	40.60	191.51	288.99	790.02
LRA	0.25	33.64 ± 46	15.82	40.60	98.66	158.92	204.75
ULA	0.94	42.91 ± 86	14.15	37.56	143.54	159.21	591.34
LLA	0.30	16.05 ± 32	6.00	17.86	39.61	52.35	214.47
URL	0.65	36.66 ± 45	19.19	56.31	83.43	176.08	203.01
LRL	0.41	10.40 ± 20	4.52	9.47	18.83	39.27	121.55
ULL	2.86	31.61 ± 29	22.35	41.92	73.81	103.84	120.48
LLL	0.09	12.59 ± 21	4.53	10.85	39.43	65.71	106.80
RH	20.13	184.37 ± 204	129.30	203.49	412.67	720.85	1188.72
LH	17.52	124.88 ± 104	93.09	154.15	244.90	321.39	578.11
TPDE	79.01	779.60 ± 902	432.97	805.56	1866.44	2520.60	5041.08
PIE	0.02	0.56 ± 0.46	0.48	0.74	1.20	1.66	2.26

URA = Upper Right Arm, LRA = Lower Right Arm, ULA = Upper Left Arm, LLA = Lower Left Arm, URL = Upper right Leg, LRL = Lower Right Leg, ULL = Upper Left Leg, LLL = Lower Left Leg, RH = Right Hand, LH = Left Hand, TPDE = Total Potential Dermal Exposure, PIE = Potential Inhalation Exposure

Table 2. Actual dermal and inhalation exposures (mg) of different body regions of 57 DDT applicators during spraying of one house for an average of 25 minutes and 12 minutes for dermal and inhalation exposures respectively.

Body parts	Minimum	Mean	Median	Percentiles			Maximum
				75th	90th	95th	
Head	0.784	136.29 ± 318	39.37	105.82	2240.46	728.07	1793.35
Chest	0.030	0.55 ± 0.98	0.20	0.64	1.21	2.06	6.66
Back	0.007	0.32 ± 0.67	0.11	0.36	0.69	1.33	4.63
URA	0.005	0.63 ± 0.46	0.16	0.41	1.92	2.89	7.90
LRA	0.003	0.34 ± 0.46	0.16	0.41	0.99	1.59	2.05
ULA	0.009	0.43 ± 0.86	0.14	0.38	1.44	1.59	5.91
LLA	0.003	0.16 ± 0.32	0.06	0.18	0.40	0.52	2.14
URL	0.006	0.37 ± 0.45	0.19	0.56	0.83	1.76	2.03
LRL	0.004	0.10 ± 0.20	0.05	0.09	0.19	0.39	1.22
ULL	0.029	0.32 ± 0.29	0.22	0.42	0.74	1.04	1.20
LLL	0.001	0.13 ± 0.21	0.05	0.11	0.39	0.66	1.07
RH	20.13	184.37 ± 204	129.30	203.49	412.67	720.85	1188.72
LH	17.52	124.88 ± 104	93.09	154.15	244.90	321.39	578.11
TADE	65.25	448.88 ± 528	306.94	429.52	956.96	1795.49	2879.14
AIE	0.02	0.56 ± 0.46	0.48	0.74	1.20	1.66	2.26

TADE = Total Actual Dermal Exposure, AIE = Actual Inhalation Exposure

Table 3. Total actual dermal exposure difference during spraying of thatched roofed houses and corrugated iron sheet roofed houses in relation to time and volume of a house.

	Volume of house (m^3)		Time to spray (min)		TADE (mg)		Ratios			
							TADE to Volume		TADE to Time	
Exposure	TRH	CRH	TRH	CRH	TRH	CRH	TRH	CRH	TRH	C RH
Mean	115	208	21	31	412	426	4.9	2.5	21.65	15.99
Median	108	160	19	25	251	315	2.4	2.4	14.26	11.97
75th	181	243	27	41	460	545	6.6	3.1	31.01	15.91
95th	212	819	35	61	1722	1423	19.2	6.1	86.29	84.72

TRH = Thatched Roofed Houses, CRH = Corrugated iron sheet Roofed Houses, TADE = Total Actual Dermal Exposure.

Table 4. Total acute absorbed dose of DDT in both dermal and inhalation route of exposures of applicators during spraying of one house per 25 minutes and 15 houses per day compared to the derived AOEL and other health-based exposure guidance values.

		Total estimated internal/absorbed dose of DDT (mg/kg bw/day)[Ψ]						
Exposure	DAR	Minimum	Mean	Median	75th percentile	95th percentile	Maximum	Noncancer endpoints for DDT (mg/kg bw/d)
During spraying of one house	1.8%	0.02	0.14	0.10	0.14	0.54	0.90	0.01 (AOEL derived)
	10%	0.11	0.76	0.51	0.73	3.00	4.84	0.0005 (RfD, USEPA 1996)
	25%	0.27	1.88	1.28	1.80	7.49	12.03	0.01 (PTDI, FAO/WHO 2000)
During spraying of 15 houses per day	1.8%	0.34	2.16	1.50	2.09	8.16	13.52	0.0005 (TDI, RIVM 2001)
	10%	1.67	11.36	7.68	10.91	44.97	72.54	0.0005 (MRL, ATSDER 2002)
	25%	4.12	28.20	19.19	27.02	112.30	180.51	

Ψ = 100% absorbed DDT through inhalation route of exposure is added to the dermally absorbed dose at each DAR, DAR = Dermal Absorption Rate

Table 5. Acute and chronic dermal and inhalation internal exposures of the 57 DDT applicators and corresponding results estimated by ConsExpo 5.0 b01 model.

		Experimental						ConsExpo
					Percentiles			
Exposure		DAF	Mean ± SD	Median	75th	95th	99th	99th
Acute Exposure	ADE (mg/kg bw)	NA	7.481 ± 8.797	5.116	7.159	29.925	47.986	5.900
	DAD (mg/kg bw)	1.8%	0.135 ± 0.158	0.092	0.129	0.539	0.864	0.106
		10%	0.748 ± 0.880	0.512	0.716	2.992	4.799	0.590
		25%	1.870 ± 2.199	1.279	1.790	7.481	11.996	1.500
	IAD (mg/kg bw)	100%	0.009 ± 0.008	0.008	0.012	0.028	0.038	0.002
Chronic Exposure	DAD (mg/kg bw/d)	1.8%	0.199 ± 0.234	0.136	0.191	0.797	1.278	0.157
		10%	1.107 ± 1.301	0.757	1.059	4.427	7.099	0.880
		25%	2.767 ± 3.254	1.892	2.648	11.068	17.748	2.200
	IAD (mg/kg bw/d)	100%	0.014 ± 0.011	0.012	0.018	0.041	0.056	0.002

SD = Standard Deviation, NA = Not Applicable, DAF = Dermal Absorption Factor, ADE = Actual Dermal Exposure, DAD = Dermally absorbed dose, IAD = Inhalatory Absorbed Dose

Table 6. Actual exposures of the 57 DDT applicators and corresponding results estimated by Spraying model 1, Spraying model 10, and ConsExpo 5.0 b01 in mg/kg bw/one spraying day.

			Percentiles			
Assessment/estimation	Exposure	Median	75th	90th	95th	99th
Experimental (Study)	Dermal	76.3	107.38	239.24	448.87	719.79
	Inhalation	0.12	0.19	0.30	0.42	0.56
Spraying Model 1	Dermal	146.50	1198.51	∓	4409.10	∓
	Inhalation	6.42	8.02	∓	24.98	∓
Spraying Model 10	Dermal	∓	∓	662.60	∓	∓
	Inhalation	∓	∓	0.004	∓	∓
ConsExpo 5.0 b01	Dermal	∓	∓	∓	∓	88.50
	Inhalation	∓	∓	∓	∓	0.02

∓ = the models do not calculate these values

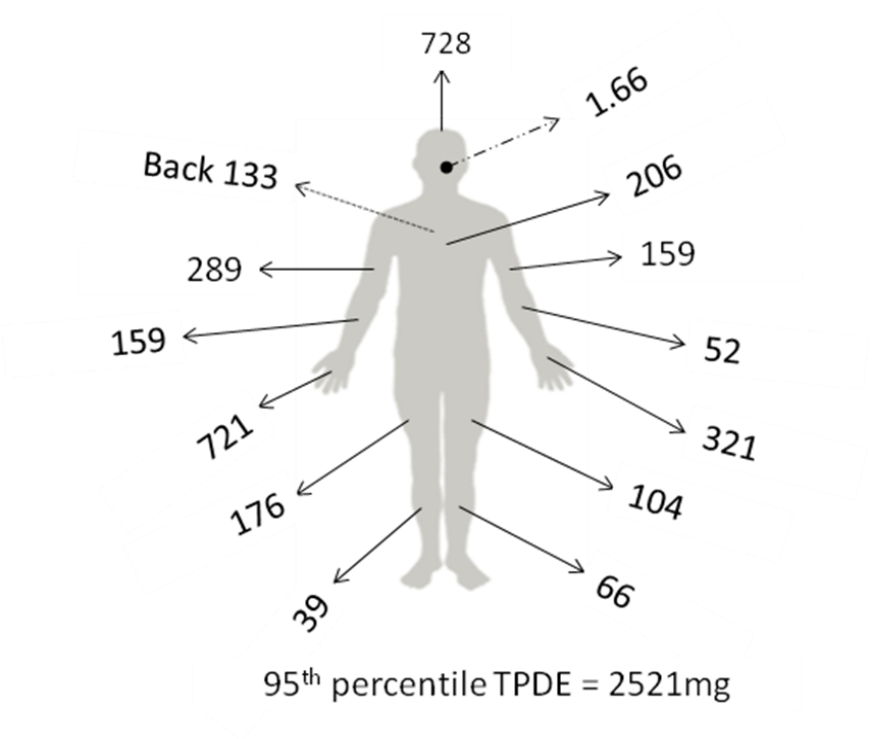

Figure 1. The 95th percentile total potential dermal exposure (TPDE) of applicators during spraying of one house.