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Infectious diseases are problematic for deployed military forces throughout the world, and, historically, more military service days have been lost to insect-vectored diseases than to combat. Because of the limitations in efficacy and availability of both vaccines and therapeutic drugs, vector management often is the best tool that military personnel have against most vector-borne pathogens. However, the use of insecticides may raise concerns about the safety of their effects on the health of the military personnel exposed to them. Therefore, our objective was to use risk assessment methodologies to evaluate health risks to deployed U.S. military personnel from vector management tactics. Our conservative tier-1, quantitative risk assessment focused on acute, subchronic, and chronic exposures and cancer risks to military personnel after insecticide application and use of personal protective measures in different scenarios. Exposures were estimated for every scenario, chemical, and pathway. Acute, subchronic, and chronic risks were assessed using a margin of exposure (MOE) approach. Our MOE was the ratio of a no-observed-adverse-effect level (NOAEL) to an estimated exposure. MOEs were greater than the levels of concern (LOCs) for all surface residual and indoor space spraying exposures, except acute dermal exposure to lambda-cyhalothrin. MOEs were greater than the LOCs for all chemicals in the truck-mounted ultra-low-volume (ULV) exposure scenario. The aggregate cancer risk for permethrin exceeded 1×10^{-6}, but more realistic exposure refinements would reduce the cancer risk below that value. Overall, results indicate that health risks from exposures to insecticides and personal protective measures used by military personnel are low.

Infectious diseases remain the third leading cause of death in the United States each year, and the second leading cause of death worldwide (WHO, 2004). Vector-borne diseases account for 17% of the estimated global burden of infectious diseases, with malaria alone responsible for 13.5% (WHO, 2004).

Infectious diseases may severely affect deployed military forces. Historically, more military service days have been lost to them than to combat (NRC, 1994). During deployment, personnel are often exposed to the bites of arthropods, which may vector pathogens that produce diseases (Gambel et al., 1998). Arthropod-borne diseases can affect the success of U.S. military missions and operations worldwide. Deployed U.S. military personnel typically are at greater risk than endemic populations because they have not acquired immunity to most of the vector-borne pathogens that they may encounter overseas (NRC, 1994), and they mostly train and operate outdoors (Garvey, 2000), increasing their exposure to arthropods. Consequently, morbidity rates may be high. Further, discomfort and dermatological effects produced by nuisance bites, psychological distress, allergic reactions, or secondary infections might compromise mission success even in the absence of disease transmission (Mehr et al., 1997), and soldiers may also transport infectious disease agents back to the United States (Thompson et al., 2005).

Although deployed U.S. military personnel may be susceptible to several vector-borne diseases, the mosquito-borne pathogens that produce malaria and dengue are most problematic. In fact, dengue and malaria were among the five most frequently diagnosed diseases associated with arthropods among members of the U.S. Armed Forces between 1995 and 1999 (Garvey,

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2000). Malaria is arguably the most important disease produced by a vector-borne pathogen that deployed forces may encounter. Endemic to more than 100 countries and territories, it has killed more people than any other disease in history, and annually infects 300–500 million people worldwide, killing 1–2.5 million per year (Addington et al., 2003; Kotwal et al., 2005; USAID, 2006).

Historically, malaria played an important role in military operations. The impact of malaria in U.S. military history is well known (Beadle & Hoffman, 1993; Bruce-Chwatt, 1985; Bunn et al., 1955; Coates et al., 1963; Peterson, 1995, Robert, 2001; Shanks & Karwacki, 1991; Wallace et al., 1996). It has affected U.S. military operations during the Revolutionary War and the American Civil War (Desowitz, 1991; Steiner, 1968). In 1992–1993, 131 U.S. Armed Forces personnel who served in Somalia were diagnosed with malaria (CDC, 1993). More recently, Army Rangers serving in Afghanistan from June to September in 2002 faced an outbreak of malaria, with an attack rate of 52.4 cases per 1000 soldiers (Kotwal et al., 2005). In 2002, 57 U.S. soldiers were diagnosed with malaria, representing more than 20 different locations worldwide (MSMR, 2002). In 2003, 40% of the Marines sent to Liberia contracted malaria (BBC, 2003). There were 71 cases of malaria recorded in the U.S. Army between January 2003 and October 2004 (USDOD, 2004).

Chemoprophylaxis is part of malaria protection for forces stationed in some endemic areas, but there may be side effects, including claims of psychoses and seizures (Thompson et al., 2005). Consequently, adherence to many of the prophylactic measures is an issue among deployed personnel (Barrett et al., 1969; Gambel et al., 1998; Murray, 2006; Newton et al., 1994). Moreover, drug-resistant strains of *Plasmodium* occur globally (Shanks & Karwacki, 1991; Thompson et al., 2005). The direct costs of malaria treatment are high, and range from $11 million to $30 million in a hypothetical situation where the attack rate is 25% of 50,000 deployed troops (Gillert, 1996). The cost of medical treatment for the 80 marines who contracted malaria while serving in Liberia was $1,483,120 (USDOD, 2004), a substantial portion of which was due to required evacuation of these patients. There are currently no effective vaccines against malaria. Although many resources and funds have been allocated to malaria vaccine research, it has proven to be a difficult task due to the size and genetic complexity of the parasite (Dubovsky, 2001).

Dengue is responsible for 50–100 million human infections per year (Diaz-Quijano et al., 2006; Monath, 1994; Rigau-Perez et al., 1998) and is a major cause of morbidity throughout the world (Gibbons & Vaughn, 2002; Monath, 1994). It has been estimated that 500,000 people with dengue hemorrhagic fever (DHF) are hospitalized each year (Calisher, 2005; Gubler, 1997). Dengue was diagnosed in 20% (74 of 389) of febrile patients at military field hospitals in Somalia between December 1992 and May 1993 (Wallace et al., 1996). There are no specific therapeutic agents for dengue, and treatment varies with the symptoms (Mairuhu et al., 2004). Similar to malaria, an effective, safe, and affordable vaccine is not yet available (Chaturvedi et al., 2005; Mairuhu et al., 2004; Rigau-Perez et al., 1998).

Because of the lack of vaccines and therapeutic drugs, vector management, including the use of personal protective measures (PPMs), is the best tool that deployed U.S. military personnel have against most vector-borne pathogens that produce disease. In preparation for military operations and force-health protection, the health risks from vector-borne pathogens that cause disease and vector management tactics need to be understood. Due to long-standing perceptions of risk from pesticides (Peterson & Higley, 1993; Slovic, 1987), the use of insecticides may raise concerns about their potential adverse health effects on military personnel. The uncertainties about exposure of the troops to pesticides led the U.S. Department of Defense to investigate the use and management of pesticides during the Gulf War (USDOD, 2003) and to raise concerns about the potential adverse health effects of pesticide exposures to service members in general.

Risk assessment is a systematic process for evaluating risk in an objective manner where all assumptions and uncertainties are clearly considered and presented (NRC, 1983, 1996). A human health risk assessment takes into account the possible harmful effects (also termed “hazard” or “toxicity”) of using the chemical as a function of exposure (NRC, 1983). To accomplish this, risk assessment typically utilizes a tiered approach extending from deterministic models (tier 1), which are based on extremely conservative assumptions, to probabilistic models (tier 4), which use refined assumptions (SETAC, 1994). Because a tier-1 risk assessment uses very conservative assumptions and parameters are overestimated, the resulting quantitative risk values typically are conservative and err on the side of safety.

The objective of this study was to use risk assessment methodologies to evaluate health risks to deployed U.S. military personnel from insect-vector management tactics. These tactics are mainly directed against adult mosquitoes, but several of them also apply to other disease-vectoring arthropods.

MATERIALS AND METHODS

Problem Formulation

Our tier-1 quantitative risk assessment of human health risks associated with mosquito management tactics focused on acute, subchronic, and chronic exposures after insecticide application and use of PPMs in different scenarios. Acute exposures were defined in this study as single-day exposures after a single application or use of the chemical. Subchronic exposures were defined as the exposure per day over 180 d with multiple spray events. For chronic exposures, it was assumed personnel might be deployed for 250 d/yr for 10 yr.

Exposures to two population subgroups, adult male and adult female, were estimated for every scenario, chemical, and pathway. Adult males were assumed to weigh 71.8 kg, which represents the mean body weight for all males (18 yr and

older), and adult reproductive females were assumed to weigh 60 kg, which represents the mean body weight for females between 13 and 54 yr (U.S. EPA, 1997a).

Hazard Identification

Risk assessments were conducted for alpha-cypermethrin, cyfluthrin, and lambda-cyhalothrin, which are used as surface residual insecticides on walls, buildings, structures, and vehicles. *d*-Phenothrin is used as an indoor space spray in buildings, tentage, and vehicles, and also as an outdoor ultra-low-volume (ULV) application. In addition to *d*-phenothrin, risk assessments were conducted for permethrin and resmethrin used as an outdoor ULV application, as well as for piperonyl butoxide, which is used to synergize pyrethroids. Assessments were also undertaken for permethrin-impregnated battle-dress uniforms (BDUs) and for bed nets impregnated with permethrin, deltamethrin, lambda-cyhalothrin, alpha-cypermethrin, or cyfluthrin.

All seven pyrethroid insecticides and the synergist piperonyl butoxide evaluated in this study are currently registered by the U.S. Environmental Protection Agency (U.S. EPA). All of these chemicals and use patterns of their commercial formulations either are approved by the U.S. Armed Forces Pest Management Board (USDOD, 2006) or have the potential to be used in certain situations (e.g., Najera and Zaim 2002; Zaim et al., 2000).

Toxicity Endpoints

Evaluation of noncancer risks. Toxicity endpoints were chosen based on U.S. EPA regulatory endpoints. Inhalation and dermal toxicity endpoints were used for each respective exposure route and duration. Dietary exposure was not used because that exposure route was assumed to be negligible for the use patterns modeled. Acute, subchronic, and chronic no-observed-adverse-effect levels (NOAELs) were identified for each active ingredient and exposure route and duration (Tables 1 and 2).

Cancer risks. Cancer risks were calculated for exposure to the chemicals classified by U.S. EPA as potential human carcinogens. Cancer risks for permethrin and resmethrin were evaluated by multiplying average daily dose by the cancer slope factor (CSF). This is a commonly used conservative model and represents the incremental probability that an

TABLE 1
Inhalation Toxic Effects and Regulatory Endpoints for the Chemicals Analyzed in the Risk Assessment

Compound	Exposure	Endpoint	MOE LOC[a]
Piperonyl butoxide (PBO)	Acute	NOAEL = 630 mg/kg/d (Tanaka et al., 1995)	100
	Subchronic	LOAEL = 0.015 mg/L (3.91 mg/kg/d) (U.S. EPA, 2005f)	300
	Chronic	LOAEL = 0.015 mg/L (3.91 mg/kg/d) (U.S. EPA, 2005f)	1000
Permethrin	Acute	NOEL = 0.042 mg/L (11 mg/kg/d) (U.S. EPA, 2006a)	100
	Subchronic	NOEL = 0.042 mg/L (11 mg/kg/d) (U.S. EPA, 2006a)	100
	Chronic	NOEL = 0.042 mg/L (11 mg/kg/d) (U.S. EPA, 2006a)	100
Resmethrin	Acute	LOAEL = 0.1 mg/L (28.2 mg/kg/d) (U.S. EPA, 2005b)	1000
	Subchronic	LOAEL = 0.1 mg/L (28.2 mg/kg/d) (U.S. EPA, 2005b)	1000
	Chronic	LOAEL = 0.1 mg/L (28.2 mg/kg/d) (U.S. EPA, 2005b)	1000
d-Phenothrin	Acute	NOEL = 0.291 mg/L (U.S. EPA, 2000)	100
	Subchronic	NOEL = 0.291 mg/L (U.S. EPA, 2000)	100
	Chronic	NOEL = 0.291 mg/L (U.S. EPA, 2000)	100
Deltamethrin	Acute	NOAEL = 1 mg/kg/d (U.S. EPA, 2004b)	100
	Subchronic	NOAEL = 1 mg/kg/d (U.S. EPA, 2004b)	100
	Chronic	NOAEL = 1 mg/kg/d (U.S. EPA, 2004b)	100
Cyfluthrin	Acute	NOAEL = 0.00026mg/L (0.07 mg/kg/d) (U.S. EPA, 2005c)	100
	Subchronic	NOAEL = 0.00009 mg/L (0.02 mg/kg/d) (U.S. EPA, 2005c)	100
	Chronic	NOAEL = 0.00009 mg/L (0.02 mg/kg/d) (U.S. EPA, 2005c)	100
Lambda-cyhalothrin	Acute	NOAEL = 0.04 mg/kg/d (U.S. EPA, 2004a)	100
	Subchronic	NOAEL = 0.04 mg/kg/d (U.S. EPA, 2004a)	100
	Chronic	NOAEL = 0.04 mg/kg/d (U.S. EPA, 2004a)	100
Alpha-cypermethrin	Acute	NOEL = 0.01 mg/L (2.7 mg/kg/d) (U.S. EPA, 2006b)	100
	Subchronic	NOEL = 0.01 mg/L (2.7 mg/kg/d) (U.S. EPA, 2006b)	100
	Chronic	NOEL = 0.01 mg/L (2.7 mg/kg/d) (U.S. EPA, 2006b)	300[b]

[a]Margin of exposure level of concern.
[b]No long-term study.

TABLE 2
Dermal Toxicological Effects and Regulatory Endpoints for the Chemicals Analyzed in the Risk Assessment

Compound	Exposure	Endpoint	MOE LOC
Piperonyl butoxide (PBO)	Acute	N/A[a] (U.S. EPA, 2005f)	N/A
	Subchronic	N/A (U.S. EPA, 2005f)	N/A
	Chronic	N/A (U.S. EPA, 2005f)	N/A
Permethrin	Acute	NOAEL = 500 mg/kg/d (U.S. EPA, 2006)	100
	Subchronic	NOAEL = 500 mg/kg/d (U.S. EPA, 2006)	100
	Chronic	NOAEL = 500 mg/kg/d (U.S. EPA, 2006)	100
Resmethrin	Acute	NOAEL = 30 mg/kg/d (U.S. EPA, 2005b)	1000[b]
	Subchronic	NOAEL = 30 mg/kg/d (U.S. EPA, 2005b)	1000[b]
	Chronic	NOAEL = 30 mg/kg/d (U.S. EPA, 2005b)	1000[b]
d-Phenothrin	Acute	NOAEL = 1000 mg/kg/d (U.S. EPA, 2000)	100
	Subchronic	NOAEL = 1000 mg/kg/d (U.S. EPA, 2000)	100
	Chronic	Oral NOAEL[c] = 7.1 mg/kg/d (U.S. EPA 2000)	100
Deltamethrin	Acute	NOEL = 1000 mg/kg/d (Barlow et al., 2001; Tsai, 2006)	100
	Subchronic	NOEL = 1000 mg/kg/d (Barlow et al., 2001; Tsai, 2006)	100
	Chronic	NOEL = 1000 mg/kg/d (Barlow et al., 2001; Tsai, 2006)	100
Cyfluthrin	Acute	NOAEL = 2.36 / 2.5 mg/kg/d (U.S. EPA, 2005c)	100
	Subchronic	NOAEL = 2.36 / 2.5 mg/kg/d (U.S. EPA, 2005c)	100
	Chronic	NOAEL = 2.4 mg/kg/d (U.S. EPA, 2005c)	100
Lambda-cyhalothrin	Acute	NOAEL = 5 mg/kg/d (U.S. EPA, 2004a)	100
	Subchronic	NOAEL = 5 mg/kg/d (U.S. EPA, 2004a)	100
	Chronic	NOAEL = 5 mg/kg/d (U.S. EPA, 2004a)	100
Alpha-cypermethrin	Acute	Oral NOAEL[d] = 10 mg/kg/d (U.S. EPA, 2006b)	100
	Subchronic	Oral NOAEL[d] = 10 mg/kg/d (U.S. EPA, 2006b)	100
	Chronic	Oral NOAEL[d] = 0.6 mg/kg/d (U.S. EPA, 2006b)	100

[a]Not applicable. No systemic, developmental and neurotoxicity concerns at the limit dose (U.S. EPA, 2005f).
[b]Due to lack of developmental neurotoxicity study.
[c]No studies available for long term skin exposure to *d*-phenothrin.
[d]According to U.S. EPA, "no hazard was identified to justify quantification of risk" through dermal exposure.

individual will develop cancer during his lifetime due to exposure to that particular chemical (U.S. EPA, 2005f).

Environmental Concentrations and Fate of Insecticides

The AERMOD version 1.0 tier-1 air dispersion model (U.S. EPA 1999) was used to predict the 7.62-m (25-ft) and 91.44-m (300-ft) air concentrations of each truck-mounted ULV insecticide within 1- and 6-h time ranges for the 3 active ingredients and the synergist piperonyl butoxide. The assumptions for the reasonable worst case scenario and the establishment of receptors followed those used by Peterson et al. (2006).

The Industrial Source Complex Short-Term (ISCST3) screening model (U.S. EPA, 1995) was used to model particle deposition of the ULV spray at 7.62 m and 91.44 m from the spray area at the 1-h average. Assumptions for ISCST3 also followed Peterson et al. (2006). Values were obtained for deposition at 7.62 m, deposition at 91.44 m, and the average deposition within 91.44 m of the spray source using a Cartesian grid similar to that used in AERMOD (Peterson et al., 2006). Furthermore, the deposition values within 91.44 m for each insecticide were used in an exponential decay model (Peterson et al., 2006) to characterize their persistence on the terrestrial environment within a spray program that included 30 sprays in 5-d clusters. Each spray event was followed through d 180 for subchronic exposure, and d 250 for chronic exposure using a multiple degradation model from the U.S. EPA (2004c).

Potential Exposure

Our tier-1 risk assessment focused on worst-case scenarios in which the deployed military personnel might be exposed to the insecticides. The five major uses of insecticide were identified as surface residual spraying, indoor space spraying, outdoor ULV spraying, insecticide-impregnated BDUs, and insecticide-impregnated bed nets (Figure 1).

Surface Residual Spraying and Indoor Space Applications

In a semipermanent or permanent camp scenario, residual insecticides may be used as a general surface application, on or

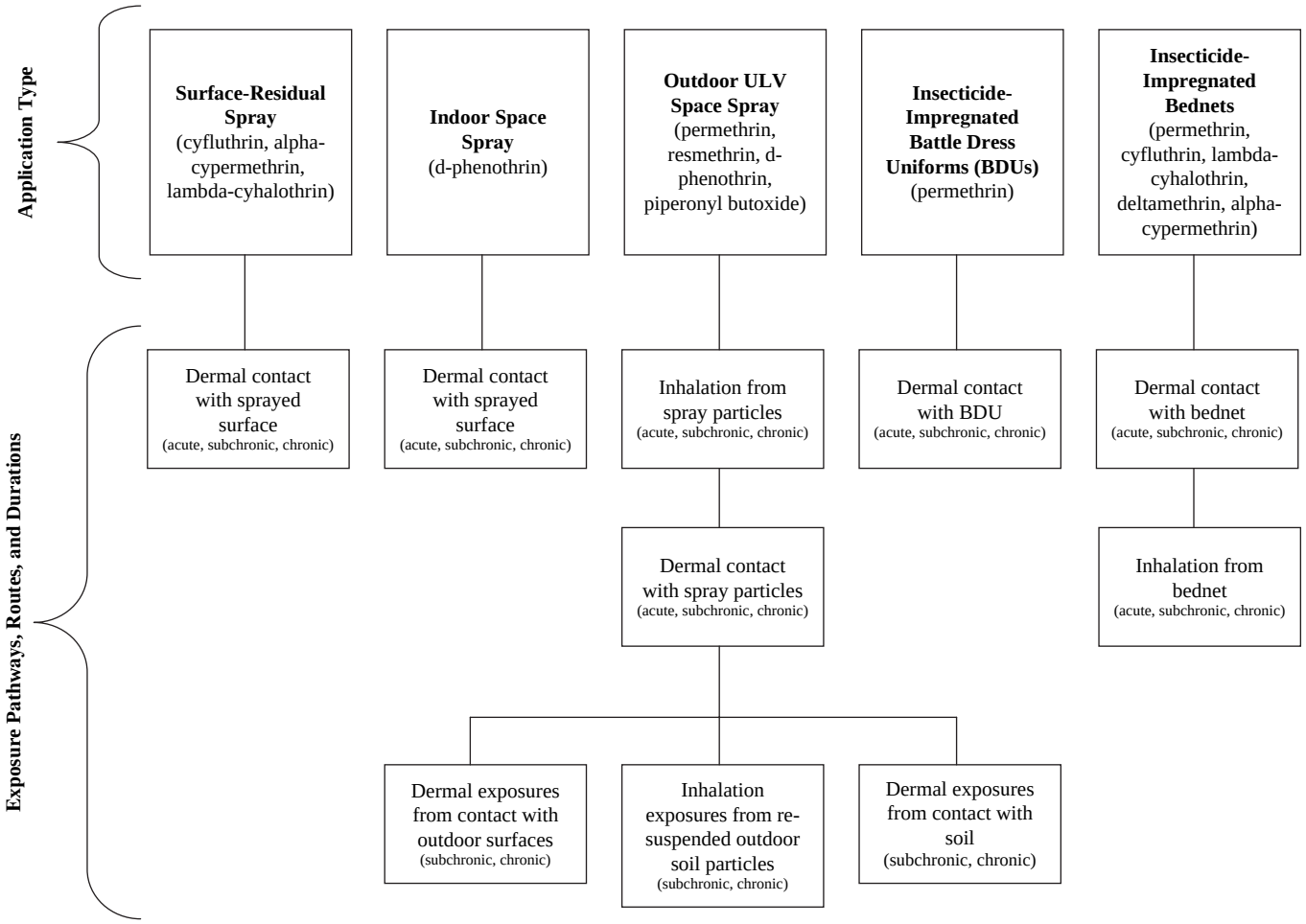

FIG. 1. Conceptual model of the scope of the exposure and risk assessment.

around walls, buildings, and structures, on various modes of transportation, and at refuse dumps. They may also be used as space sprays inside buildings, in vehicles, and in tentage. Some chemicals used as surface residuals are cyfluthrin, alpha-cypermethrin, and lambda-cyhalothrin. Aerosol formulations of *d*-phenothrin may also be used as an indoor space spray.

For these scenarios, inhalation exposures were assumed to be negligible because of use pattern, low vapor pressure, and low concentrations of all active ingredients (U.S. EPA, 1997b). Dermal exposures from contact with sprayed surfaces were assessed for three exposure durations: acute immediately after a single-spray event, subchronic after multiple spray events over 180 d, and chronic after multiple spray events for 250 d each year over 10 yr.

Acute dermal exposure from contact with sprayed surfaces. Acute dermal exposures from contact with surfaces after a residual spray event were estimated as:

$$PE = (SA \times AbR \times TSR) / BW \quad (1)$$

where PE is potential exposure (mg/kg body weight [BW]), SA is body surface area in contact with surface (m^2), AbR is dermal absorption rate, TSR is transferable surface residue, and BW is body weight (kg). The body surface area in contact with the surface was assumed to be 50% of the surface area for hands, arms, and trunk; therefore, it was assumed the person would contact treated surfaces with half the total surface area of his hands, arms, and trunk within 24 h after spraying. Body-surface area data were obtained from U.S. EPA (1997a). The transferable surface residue was assumed to be 20% (Williams et al., 2003); that is, 20% of the chemical applied would be transferred from the surface to the skin. The values for dermal absorption are chemical specific and were only incorporated into the equation when the study that originated the NOAEL in question was not a dermal study (the dermal absorption in those cases represented systemic exposure). Values for dermal absorption were 2.5% for alpha-cypermethrin (U.S. EPA, 2006b) and 5% for cyfluthrin (U.S. EPA, 2005c).

Subchronic dermal exposure from contact with sprayed surfaces. Subchronic dermal exposures from contact with surfaces after spray events were estimated as:

$$PE = \left(PE_{acute} \times SE\right) / D \quad (2)$$

where PE is potential exposure (mg/kg BW/d), PE_{acute} is the acute exposure from each spray event (mg/kg BW), SE is the number of spray events, and *D* is the duration of exposure (d). It was assumed that there were 6 spray events and the exposure duration was 180 d.

Chronic dermal exposure from contact with sprayed surfaces. Chronic dermal exposures from contact with surfaces after spray events were estimated as:

$$PE = \left[\left(PE_{acute} \times SE\right) / D \times Y\right] / AT, \quad (3)$$

where PE is potential exposure (mg/kg BW/d), PE_{acute} is the acute exposure from each spray event (mg/kg BW), SE is the number of spray events, *D* is the duration of exposure in days, *Y* is the duration of exposure in years, and AT is averaging time. It was assumed that there were 9 spray events and the exposure duration was 250 d each year for 10 yr. Time was averaged (AT) to account for total number of days in 10 yr (365×10).

Outdoor Truck-Mounted ULV Applications

Deployed personnel potentially may be exposed to ULV applications of insecticides when outside. Chemicals used in truck-mounted ULV outdoor applications are permethrin, resmethrin, *d*-phenothrin, and piperonyl butoxide.

Acute exposure. Two major routes of exposure immediately after a single-spray event were assumed: inhalation and dermal contact with spray. It was also assumed that personnel did nothing to limit their exposure to the spray (see below for specific exposure assumptions).

Acute inhalation exposures from spray particles. Acute inhalation exposures from contact with spray after a single spray event were estimated as:

$$PE = \left(EEC \times RR \times D\right) / BW \quad (4)$$

where PE is potential exposure (mg/kg BW), EEC is the 1-h average estimated environmental concentration of a chemical in the air within 91.44 m from the spray source (mg/m^3), RR is respiratory rate under moderate activity (m^3/h), *D* is duration of exposure (h), and BW is body weight (kg).

Respiratory rates were assumed to be 1.6 m^3/h for both adult females and males and are indicative of moderate physical activity (U.S. EPA, 1997a). The assumed duration of exposure was 1 h. Therefore, the assumption was that the person was outside, within 91.44 m from the spray truck when it passed him or her. Moreover, the person remained outside for 1 h, respiring as if under moderate physical activity during the entire time. Because of the nature of ULV applications and dispersion rate of the droplets, inhalation exposures after the first hour were not assumed. Body weight for the different age groups was discussed earlier.

Acute dermal exposures from contact with spray. Acute dermal exposures after a single spray event were estimated as:.

$$PE = \left(TDE \times AbR\right) / BW \quad (5)$$

where PE is potential exposure (mg/kg BW), TDE is total dermal exposure (mg), AbR is dermal absorption rate, and BW is body weight (kg). Values for dermal absorption were 10% for resmethrin (U.S. EPA, 2005b) and 70% for *d*-phenothrin (U.S. EPA, 2000).

The U.S. EPA Pesticide Handler Exposure Database (PHED, v. 1.1) (U.S. EPA, 1998) was used as a conservative surrogate for dermal deposition immediately after truck-mounted ULV applications (Peterson et al., 2006). For the acute dermal exposure assessment, the PHED exposure scenario of a flagger exposure to a liquid insecticide application was used. The scenario assumed that the person was only wearing shorts and that exposure was 100-fold greater than the flagger scenario. This scenario conservatively estimates deployed military personnel dermal exposure because a 100-fold increase in exposure was added, and other risk assessments conducted by the U.S. EPA have not considered acute dermal contact from ULV applications (e.g., piperonyl butoxide and permethrin) because it was believed to be negligible (U.S. EPA, 2005e, 2005f, 2006a).

Subchronic exposure. Multiroute exposures per day were assumed over 180 d after multiple spray events. Routes of insecticide exposure included inhalation of spray particles, inhalation of resuspended outdoor soil particles, and dermal contact with spray, soil, and outdoor surfaces.

Subchronic inhalation exposures from spray particles and subchronic dermal exposures from contact with spray. Subchronic inhalation and dermal exposures from contact with spray were estimated using the same equation used for subchronic dermal exposure from contact with surfaces sprayed with residual insecticides [see Eq. 2]. It was assumed that there were 21 spray events and the exposure duration was 180 d.

Subchronic inhalation exposures from resuspended outdoor soil particles. Subchronic inhalation exposures from re-suspended soil were estimated as:

$$PE = \left(EEC/SW \times CA \times CF \times RR\right) / BW \quad (6)$$

where EEC is the 180-d average concentration of the insecticide deposited on soil (mg/mg soil), SW is soil weight (mg/m^2), CA

is concentration of particulate matter in air ($\mu g/m^3$), CF is conversion factor (from μg to mg, 0.001), RR is respiratory rate (m^3/d), and BW is body weight (kg). Soil weight was assumed to be 481 kg/m^3 (13.62 kg/ft^3) based on reported densities for Scotts garden soil. It was assumed that the concentration of particulate matter in air is the PM_{10} standard of 60 $\mu g/m^3$ (NYCDOH, 2001) and that this concentration is in the breathing zone. It was further assumed that all the suspended PM was from soil, 100% was retained in the lungs, and 100% was absorbed. The respiratory rate used was 15.2 m^3/d for adult males and 11.3 m^3/d for adult females (U.S. EPA, 1997a). Assumptions for body weight are discussed earlier.

Subchronic dermal exposures from contact with soil. Subchronic dermal exposures were estimated as:

$$PE = \left(CS \times SA \times SS \times AbR \times DR\right) / BW \quad (7)$$

where PE is potential exposure (mg/kg BW/d), CS is the 180-d average concentration of the insecticide deposited on soil (mg/mg soil), SA is body surface area in contact with soil (cm^2), SS is mass of soil adhered to skin (mg/cm^2), AbR is dermal absorption rate, DR is dislodgeable residue, and BW is body weight (kg). The concentration of the active ingredient on the soil (CS) was calculated from the 180-d average deposition on soil, assuming the insecticide is deposited within the first cm layer of soil (1 m × 1 m × 1 cm = 0.01 m^3), and soil weight, which was assumed to be 481 kg/m^3 (13.62 kg/ft^3). The body surface area in contact with soil was assumed to be the sum of surface areas for hands, arms, trunk, legs, and face (head/2) (U.S. EPA, 1997a). Therefore, it was assumed personnel were clothed in only shorts and shoes while outside. Contact with soil was associated with an activity such as rugby (1.089 mg soil/cm^2 skin) (U.S. EPA, 1997a). It was assumed that the same person was engaged in these activity patterns each day over the 180 d. Dislodgeable insecticide residue (*DR*) from soil was assumed to be 20% (U.S. EPA, 1997a). The assumptions for dermal absorption rate were discussed earlier.

Subchronic dermal exposures from contact with outdoor surfaces. Subchronic dermal exposures were estimated as:

$$PE = \left(EEC \times SA \times AbR \times DR\right) / BW \quad (8)$$

where PE is potential exposure (mg/kg BW/d), EEC is the 180-d average environmental concentration of the insecticide deposited on soil within 91.44 m from the spray source (mg/m^2), SA is body surface area in contact with surface (cm^2), AbR is dermal absorption rate, DR is dislodgeable residue, and BW is body weight (kg). The assumptions for surface area, dermal absorption rate, and dislodgeable residue were discussed earlier.

Chronic exposure. Multiroute exposures were assumed per day over 250 d after multiple spray events each year for 10 yr. Routes of insecticide exposure included inhalation of spray particles, inhalation of resuspended outdoor soil particles, and dermal contact with spray, soil, and outdoor surfaces. Estimates for all routes followed equations used for subchronic exposures, and time was averaged to account for 250 d of exposure per year over 10 yr [see Eqs. 6–8]. A total of 30 spray events in 250 d was assumed.

Cancer risk. Of the seven active ingredients plus one synergist assessed in this study, three are tentatively classified by U.S. EPA as possible or likely human carcinogens—permethrin, resmethrin, and alpha-cypermethrin (U.S. EPA, 2005a, 2005b, 2005d, 2005f, 2006a, 2006b— but no quantification is currently required for alpha-cypermethrin (U.S. EPA, 2005d, 2006b). Therefore, resmethrin [$Q^* = 5.621 \times 10^{-2}$ $(mg/kg/d)^{-1}$; U.S. EPA, 2005a, 2005b] and permethrin [$Q^* = 9.567 \times 10^{-3}$ $(mg/kg/d)^{-1}$; U.S. EPA, 2005f, 2006a] were included in our analysis of cancer risk. The term Q^* is the cancer potency factor derived from animal experiments.

Potential exposures (PE) were estimated according to exposure route and then used to calculate cancer risk:

$$\text{Cancer risk} = PE \times Q^* \quad (9)$$

Exposure duration per year was 0.685 (250 d of exposure in 365 d/yr) for all cancer risk estimates. Years of exposure were averaged by dividing 10 yr of exposure by 75 yr in a lifetime (0.133).

Insecticide-Impregnated BDUs

The human health risks were assessed from the use of BDUs impregnated with permethrin. Because field operations may require military personnel to use the permethrin-impregnated uniforms on a continuous basis, it was assumed that these would be used for 18 h/d for 250 d/year. Inhalation exposures were determined to be negligible because of the low vapor pressure of permethrin and this particular use pattern (U.S. EPA, 2005f, 2006a). For estimates of potential exposure through the dermal route, it was assumed the clothing residue concentration in the treated uniform to be 0.125 mg permethrin/cm^2, and the surface area in contact with the uniform to be the area of arms, hands, and legs (U.S. EPA, 1997a), with the use of undershirt and briefs underneath the BDU. This assumption is sufficiently conservative because U.S. EPA only considered the surface areas of legs and arms in their estimates (U.S. EPA, 2005f, 2006a). The transfer factor of the chemical from the clothing to the skin was assumed to be 0.49% (Snodgrass, 1992). As a worst-case scenario, it was assumed there was no wash-off or degradation of the permethrin on the BDU over time. As with the other scenarios, acute (1 d exposure), subchronic (180 d), and chronic (250 d each year over 10 yr) potential exposures were assessed. Cancer risk was also assessed because permethrin is classified by the U.S. EPA as a possible human carcinogen (U.S. EPA, 2005f, 2006a).

Acute and subchronic dermal exposures.

$$PE = (CR \times SA \times TF \times AbR \times EF)/BW \quad (10)$$

where PE is potential exposure (mg/kg BW), CR is clothing residue (mg a.i./cm^2), SA is surface area (cm^2), TF is transfer factor from the clothing to the skin, AbR is dermal absorption rate, EF is exposure frequency (h/d), and BW is body weight (kg).

Chronic dermal exposures.

$$PE = (CR \times SA \times TF \times AbR \times EF)/BW \times (D \times Y)/AT \quad (11)$$

where PE is potential exposure (mg/kg BW), CR is clothing residue (mg a.i./cm^2), SA is surface area (cm^2), TF is transfer factor from the clothing to the skin, AbR is dermal absorption rate, BW is body weight (kg), EF is exposure frequency (h/d), *D* is exposure duration (d), *Y* is number of years, and AT is averaging time (365 d × 10 yr = 3650).

Cancer risk—Dermal exposures. For the cancer assessment, it was assumed that permethrin-impregnated BDUs were worn 18 h/d, 250 d/yr, over 10 yr in a lifetime. Potential exposures (PE) were estimated according to exposure route and then used to calculate cancer risk.

Insecticide-Impregnated Bed Nets

It was assumed bed nets might be impregnated with permethrin (60.33 mg/m^2 target dose, U.S. EPA 2005f, or 500 mg/m^2 target dose, Najera & Zaim, 2002), deltamethrin (25 mg/m^2 target dose, Barlow et al., 2001), lambda-cyhalothrin (20 mg/m^2 target dose, Zaim et al., 2000), alpha-cypermethrin (40 mg/m^2 target dose, Zaim et al., 2000), or cyfluthrin (50 mg/m^2 target dose, Bomann, 1995) and that the size of the bed net was 15 m^2 (Najera & Zaim, 2002). Military personnel were assumed to spend 8 h/night under the bed net, and, as for the impregnated BDUs, acute (1 d), subchronic (180 d), chronic (250 d for 10 yr), and cancer (250 d each year for 10 yr in a lifetime) risks were assessed.

Acute inhalation exposures.

$$PE = (AC \times RR \times T \times CF)/BW \quad (12)$$

where PE is potential exposure (mg/kg BW), AC is air concentration under net (μg/m^3), RR is respiratory rate (m^3/h), *T* is time spent under net (h), CF is conversion factor from μg to mg (0.001), and BW is body weight (kg). The air concentration under the net was assumed to be 0.55 μg/m^3 for cyfluthrin (Bomann, 1995), and this value was extrapolated to the other pyrethroids analyzed, depending on their target doses and vapor pressures (Barlow et al., 2001). The respiratory rate was assumed to be 0.4 m^3/h, which corresponds to the respiratory rate of an adult at rest (U.S. EPA, 1997a). Assumptions for time and body weight were discussed earlier.

Acute dermal exposures.

$$PE = (TD \times SA \times TC \times AbR)/BW \quad (13)$$

where PE is potential exposure (mg/kg BW), TD is target dose (mg a.i./m^2), SA is surface area potentially in contact with net (m^2), TC is transfer coefficient, AbR is chemical specific absorption rate, and BW is body weight (kg). The surface area potentially in contact with the net was assumed to be 50% of the total area of head, trunk, arms, legs, hands, and feet (U.S. EPA, 1997a). Transfer coefficient is 2.5% (Najera & Zaim, 2002). Assumptions for target dose, absorption rates, and body weight were discussed earlier.

Subchronic inhalation and dermal exposures were calculated using the equation for acute inhalation and dermal exposures considering the time spent under net, which was assumed to be 8 h/d (8/24 = 0.333). Chronic inhalation and dermal exposures were assumed to be 8 h/d, for 250 d over 10 yr.

Cancer risk was assessed for permethrin-impregnated bed nets. For cancer risk estimates, it was assumed that a person would be deployed for 10 yr and would sleep 8 h/d under a permethrin-impregnated bed net everyday for 250 d/yr, over a 75-yr lifetime.

Risk Characterization

Human health risks were assessed by integrating toxicity and exposure. Acute, subchronic, and chronic risks were assessed using a margin of exposure (MOE) approach. Our MOE was the ratio of a NOAEL to an estimated exposure. For each population subgroup, an MOE was calculated by dividing the NOAEL by the potential exposure (PE). The target levels of concern (LOCs) or MOEs for dermal and inhalation exposures to permethrin, *d*-phenothrin, deltamethrin, cyfluthrin, and lambda-cyhalothrin were based on the conventional uncertainty factor of 100 × (10 × for intraspecies extrapolation and 10 × for interspecies variation) for all durations. For dermal and inhalation exposures to resmethrin and alpha-cypermethrin, the target LOCs or MOEs were 1000 × (additional 10 ×) due to the absence of developmental neurotoxicity studies. This does not imply that there are no neurotoxicity studies for these insecticides, but rather that there are no developmental neurotoxicity studies. The target LOC or MOE for inhalation exposure to piperonyl butoxide was 100 for acute, 300 for subchronic (3 × due to the use of a LOAEL), and 1000 for chronic (10 × to account for "lesions in the respiratory tract that might progress into long term adverse effects") (U.S. EPA, 2005e).

Exposures by similar route of exposure and duration for each chemical (e.g., subchronic dermal contact with spray, soil, and outdoor surfaces) were added for the determination of the

MOE for that route (subchronic dermal total exposure). For multiroute exposures (dermal + inhalation) to each active ingredient, an aggregate MOE was calculated by:

$$\text{Aggregate MOE} = 1/(1/\text{MOE}_{\text{dermal}} + 1/\text{MOE}_{\text{inhalation}}), \quad (14)$$

Exposures by all routes and all scenarios for each chemical were also added to calculate an aggregate MOE for that particular chemical. For example, permethrin can be used as an outdoor ULV, in BDUs, and in bed nets, and the aggregate MOE was calculated by:

$$\text{Aggregate MOE}_{\text{permethrin}} = 1/(1/\text{MOE}_{\text{ULV}} + 1/\text{MOE}_{\text{BDU}} + 1/\text{MOE}_{\text{bed net}}) \quad (15)$$

RESULTS

Surface Residual Spraying and Indoor Space Spraying

Table 3 shows the calculated dermal MOEs for each active ingredient and exposure duration. Potential acute dermal exposures through contact with sprayed surfaces ranged from 3×10^{-3} to 1.98×10^{-1} mg/kgBW/d. Subchronic exposures ranged from 1×10^{-4} to 6×10^{-3} mg/kgBW/d. Chronic exposures ranged from 3.15×10^{-7} to 1.87×10^{-5} mg/kgBW/d. MOEs were greater than the LOCs for all exposures except acute post-application dermal exposure to lambda-cyhalothrin (Table 3).

Outdoor Truck-Mounted ULV Spraying

Acute, subchronic, and chronic MOEs were calculated for each chemical by route of exposure and duration. Table 4 shows the estimated aggregate MOEs and cancer risk, which was calculated for permethrin and resmethrin. Potential inhalation exposures ranged from 3.3×10^{-5} to 3×10^{-4} mg/kgBW/d (acute exposures), 3.85×10^{-6} to 4×10^{-5} mg/kgBW/d (subchronic exposures), and 1.08×10^{-8} to 1.13×10^{-7} mg/kgBW/d (chronic exposures). Potential dermal exposures to the adulticides ranged from 1.03×10^{-6} to 3×10^{-4} mg/kgBW/d (acute exposures), 2×10^{-4} to 3.2×10^{-2} mg/kgBW/d (subchronic exposures), and 1.59×10^{-5} to 2.3×10^{-2} mg/kgBW/d (chronic exposures). Acute aggregate MOEs ranged from 4307 to > 2,000,000 and subchronic and chronic MOEs ranged from 15,337 to 504,459 and from 7,456 to >41,000,000, respectively. An MOE of 4307 means that the estimated exposure was 4307 times less than the NOAEL. MOEs were greater than the LOCs for all chemicals in the truck-mounted ULV exposure scenario. The lowest acute aggregate MOE was to permethrin and the highest aggregate acute MOE was to piperonyl butoxide (Table 4). The lowest and highest aggregate MOEs were to permethrin and *d*-phenothrin, respectively (Table 4), for subchronic exposures, and to *d*-phenothrin and piperonyl butoxide for chronic exposures.

Cancer risk for truck-mounted ULV spraying of resmethrin was estimated to be 1.73×10^{-7}. The greatest estimate of cancer risk for ULV spraying of permethrin was 4.38×10^{-6}, exceeding the LOC of 1×10^{-6} (Table 4). Dermal exposure from contact with outdoor surfaces represented the greatest exposure for permethrin.

Impregnated BDUs

Table 5 shows the calculated dermal MOEs for each active ingredient by exposure duration for permethrin-impregnated BDUs. Potential dermal exposures through contact with the BDUs were 0.066 mg/kgBW/d (acute and subchronic exposures), and 0.045 mg/kgBW/d (chronic exposures). Dermal exposures to permethrin-impregnated BDUs were below LOCs for all exposure durations. Cancer risk for permethrin-impregnated BDUs is also shown in Table 5.

TABLE 3
Margins of Exposure (MOE) for Surface Residual and Indoor Space Spray Active Ingredients by Duration of Dermal Exposure

Chemical	Application rate	Subgroup	Acute MOE[a]	Subchronic MOE	Chronic MOE
Cyfluthrin	215.8 mg/m^2	Adult male	139	4173	>1,000,000
		Adult female	147	4420	>1,500,000
Lambda-cyhalothrin	120.56 mg/m^2	Adult male	26	791	>200,000
		Adult female	28	838	>200,000
Alpha-cypermethrin	125.9 mg/m^2	Adult male	2021	>30,000	>12,000,000
		Adult female	2140	>30,000	>13,000,000
d-Phenothrin	2.15 mg/m^2	Adult male	>200,000	>8,000,000	>20,000,000
		Adult female	>300,000	>9,000,000	>20,000,000

[a]Margin of exposure (MOE = NOAEL/exposure).

TABLE 4
Margins of Exposure (MOE) for Outdoor Truck-Mounted ULV Chemicals by Duration of Aggregate Exposure and Cancer Risk

Chemical	Application rate	Subgroup	Acute MOE	Subchronic MOE	Chronic MOE	Cancer Risk
PBO	0.0392 kg/ha	Adult male	>2,000,000	>100,000	>40,000,000	N/A[a]
		Adult female	>1,500,000	>97,000	>34,000,000	N/A
Permethrin	0.0078 kg/ha	Adult male	4307	>15,000	>20,000	4.38×10^{-6}
		Adult female	4407	>15,000	>20,000	4.31×10^{-6}
Resmethrin	0.0078 kg/ha	Adult male	>40,000	>100,000	>1,500,000	1.63×10^{-7}
		Adult female	>30,000	>100,000	>1,500,000	1.73×10^{-7}
d-Phenothrin	0.004 kg/ha	Adult male	>1,000,000	>400,000	7456	N/A
		Adult female	>1,000,000	>500,000	7618	N/A

[a]Not applicable.

TABLE 5
Margins of Exposure (MOE) for Active Ingredients in Insecticide-Impregnated BDUs and Bed Nets by Duration of Aggregate Exposure and Cancer Risk

Chemical	Target dose	Subgroup	Acute MOE	Subchronic MOE	Chronic MOE	Cancer Risk
Permethrin (BDUs)	0.125 mg/cm^2	Adult male	7587	7587	>10,000	8.64×10^{-6}
		Adult female	7594	7594	>10,000	8.63×10^{-6}
Permethrin (bed nets)	500 mg/m^2	Adult male	2830	8497	>10,000	7.71×10^{-6}
		Adult female	2878	8642	>10,000	7.58×10^{-6}
Permethrin (bed nets)	60.33 mg/m^2	Adult male	>20,000	>70,000	>100,000	9.31×10^{-7}
		Adult female	>20,000	>70,000	>100,000	9.15×10^{-7}
Deltamethrin (bed nets)	25 mg/m^2	Adult male	>80,000	>300,000	>400,000	N/A[a]
		Adult female	>80,000	>300,000	>400,000	N/A
Lambda-cyhalothrin (bed nets)	20 mg/m^2	Adult male	677	2113	3085	N/A
		Adult female	683	2146	3134	N/A
Alpha-cypermethrin (bed nets)	40 mg/m^2	Adult male	>20,000	>40,000	>70,000	N/A
		Adult female	>20,000	>40,000	>70,000	N/A
Cyfluthrin (bed nets)	50 mg/m^2	Adult male	2664	8018	>10,000	N/A
		Adult female	2707	8154	>10,000	N/A

[a]Not applicable.

Impregnated Bed Nets

Table 5 shows the calculated aggregate MOEs for each exposure duration and insecticide for impregnated bed nets and cancer risk for permethrin-impregnated bed nets. Potential dermal exposures through contact with the bed nets ranged from 3×10^{-4} to 0.177 mg/kgBW/d (acute exposures), 1×10^{-4} to 0.059 mg/kgBW/d (subchronic exposures), and 8.06×10^{-5} to 0.04 mg/kgBW/d (chronic exposures). Potential inhalation exposures from sleeping under the bed nets ranged from 2.45×10^{-6} to 5.87×10^{-6} mg/kgBW/d (acute exposures), 1.02×10^{-7} to 2.44×10^{-7} mg/kgBW/d (subchronic exposures), and 6.99×10^{-8} to 1.67×10^{-7} mg/kgBW/d (chronic exposures). Exposures to all pyrethroid-impregnated bed nets assessed in this study were below levels of concern (i.e., MOEs were greater than LOCs).

Aggregate Risk

Aggregate MOEs ranged from 677 to 88,601 (acute exposure), from 2113 to 331,671 (subchronic), and from 3085 to 484,239 (chronic). The lowest and highest aggregrate MOEs were for exposure to lambda-cyhalothrin and deltamethrin, respectively,

for all exposure durations (Table 5). Cancer risk for permethrin-impregnated bed nets is also shown in Table 5. Aggregate cancer risk for permethrin (outdoor truck-mounted ULV spraying, impregnated BDUs, and impregnated bed nets) was 8.7×10^{-6}.

DISCUSSION

A number of exposure scenarios were considered and, although deployments may often present situations that are different than those presented here, it is believed that exposure was overestimated and that the scenarios analyzed were reasonable worst cases.

The highest aggregate MOE (least risk) was for chronic exposure to piperonyl butoxide and the lowest (most risk) was for acute exposure to lambda-cyhalothrin applied as a surface residual insecticide. Risks exceeded LOCs for acute dermal exposure to lambda-cyhalothrin applied as a surface residual spray. The MOE in this case was 26, meaning that the estimated exposure was 26 times less than the NOAEL, but not 100-fold less, which would be needed to be below the LOC. In our assessment, it was not assumed there was any degradation of lambda-cyhalothrin after application to surfaces. More realistic assumptions of degradation and/or less than 50% body (i.e., skin) surface area in contact with sprayed surfaces over the 24 h after application might reduce exposure and therefore risk.

For the permethrin-impregnated BDUs scenario, the greatest cancer risk estimate was 8.64×10^{-6}. Our assumptions were conservative and likely overestimated exposure because an initial health effects assessment of impregnated BDUs conducted by the U.S. National Research Council used a dermal absorption rate of 2% for permethrin instead of 15% (Bartelt and Hubbell, 1987; NRC, 1994). The cancer risk using the 2% absorption rate would be 1.15×10^{-6}. One did not account for wash-off of permethrin from the BDUs over time (i.e., the time-weighted average percent of permethrin remaining on fabric through washings) (NRC, 1994; U.S. EPA, 2006a), which would further reduce estimates of cancer risk.

Cancer risk LOCs were also exceeded for exposure to truck-mounted ULV spraying of permethrin. Our assumptions were conservative and an absorption rate of 15% was used for permethrin. If one used a dermal absorption rate of 2% instead of 15% (Bartelt & Hubbell, 1987; NRC, 1994), the cancer risk estimate would be 6.24×10^{-7}. There was also conservatism in our assumptions of body area exposed for contact with surfaces, by assuming that the person is minimally clothed, and that the area in contact would be the total surface area of face, trunk, arms, legs, and hands (i.e., the individual was only wearing shorts and shoes). Finally, it may be possible to entirely discount dermal exposures. In its re-registration eligibility document, the U.S. EPA did not include a dermal exposure estimate for permethrin when applied via ULV equipment for mosquito control because it was not considered a significant exposure route (U.S. EPA, 2006a). If dermal exposures are discounted from our risk assessment, the cancer risk would be 6.68×10^{-9}.

Cancer risk estimates for bed nets impregnated with 500 mg permethrin/m^2 exceeded the 1×10^{-6} LOC. According to our tier-1 assessment, the highest dose of permethrin for impregnated bed nets that would not exceed LOCs is 65 mg/m^2, which is more than the maximum application rate of 0.09 g a.i./bed net maximum application rate recommended by the U.S. EPA (2005f). In this assessment, the dermal absorption rate of 15% was used for permethrin. If the 2% absorption rate is used (Bartelt & Hubbell, 1987; NRC, 1994), the cancer risk estimate is 1.03×10^{-6} for the 500-mg/m^2 application rate.

One can also calculate aggregate MOEs assuming that one chemical is used for all the possible exposure pathways and scenarios in which it is currently registered for use. For example, one can conservatively assume that permethrin is used for outdoor ULV truck-mounted application, BDUs, and bed nets, and the person would then be exposed at the same time through all of these use patterns. Using this approach, the aggregate MOEs would still be greater than the LOCs, ranging from 5071 to 7349. *d*-Phenothrin can be used as an indoor space spray and outdoor ULV. The aggregate MOEs for *d*-phenothrin range from 7628 (chronic exposure) to 478,764 (subchronic exposure). If one applies the same assumptions to cyfluthrin and alpha-cypermethrin, which can be used as surface-residual sprays and impregnate bed nets, all MOEs would also be greater than LOCs, ranging from 132 (acute aggregate exposure to cyfluthrin) to 75,089 (chronic aggregate exposure to alpha-cypermethrin).

Currently, methodologies have not been developed to conduct cumulative risk assessments considering concomitant exposure to different pyrethroids (U.S. EPA, 2002). This is because of the uncertainty regarding common toxicological mechanisms of action of the active ingredients. However, unless there are highly synergistic adverse effects between the pyrethroid active ingredients evaluated in this study, our conservatively estimated exposures indicate that cumulative exposures would still be less than toxicological effect levels.

Uncertainties

Although it is possible the risk assessments presented here were sufficiently conservative and likely overestimated risk, as in any risk assessment, a number of uncertainties were revealed. Some uncertainties were discussed with the assumptions for the scenarios. Exposures to all active ingredients analyzed in the truck-mounted ULV scenario were below U.S. EPA LOCs. It is possible our tier-1 risk assessment of the adulticides applied through truck-mounted ULV spraying was sufficiently conservative and most likely overestimated risk, but there have been few studies addressing actual aerial concentrations or surface deposition of chemicals applied through ULV spraying (Knepper et al., 1996; Moore et al., 1993; Tietze et al., 1994, 1996). ULV insecticides are usually thought to

have low deposition rates because of the nature of their application and concentrations of the chemicals in the air and deposition values are likely much lower than those predicted by AERMOD and ISCST3 tier-1 models. For example, Knepper et al. (1996) found that ULV-applied permethrin and malathion did not persist for more than 24 h on grass surfaces at 91.4 m from the application source. Higher-tiered risk assessments using more realistic exposures would most likely result in higher MOEs, and therefore less risk than presented in our tier-1 assessment.

Piperonyl butoxide, present in many formulations of pyrethroids, increases the mosquito toxicity of the pyrethroids approximately 10-fold, but mammalian toxicity is not likely to be proportionally increased (Knowles, 1991). Human exposures to solvents and other inert ingredients are likely to be very low, resulting in low risks (NYCDOH, 2001).

Our risk assessments did not consider other effects such as skin and nasal irritation associated with the use of pyrethroid-impregnated bed nets (Barlow et al., 2001). Moreover, to our knowledge there are no studies that tested the air concentrations of many of the pyrethroids under the bed nets. A study was conducted for cyfluthrin (Bomann, 1995), and those results were extrapolated to the other pyrethroids based on their target rate and vapor pressure.

Another uncertainty is the mechanism of action of pyrethroids. It is known that pyrethroids act on the nerve membrane sodium channels, altering nerve function by modifying its normal biochemistry and physiology. But there are multiple types of sodium channels and it is currently not known whether all pyrethroids have the same effects on all channels or whether there could be additive, subtractive, or synergistic effects due to modifications of different types of sodium channels (U.S. EPA, 2005c).

It is possible our risk assessments were sufficiently conservative and indicate that health risks to military personnel from exposures to vector-control insecticides and personal protective measures may be low. Our results most likely do not warrant significant refinements for regulatory decision making, but data on actual use patterns, timing, and areas treated, and data on actual air concentrations and deposition rates would better characterize risks. Also, as further additional toxicological data become available, and new areas of concern emerge, these risk assessments need to be revised.

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