A Probabilistic Risk Assessment for Deployed Military Personnel After the Implementation of the "Leishmaniasis Control Program" at Tallil Air Base, Iraq

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ABSTRACT Leishmaniasis has been of concern to the U.S. military and has re-emerged in importance because of recent deployments to the Middle East. We conducted a retrospective probabilistic risk assessment for military personnel potentially exposed to insecticides during the "Leishmaniasis Control Plan" (LCP) undertaken in 2003 at Tallil Air Base, Iraq. We estimated acute and subchronic risks from resmethrin, malathion, piperonyl butoxide (PBO), and pyrethrins applied using a truck-mounted ultra-low-volume (ULV) sprayer and lambda-cyhalothrin, cyfluthrin, bifenthrin, chlorpyrifos, and cypermethrin used for residual sprays. We used the risk quotient (RQ) method for our risk assessment (estimated environmental exposure/toxic endpoint) and set the RQ level of concern (LOC) at 1.0. Acute RQs for truck-mounted ULV and residual sprays ranged from 0.00007 to 33.3 at the 95th percentile. Acute exposure to lambda-cyhalothrin, bifenthrin, and chlorpyrifos exceeded the RQ LOC. Subchronic RQs for truck-mounted ULV and residual sprays ranged from 0.00008 to 32.8 at the 95th percentile. Subchronic exposures to lambda-cyhalothrin and chlorpyrifos exceeded the LOC. However, estimated exposures to lambda-cyhalothrin, bifenthrin, and chlorpyrifos did not exceed their respective no observed adverse effect levels.

KEY WORDS organophosphate, pyrethroid, sand fly, *Phlebotomus*, *Leishmania*

Leishmaniasis has been of concern to U.S. military personnel in the 20th century and has re-emerged in importance because of recent deployments to the Middle East (Magill et al. 1993, AFPMB 1999, Weina et al. 2004). Although leishmaniasis is not considered a disease of strategic military significance, it may pose a significant threat to mission objectives (AFPMB 1999). Leishmaniasis is a disease complex caused by 17–20 species of protozoan parasites of the genus *Leishmania,* which are vectored by phlebotomine sand flies (Croft et al. 2006). There are three clinical subtypes of leishmaniasis: cutaneous, mucocutaneous, and visceral. The most common subtype is cutaneous leishmaniasis, with 1.5–2 million cases per year worldwide, and the more serious subtype, visceral leishmaniasis, infects 500,000 people per year worldwide (Herwaldt 1999, Croft et al. 2006, Ameen 2007). Cutaneous leishmaniasis alone normally does not cause death, although secondary infections by bacteria can be fatal (Piscopo and Mallia 2006). Untreated visceral leishmaniasis has a case-mortality rate of 30–60%, depending on the region and the strain (Seaman et al. 1996). Mucosal leishmaniasis is generally a New World disease and is relatively rare (Kenner et al. 1999). In 1990 and 1991, there were 20 cases of cutaneous leishmaniasis and 12 cases of visceral leishmaniasis in soldiers deployed to the Arabian Peninsula during Operations Desert Shield and Storm (AFPMB 1999). The majority of cases in Iraq since the beginning of Operation Iraqi Freedom in 2003 are associated with increased exposure to infected sand flies (Coleman et al. 2006). The increased exposure is caused by increased numbers of breeding sites because of the destruction of water and sanitation systems, shortage of insecticides, equipment, accumulation of garbage, and the increase in the numbers of dogs in the streets (Jassim et al. 2006).

In 2003 and 2004, the annual incidence rates of leishmaniasis in the U.S. military were 40.9 and 24.4 per 100,000 person-years (Lay 2004), respectively, although the rate could be as high as 10% of soldiers stationed in the Persian Gulf (Pehoushek et al. 2004). From January 2003 to November 2004, there were 1,178 cases of leishmaniasis in service members of the U.S. military, with a rate of 51.4 cases per month. Most of the affected soldiers served in Iraq and/or Kuwait (Lay 2004). In 2003, the estimated case rate for soldiers stationed near the Iraq–Iran boarder was ≈200 per 1,000 deployed persons (Aronson 2007a). From

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2001 to 2006, the incidence rate in Iraq and Afghanistan was 2.31 cases per 1,000 person-years of service, with the largest numbers of leishmaniasis cases occurring in late summer and fall of 2003 (Aronson 2007b).

There has been a sharp reduction in leishmaniasis cases in Iraq/Afghanistan, most likely because of improvements in tents and buildings, as well as emphasis on personal protective measures (PPMs) (Aronson 2007b). Of the 1,287 cases of leishmaniasis diagnosed from 2001 to 2006, only 4 have been visceral (Aronson 2007b). During Operations Desert Shield and Storm, the estimated cost of leishmaniasis to the U.S. military was approximately $18,000 and 92 lost duty days per patient (Grogl et al. 1993, Gambel and Aronson 1997, Martin et al. 1998, AFPMB 1999). Assuming the 2003 and 2004 incidence rates of leishmaniasis, the estimated overall cost of treatment and lost duty days would be $867,000 to $918,000 per month.

To prevent sand fly bites, the U.S. military provides PPMs to military personnel, including insect repellents (DEET), insecticide treated bednets, and permethrin-impregnated battle dress uniforms (BDUs) (Martin et al. 1998, AFPMB 1999, Coleman et al. 2006). However, when PPMs were available to U.S. military personnel at Tallil Air Base, Iraq, only 31% of men and 12% of women used these measures. Use rates were low because of the intense heat, blowing sand, and a lack of knowledge about how to use them (Coleman et al. 2006).

At Tallil Air Base in 2003, the U.S. military adopted the "Leishmaniasis Control Plan" (LCP) to reduce sand fly populations. During the LCP, the military used truck-mounted ultra-low-volume (ULV) insecticides and residual sprays in and around tents, as well rodent and canine control (Coleman et al. 2006). The U.S. Armed Forces Pest Management Board (AFPMB) recommends each of the control measures undertaken at Tallil Air Base as well as the use of PPMs for the control and prevention of sand fly bites (AFPMB 1999, 2008). However, little or no impact on sand fly populations was seen after the extensive control activities at Tallil Air Base (Coleman et al. 2006).

Macedo et al. (2007) performed a reasonable worst-case, deterministic human-health risk assessment of acute, subchronic, and chronic risks after truck-mounted ULV, indoor space sprays, surface-residual sprays, insecticide-impregnated BDUs, and insecticide-impregnated bednets, used for the management of mosquitoes. They showed that the risks to military personnel exposed to PPMs and mosquito management tactics are most likely negligible. The vector control measures evaluated by Macedo et al. (2007) are similar to those used at Tallil Air Base for the control of sand flies. However, the mosquito management tactics differ from the tactics used at Tallil Air Base for the control of sand flies in number of applications, environment, and target vector. Therefore, we performed a retrospective probabilistic risk assessment on the management tactics (truck-mounted ULV and indoor residual sprays) used for sand flies at Tallil Air Base during the LCP.

Materials and Methods

Problem Formulation. We performed a reasonable worst-case probabilistic risk assessment of acute and subchronic human exposures after the LCP was adopted during Operation Iraqi Freedom to protect all coalition forces in the vicinity of Tallil Air Base. Risk assessment is the formalized basis for the objective evaluation of risk in which all assumptions and uncertainties are clearly considered and presented (NRC 1983). Reasonable worst-case risk assessments err on the side of safety through deliberate overestimation of the risks to humans and the environment. Probabilistic analysis incorporates sampling from the statistical distribution of each input variable and propagates each variable into output of estimated exposures. Acute exposures were defined in this study as single-day exposures after a single insecticide application. Subchronic exposures to insecticides were defined as the exposure to insecticides per day over 165 d that the LCP was instituted, during and after truck-mounted ULV and residual spray events (Coleman et al. 2006). Exposures to two population groups, adult men and adult women (18–65 yr of age), were estimated for each scenario, chemical, route, and pathway.

Hazard Identification. We assessed the three active ingredients resmethrin, malathion, and pyrethrins and the synergist piperonyl butoxide (PBO) used for the truck-mounted ULV applications. We also assessed the five active ingredients lambda-cyhalothrin, cyfluthrin, bifenthrin, chlorpyrifos, and cypermethrin used for residual applications.

Toxicity and Dose–Response Relationships. Dose–response information for each compound was reviewed, and endpoints were chosen based on acute and subchronic exposures. The toxicity thresholds used in this assessment were ingestion reference doses (RfDs), which are established by the U.S. Environmental Protection Agency (U.S. EPA). Ingestion RfDs were based on the no observed adverse effect level (NOAEL) with a 100-fold safety factor for intra- and interspecies extrapolation uncertainties. The acute oral RfDs for resmethrin, malathion, PBO, pyrethrins, lambda-cyhalothrin, cyfluthrin, bifenthrin, chlorpyrifos, and cypermethrin are 0.1, 0.14, 6.3, 0.07, 0.0025, 0.02, 0.01, 0.005, and 0.1 mg/kg body weight (BW)/d, respectively (U.S. EPA 1998a, 2000b, 2002, 2004a, 2005a, 2006a, b, c, 2008). The subchronic oral RfDs for resmethrin, malathion, PBO, pyrethrins, lambda-cyhalothrin, cyfluthrin, bifenthrin, chlorpyrifos, and cypermethrin are 0.1, 0.07, 0.16, 0.044, 0.001, 0.024, 0.015, 0.0003, and 0.06 mg/kg BW/d, respectively (U.S. EPA 1998a, 2000b, 2002, 2004a, 2005a, 2006a, b, c, 2008).

Estimation of Environmental Concentrations. We used AERMOD tier-1 air dispersion model (U.S. EPA 1999) in conjunction with BEEST software (Version 9.65; Oris Solutions, Austin, TX) to predict the air concentrations and surface deposition for the three

Table 1. Input distributions for spray deposition and aerial concentrations for each chemical used for truck-mounted ultra-low-volume applications

Input	Distribution type	Parameter	Resmethrin	Malathion	PBO	Pyrethrins	Units
Aerial concentrations	Gamma (truncated)	Location	1.31	10.45	2.24	1.47	$\mu g/m^3$
		Scale	1.76	14.02	0.22	1.98	
		Shape	1.81	1.81	2	1.81	
Spray deposition	Weibull (truncated)	Location	0.0003	0.002	2.24	0.0003	g/m^2
		Scale	0.001	0.008	0.22	0.001	
		Shape	0.91	0.91	2	0.91	

PBO, piperonyl butoxide.

active ingredients and PBO within 6 h after truck-mounted ULV application. In BEEST, we created a camp layout with 19 tents set back-to-back in six rows to simulate the tent setup at Tallil Air Base. The assumptions included: (1) each chemical had a 24-h half-life in the air; (2) the insecticides were applied at the maximum application rate as stated on each label; (3) all of the insecticides were susceptible to the same weather conditions using standardized weather data from Albuquerque, NM, from July 1993 to June 1994; (4) all spray events occurred at 2100 hours; (5) each spray release was at 1.5 m; and (6) receptors were positioned radially from the center of the camp, to ≈230 m in all directions and placed at ≈14-m intervals throughout the camp both along the truck route and in between tents. We chose weather data from Albuquerque because the area is a desert environment that has standardized weather data for use with the AERMOD downloader. The maximum application rates for truck-mounted ULV resmethrin, malathion, PBO, and pyrethrins are 7.85, 71.62, 43.94, and 10.09 g (AI)/ha, respectively (Table 1).

Acute Exposure

Truck-Mounted ULV Applications. We assumed that multiroute exposures immediately after a single-spray event were limited to 24 h. Routes of insecticide exposure to each group were inhalation and dermal. Assumptions of body weight, respiration rate, and percent area of two hands are presented in Table 2. We assumed that each group would be outside when the spray truck passed, and the duration of the exposure was 6 h. The exposure modeling assumptions followed Schleier et al. (2008) and Peterson et al. (2006), which are briefly reviewed here.

Acute inhalation exposure was estimated by

$$PE_{inhalation} = (EEC \times RR \times D)/BW, \quad [1]$$

where $PE_{inhalation}$ is potential exposure from inhalation (mg/kg BW), EEC is the estimated environmental air concentrations as estimated by AERMOD ($\mu g/m^3$; Table 1), RR is respiratory rate for each group that is indicative of light activity dominated by moderate movement or periods of rest (m^3/h; Table 2), D is duration of exposure (h), and BW is body weights for each group representing the general U.S. population (kg; Table 2).

Acute dermal exposure from spray deposition onto the group was estimated by

$$PE_{dermal} = (ADE \times CF \times AR \times AB)/BW, \quad [2]$$

where PE_{dermal} is potential exposure from dermal contact (mg/kg BW), ADE is adjusted dermal exposure (mg/lb [AI]), and CF is the dermal conversion factor that is the increase in exposure from the flagger scenario. There is limited publicly available information on dermal deposition immediately after truck-mounted ULV sprays, so we used the U.S. EPA Pesticide Handler Exposure Database (PHED) as a conservative surrogate (U.S. EPA 1998b). The PHED contains pesticide-handler scenarios derived from field studies and exposure estimates based on physical factors such as application rate, hectares treated per day, type of clothing worn, methods of application, and formulation type. We used the PHED scenario in

Table 2. Assumptions for body weight, respiration rate, and percent surface area of two hands for adult males and females

Input variables	Group	Parameter	Values	Units	Distribution	Source
Body weight	Adult males	Mean	78.65	kg	Log-normal (truncated)	Portier et al. (2007)
		SD	13.23			
	Adult females	Mean	65.47	kg		
		SD	13.77			
Respiration rate	Adult males	Mean	15.14	liters/min	Log-normal (truncated)	Allan et al. (2008)
		SD	5.3			
	Adult females	Mean	13.26	liters/min		
		SD	4.64			
Percent surface area of two hands	Adult males	Mean	5.2	%	Normal (truncated)	U.S. EPA (1997)
		SD	0.5			
	Adult females	Mean	5.1	%		
		SD	0.3			

which a flagger (person marking the location for pesticide application while the application is occurring) was exposed to a liquid application. We used a uniform distribution and assumed a person would be exposed 10–100 times more than in the flagger scenario (Schleier et al. 2008). AR is application rate (kg [AI] /ha), AB is dermal absorption rate for each chemical, D is duration of exposure (h), and BW is body weight (kg; Table 2). Surface area for all groups was estimated using

$$SA = (4 \times BW + 7)/(BW + 90), \quad [3]$$

where SA is surface area and BW is body weight (kg; Table 2) of the group being assessed (U.S. EPA 1997). To adjust the flagger exposure for adult women, we used

$$ADE = FE \times (SA_{female}/SA_{male}), \quad [4]$$

where ADE is the adjusted dermal exposure (mg/lb [AI]), FE is the flagger exposure, SA_{female} is the surface area of an adult woman as estimated by equation 3, and SA_{male} is the surface area of an adult man as estimated by equation 3. We assumed a triangular distribution, with the maximum exposure being a flagger with no clothing (0.053 mg/lb [AI]), a minimum exposure being a single layer of clothing with no gloves (0.011 mg/lb [AI]), and the most likely exposure being a person with his or her face, arms, legs, hands, and feet exposed (0.0327 mg/lb [AI]) (U.S. EPA 1997, 1998b). The dermal absorption rates for resmethrin, malathion, PBO, and pyrethrins are 2, 10, 2, and 0.22%, respectively (U.S. EPA 2000a, 2005b, c, 2006d).

Acute dermal hand contact with sprayed surfaces was estimated by

$$PE_{hand\ contact} = (SA \times PSA \times EEC \times AB \times TC \times HC)/BW, \quad [5]$$

where $PE_{hand\ contact}$ is potential exposure from hand contact with sprayed surfaces (mg/kg BW), SA is surface area of the group (m^2), PSA is the percent surface area of the hands (Table 2), EEC is the estimated environmental concentration for spray deposition as estimated by AERMOD (mg/m^2; Table 1), AB is dermal absorption rate for each chemical, TC is the transferable surface residue of insecticides, which we assumed to be 20% (Williams et al. 2003), HC is the number of times one half of one hand contacted a surface with insecticide present, which we assumed a uniform distribution of 1–10 times, and BW is body weight (kg; Table 2).

Total acute exposure to active ingredients after truck-mounted ULV applications for each group was estimated by

$$PE_{acute\ ULV} = PE_{inhalation} + PE_{dermal} + PE_{hand\text{-}contact} \quad [6]$$

Surface Residual Spraying. Dermal exposure from contact with surfaces after residual spray events were estimated by

$$PE_{surface\ residual} = (AR \times SA \times DAR \times TC)/BW, \quad [7]$$

where $PE_{surface\ residual}$ is the potential exposure from contact with surface residual sprays (mg/kg BW), AR is the maximum application rate (mg/m^2), SA is the body surface area (equation 3) in contact with the sprayed surface (m^2), where we assumed that 50% of the body would contact the sprayed area, DAR is the dermal absorption rate, TC is the transferable surface residue of insecticides, which we assumed to be 20% (Williams et al. 2003), and BW is body weight (kg). The maximum application rates for lambda-cyhalothrin, cyfluthrin, bifenthrin, chlorpyrifos, and cypermethrin are 120.56, 21.53, 26.12, 112.08, and 125.88 mg/m^2, respectively. The dermal absorption rates for lambda-cyhalothrin, cyfluthrin, bifenthrin, chlorpyrifos, and cypermethrin are 25, 5, 25, 3, and 2.5%, respectively (U.S. EPA 1998a, 2002, 2004a, b, 2005a).

Subchronic Exposure

We assumed multiroute exposures per day after multispray events over the 165 d in which the LCP was implemented. Routes of insecticide exposure were from inhalation and dermal. The same assumptions about body weight, inhalation rate, and surface area were used as stated above for acute exposure.

Subchronic exposures for truck-mounted ULV were estimated by

$$PE_{subchronic\ ULV} = (PE_{acute\ ULV} \times SE)/D, \quad [8]$$

where $PE_{subchronic\ ULV}$ is the potential subchronic exposure from truck-mounted ULV (mg/kg BW/d), $PE_{acute\ ULV}$ is the acute potential exposure for inhalation, dermal, and hand contact with sprayed surfaces as estimated by equation 6 (mg/kg BW/d), SE is the number of spray events, and D is the 165-d duration of the exposure. The number of spray events for resmethrin, malathion, PBO, and pyrethrins are 59, 26, 68, and 9, respectively (Coleman et al. 2006). Because PBO is present in both resmethrin and pyrethrins formulations, we added the number of spray events for both chemicals to obtain the number of spray events for PBO.

Subchronic exposures from surface residual spraying were estimated by

$$PE_{subchronic\ surface\ residual} = (PE_{total\ acute} \times SE)/D, \quad [9]$$

where $PE_{subchronic\ surface\ residual}$ is the potential subchronic exposure from surface residual sprays (mg/kg BW/d), $PE_{surface\ residual}$ is the acute potential exposure from surface residual sprays as estimated by equation 7 (mg/kg BW/d), SE is the number of spray events, and D is the 165-d duration of the exposure. The number of spray events for lambda-cyhalothrin, cyfluthrin, bifenthrin, chlorpyrifos, and cypermethrin are 65, 24, 9, 7, and 3, respectively (Coleman et al. 2006).

Table 3. Adult male acute and subchronic probabilistic total potential exposure (PE_{total})[a] (mg/kg BW/d) and risk quotients (RQs)[b] at the 50th, 90th, and 95th percentiles

	Percentile	Acute exposure			Subchronic exposure		
		50th	90th	95th	50th	90th	95th
Resmethrin	PE_{total}	0.0003	0.0007	0.0009	0.0001	0.0002	0.0003
	RQ	0.003	0.007	0.009	0.001	0.002	0.003
Malathion	PE_{total}	0.003	0.006	0.007	0.0004	0.0008	0.001
	RQ	0.02	0.042	0.051	0.005	0.011	0.014
PBO	PE_{total}	0.0002	0.0004	0.0004	0.00009	0.0001	0.0002
	RQ	0.00004	0.00006	0.00007	0.0006	0.0009	0.001
Pyrethrins	PE_{total}	0.0004	0.0008	0.002	0.00003	0.00006	0.00008
	RQ	0.005	0.011	0.014	0.0006	0.001	0.002
Lambda-cyhalothrin	PE_{total}	0.074	0.081	0.083	0.028	0.032	0.033
	RQ	29.42	32.45	33.32	28.97	31.97	32.83
Cyfluthrin	PE_{total}	0.0026	0.0028	0.003	0.0003	0.0004	0.0004
	RQ	0.13	0.14	0.015	0.016	0.018	0.018
Bifenthrin	PE_{total}	0.016	0.017	0.018	0.0008	0.0009	0.001
	RQ	1.59	1.76	1.81	0.058	0.064	0.066
Chlorpyrifos	PE_{total}	0.008	0.009	0.0092	0.0003	0.0004	0.0004
	RQ	1.64	1.81	1.86	1.16	1.28	1.32
Cypermethrin	PE_{total}	0.0076	0.0085	0.0087	0.0027	0.003	0.0031
	RQ	0.077	0.085	0.1	0.0001	0.0002	0.0002

[a] PE_{total} is estimated by equations 6–9.
[b] RQ = PE_{total}/reference dose.
BW, body weight; PBO, piperonyl butoxide.

Risk Characterization. We used the risk quotient (RQ) method for our risk assessment, which is calculated by dividing the total potential exposure as estimated by equations 6–9 for each group, chemical, and duration of exposure by its respective ingestion toxic endpoint value (RfD). The multiroute exposure in our assessment was compared with the ingestion RfD because it provided a conservative endpoint, which is based on the most sensitive NOAEL. Estimated RQs are compared with a RQ level of concern (LOC), which is set by the U.S. EPA or another regulatory agency to determine whether regulatory action is needed. The RQ LOC used in our assessment was 1.0. An RQ >1.0 means the estimated exposure is greater than the relevant RfD.

Probabilistic Analysis. Probabilistic risk assessments differ from deterministic risk assessments by sampling values from the distributions of exposures and biological parameters. To perform the probabilistic risk assessment, we used Monte Carlo simulation (Crystal Ball 7.3; Decisioneering, Denver, CO) to generate the exposures and RQs. Probabilities of occurrence of RQ values were determined by incorporating sampling from the statistical distribution of each input variable used to calculate the RQs. Each of the input variables was sampled so that its distribution shape was reproduced. The variability for each input was propagated into the output of the model so that the model output reflected the probability of values that could occur. We performed this by using 20,000 iterations with the assumptions outlined in Tables 1 and 2. We truncated respiratory rate, body weight, percent surface area of two hands, air concentrations, and spray deposition at zero because it is not possible for these quantities to have negative values.

Sensitivity analysis was performed using 20,000 iterations on uncertain parameters (air concentrations, spray deposition, dermal conversion factor, and dermal exposure) to determine percent contribution of the input variable to the output variance of the model for each group and chemical for the truck-mounted ULV. Sensitivity analysis is designed to identify inputs that are having a significant impact on the variance of the model output (Cullen and Frey 1999). We chose only uncertain and not variable parameters to help direct future research examining the fate of the insecticides in desert environments. Sensitivity analysis was not performed on surface residual sprays because of the lack of uncertain parameters.

Results

Acute Risk

Truck-Mounted ULV. Risk quotients did not exceed the RQ LOC at the 50th, 90th, and 95th percentiles of exposure for any group and chemical (Tables 3 and 4). Adult male and female exposures at the 95th percentile ranged from 0.0004 to 0.007 mg/kg BW/d (Tables 3 and 4). Malathion had the highest and PBO had the lowest RQs of the chemicals assessed (Tables 3 and 4).

Surface Residual Spray. Adult male and female exposure to lambda-cyhalothrin, bifenthrin, and chlorpyrifos exceeded the RQ LOC at the 50th, 90th, and 95th percentiles (Tables 3 and 4). Cyfluthrin and cypermethrin were below the RQ LOC for both groups (Tables 3 and 4). Adult male exposure at the 95th percentile ranged from 0.003 to 0.083 mg/kg BW/d (Table 3). Adult female exposure at the 95th percentile ranged from 0.003 to 0.09 mg/kg BW/d (Table 4). Lambda-cyhalothrin had the highest and cypermethrin had the lowest RQs of the chemicals assessed (Tables 3 and 4).

Table 4. Adult female acute and subchronic probabilistic total potential exposure (PE_{total})[a] (mg/kg BW/d) and risk quotients (RQ)[b] at the 50th, 90th, and 95th percentiles

	Percentile	Acute exposure			Subchronic exposure		
		50th	90th	95th	50th	90th	95th
Resmethrin	PE_{total}	0.0003	0.0006	0.0008	0.0001	0.0002	0.0003
	RQ	0.003	0.006	0.008	0.001	0.002	0.003
Malathion	PE_{total}	0.002	0.005	0.007	0.0004	0.0008	0.001
	RQ	0.017	0.038	0.048	0.005	0.012	0.015
PBO	PE_{total}	0.0002	0.0004	0.0004	0.00009	0.0001	0.0002
	RQ	0.00004	0.00006	0.00007	0.0006	0.001	0.0011
Pyrethrins	PE_{total}	0.0003	0.0007	0.0009	0.00002	0.00004	0.00005
	RQ	0.0045	0.01	0.013	0.0004	0.0009	0.0011
Lambda-cyhalothrin	PE_{total}	0.08	0.009	0.09	0.031	0.035	0.036
	RQ	32.17	35.91	36.93	31.62	35.36	36.39
Cyfluthrin	PE_{total}	0.0029	0.0032	0.0033	0.00042	0.00047	0.00048
	RQ	0.14	0.16	0.017	0.017	0.019	0.02
Bifenthrin	PE_{total}	0.017	0.019	0.02	0.0009	0.001	0.0011
	RQ	1.74	1.94	1.99	0.063	0.071	0.073
Chlorpyrifos	PE_{total}	0.009	0.01	0.011	0.0003	0.00041	0.00043
	RQ	1.79	2	2.06	1.27	1.42	1.46
Cypermethrin	PE_{total}	0.008	0.009	0.01	0.0001	0.00017	0.00018
	RQ	0.084	0.094	0.1	0.003	0.0034	0.0035

[a] PE_{total} is estimated by equations 6–9.
[b] RQ = PE_{total}/reference dose.
BW, body weight; PBO, piperonyl butoxide.

Subchronic Risk

Truck-Mounted ULV. Risk quotients did not exceed the RQ LOC at the 50th, 90th, and 95th percentiles for any group and chemical (Tables 3 and 4). Total adult male exposure at the 95th percentile ranged from 0.00008 to 0.001 mg/kg BW/d (Table 3). Total adult female exposure at the 95th percentile ranged from 0.00005 to 0.001 mg/kg BW/d (Table 4). Malathion had the highest, whereas pyrethrins had the lowest, RQs of the chemicals assessed (Tables 3 and 4).

Surface Residual Sprays. Adult male and female exposure to lambda-cyhalothrin and chlorpyrifos exceeded the RQ LOC at the 50th, 90th, and 95th percentiles (Tables 3 and 4). Cyfluthrin, bifenthrin, and cypermethrin were below the RQ LOC for both groups (Tables 3 and 4). Adult male exposure at the 95th percentile ranged from 0.0004 to 0.03 mg/kg BW/d (Tables 3 and 4). Adult female exposure at the 95th percentile ranged from 0.0001 to 0.036 mg/kg BW/d (Tables 3 and 4). Lambda-cyhalothrin had the highest and cypermethrin had the lowest RQs of any chemical assessed (Tables 3 and 4).

Sensitivity Analysis

Sensitivity analysis of acute and subchronic exposures from truck-mounted ULV chemicals showed that air concentrations contributed the largest amount of variance to the output, followed by spray deposition, dermal conversion factor, and dermal exposure for adult men and women (Table 5).

Discussion

Although the LCP's use of residual sprays resulted in exposures to lambda-cyhalothrin, bifenthrin, and chlorpyrifos that may have exceeded the RQ LOC, they did not exceed the NOAELs. For example, acute adult female exposure at the 95th percentile for lambda-cyhalothrin, bifenthrin, and chlorpyrifos was 37, 2, and 2% of the NOAEL, respectively. Subchronic adult female exposure at the 95th percentile for lambda-cyhalothrin, bifenthrin, and chlorpyrifos was 36, 1.9, and 1.5% of the NOAEL. With our conservative

Table 5. Sensitivity analysis (percent contribution of the input variable to the output variance) of uncertain factors (air concentrations, spray deposition, dermal conversion factor, and dermal exposure) used in the truck-mounted ultra-low-volume acute and subchronic exposures for resmethrin, malathion, PBO, and pyrethrins

	Acute exposure		Subchronic exposure	
	Adult males	Adult females	Adult males	Adult females
Resmethrin				
Air concentrations	90.7[a]	99.9	96.8	100.0
Spray deposition	9.2	0.1	3.2	0
Dermal conversion factor	0	0	0	0
Dermal exposure	0	0	0	0
Malathion				
Air concentrations	88.6	98.9	99.3	99.2
Spray deposition	10.9	0.8	0.5	0.6
Dermal conversion factor	0.4	0.2	0.2	0.2
Dermal exposure	0.1	0	0	0
PBO				
Air concentrations	56.8	49.8	47.6	47.7
Spray deposition	33.0	36.2	43.2	35.5
Dermal conversion factor	7.8	11.1	6.5	12.6
Dermal exposure	2.4	2.9	2.7	4.2
Pyrethrins				
Air concentrations	89.8	100.0	71.3	99.7
Spray deposition	10.2	0	28.6	0.3
Dermal conversion factor	0	0	0	0
Dermal exposure	0	0	0	0

[a] Percent contribution of the input variable to the output variance.
PBO, piperonyl butoxide.

assumptions, exposures at the 95th percentile most likely would not result in adverse effects to adult men and women. Despite the frequent applications in the LCP, our results support previous risk assessment results that exposure to truck-mounted ULV insecticides are most likely negligible (Peterson et al. 2006, Macedo et al. 2007, Schleier et al. 2008).

To predict deposition and air concentrations, we used AERMOD, which is an industrial plume model that is not designed for ULV applications. However, AERMOD was the most appropriate model for air concentrations and deposition onto surfaces because there is a substantial data gap in air concentrations and fate of insecticides in desert environments. Previous studies of truck-mounted ULV applications in temperate and subtropical climates have observed 1–22.3% of the insecticide sprayed during application settled onto the ground, with concentrations decreasing substantially over 36 h (Tucker et al. 1987, Moore et al. 1993, Tietze et al. 1994, Knepper et al. 1996). Concentrations found in previous field studies are ≈0.6–12.5% of what was modeled using AERMOD.

In addition to deposition onto surfaces, we used a flagger exposure scenario to model deposition onto skin, which was designed for agricultural applications. The default flagger scenario in the U.S. EPA PHED overestimates exposure by ≈40%, supporting the conservatism of the model (Driver et al. 2007).

For the residual sprays, we assumed that there was no degradation during the 165-d period. Previous studies examining d-phenothrin, d-tetramethrin, and resmethrin showed that the half-life of the insecticides was ≈31–75 d on floors and walls (Matoba et al. 1998a, b). However, these studies were carried out in houses and not tents; therefore, more data are needed on the persistence of residual sprays on tent surfaces.

In addition to uncertainties in deposition, air concentrations, and breakdown of insecticides, there are also toxicological uncertainties with respect to PBO. PBO has been shown to increase the toxicity of pyrethroids and pyrethrins to aquatic organisms, but there is no indication that PBO acts as a synergist in mammals (Knowles 1991, Paul et al. 2005, Amweg et al. 2006, U.S. EPA 2006a). If a 10-fold uncertainty factor was applied to the RfDs based on the toxicological uncertainties of PBO synergizing with resmethrin or pyrethrins, neither would exceed the RQ LOC, which is comparable to past risk assessments (Peterson et al. 2006, Macedo et al. 2007, Schleier et al. 2008).

Our truck-mounted ULV sensitivity analysis is similar to the study performed by Schleier et al. (2008), showing that air concentrations and deposition of insecticides onto surfaces contributed the largest amount of variance to the model output. Acute and subchronic inhalation exposure, hand contact with sprayed surfaces, and dermal exposure contributed 95, 4, and 1.5% on average to the overall exposure, respectively, which is comparable to past risk assessments (Peterson et al. 2006, Macedo et al. 2007, Schleier et al. 2008).

In this analysis of risks, we did not probabilistically assess PPMs such as permethrin-impregnated BDUs, bednets, and repellents because of the lack of documented variability data for these exposure scenarios. Macedo et al. (2007) showed that the use of permethrin-impregnated BDUs and bednets presented negligible risk to military personnel for acute, subchronic (<180 d), and chronic exposures (>180 d). An exposure assessment of permethrin-impregnated BDUs in the German military showed that the conservative risk estimates of Macedo et al. (2007) sufficiently protected human health (i.e., they overestimated exposures by ≈16-fold) (Appel et al. 2008). Antwi et al. (2008) showed that adult men and women exposed to DEET concentrations ≥40% exceed the LOC for subchronic (<180 d) exposures, but exposures did not exceed the LOC for the acute and chronic (>180 d) scenarios.

In addition to risk from the insecticides, there are also risks of contracting leishmaniasis. The minimum field infection rate of female sand flies was 1.5% in 2003 and 2% in 2004, with ≈15% of those female sand fly pools (≈12 sand flies per pool) testing positive for leishmaniasis parasites that cause human disease (Coleman et al. 2006). This indicates the probability that a bite could result in leishmaniasis infection was ≈0.3%. With each additional bite, their risk increased, and some soldiers at the base received >1,000 bites per night (Coleman et al. 2006).

The risks are not limited to the insecticides and infection by leishmaniasis; there are also risks from the curative medical treatments. Currently there are three approved medications that have shown effectiveness in treating leishmaniasis: antimonials, miltefosine, and amphotericin B deoxycholate. Antimonials are used as the first line of treatment in leishmaniasis, whereas miltefosine is used when patients do not respond to antimonials or relapse (Aronson et al. 1998). The cost effectiveness (U.S. $/death averted) of treatment is highest for miltefosine and antimonials because of the relatively low cost; however, the most effective treatment for leishmaniasis has been shown to be amphotericin B deoxycholate, which costs $30 to $40 more per patient than antimonials (Vanlerberghe et al. 2007).

Antimonials must be administered by the U.S. military under an experimental protocol at approved medical treatment facilities because they are not registered for use in the U.S. (AFPMB 1999, Weina et al. 2004). During treatment, 3.2–60% of patients experienced arthralgias, myalgias, anorexia, herpes zoster, nausea, vomiting, diarrhea, abdominal pain, chest pain, local pain, headache, rash, itching, and fever (Aronson et al. 1998, Mohebali et al. 2007). Sodium stibogluconate and meglumine antimoniate have shown cure rates of 88.3–97% (Aronson et al. 1998, Mohebali et al. 2007). The side effects of miltefosine are nausea, vomiting, diarrhea, motion sickness, abdominal pain, coughing, headache, itching, and fever and have been observed in 1–41.4% of patients during treatment (Soto et al. 2004a, Mohebali et al. 2007). The cure rate for miltefosine was ≈50% (Soto et al. 2001,

2004a, b; Mohebali et al. 2007). Amphotericin B deoxycholate has been approved by the U.S. Food and Drug Adminstration for the treatment of leishmaniasis (Herwaldt 1999). The side effects of amphotericin B deoxycholate are back pain, sweating, headache, diarrhea, itching, shivering, respiratory distress, and/or cardiac arrhythmia, which have been observed in <40% of patients (Berman et al. 1998, Mueller et al. 2008). Treatment with amphotericin B deoxycholate has a cure rate of ≈92% after 6 mo (Sundar et al. 1997, Mueller et al. 2008).

Despite frequent applications and multipathway exposures, our probabilistic estimates of exposure to lambda-cyhalothrin, bifenthrin, and chlorpyrifos exceeded the RQ LOC but did not exceed their respective NOAELs. Because the residual spray applications did not seem to affect sand fly populations or protect soldiers, future uses could be discontinued to lower the risks from insecticides. Furthermore, the health risks from contracting leishmaniasis and adverse reactions during treatment for the disease are most likely greater than the risks from exposure to the insecticides used.

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