Environmental Toxicology and Chemistry, Vol. 24, No. 5, pp. 1029–1034, 2005
© 2005 SETAC
Printed in the USA
0730-7268/05 $12.00 + .00

WIDESPREAD DETECTION OF *N*,*N*-DIETHYL-*m*-TOLUAMIDE IN U.S. STREAMS: COMPARISON WITH CONCENTRATIONS OF PESTICIDES, PERSONAL CARE PRODUCTS, AND OTHER ORGANIC WASTEWATER COMPOUNDS

MARK W. SANDSTROM,*† DANA W. KOLPIN,‡ E. MICHAEL THURMAN,§ and STEVEN D. ZAUGG†
†U.S. Geological Survey, P.O. Box 25046, MS 407, Denver, Colorado 80225
‡U.S. Geological Survey, 400 S. Clinton St., Box 1230, Iowa City, Iowa 52244
§Department of Analytical Chemistry, University of Almeria, Carreterra Sacramento, LaCañada de San Urbano, 04120 Almeria, Spain

(*Received* 16 *June* 2004; *Accepted* 4 *October* 2004)

Abstract—One of the most frequently detected organic chemicals in a nationwide study concerning the effects of wastewater on stream water quality conducted in the year 2000 was the widely used insect repellant *N*,*N*-diethyl-*m*-toluamide (DEET). It was detected at levels of 0.02 μg/L or greater in 73% of the stream sites sampled, with the selection of sampling sites being biased toward streams thought to be subject to wastewater contamination (i.e., downstream from intense urbanization and livestock production). Although DEET frequently was detected at all sites, the median concentration was low (0.05 μg/L). The highest concentrations of DEET were found in streams from the urban areas (maximum concentration, 1.1 μg/L). The results of the present study suggest that the movement of DEET to streams through wastewater-treatment systems is an important mechanism that might lead to the exposure of aquatic organisms to this chemical.

Keywords—Insect repellant Personal care products Surface water

INTRODUCTION

Concern for potential adverse human and ecological health effects resulting from the production, use, and disposal of numerous chemicals used in industry, agriculture, medical treatment, and personal care products has led to an awareness of the need for monitoring and regulation of these chemicals in water resources. However, household chemicals, pharmaceuticals, and other consumer products are groups of chemicals that until recently had not generally been monitored in natural-water systems. A major pathway for the movement of these chemicals into the environment is their direct release after passing through wastewater-treatment plants or domestic septic systems [1]. These systems often are not designed to remove these types of chemicals from the effluent [1,2].

A nationwide study was conducted by the U.S. Geological Survey in 1999 and 2000 to determine if organic wastewater compounds (OWCs) were present in 139 U.S. streams considered to be subject to sources of wastewater (i.e., downstream from intense urbanization or livestock production) [3]. The insect repellent *N*,*N*-diethyl-*m*-toluamide (DEET) was one of the most frequently detected compounds, being found in 73.2% of the 56 streams sampled in the year 2000. Other studies also have found DEET in rivers [4], groundwater [5], and seawater [6]. Surprisingly, little is known about the environmental fate and effects of DEET, because as a residential-use pesticide [7], it traditionally has been considered to have little potential for environmental effects. Previous research, however, has shown that DEET enhances the activity of cholinesterase inhibitors [8,9].

Repellants containing DEET are used to provide protection from biting flies, mosquitoes, and a variety of small flying insects. The chemical was first registered for use in the United States in 1957 after being developed by the U.S. Army in 1946 for use by military personnel in insect-infested areas. It has been marketed commercially as a personal insect repellent since 1965 [7]. It repels insects by masking the sensory perception of lactic acid on the skin, which is one of the main stimuli involved in mosquito attraction to, and landing on, a host [10,11].

More than 225 DEET products are registered in the United States, with the majority being formulated for direct application to the skin or clothing [7]. Product concentrations range from approximately 4 to 100% active ingredient. Most DEET use is for humans, with a lesser amount being used for veterinary purposes. Approximately 30% of the U.S. population uses DEET annually as an insect repellent [7]. During 2002, the rapid spread of West Nile virus in the United States elicited frequent official recommendations that residents in affected areas use insect repellents containing DEET, which likely increased the use of products containing this compound in the United States.

The average annual domestic use of DEET is estimated to be 1.8 million kg of the active ingredient, based on pesticide-use information, mainly for 1990 [7]. This amount is comparable to the mass of some insecticides used annually for agricultural applications in the United States, such as aldicarb, carbaryl, methyl parathion, and carbofuran, which range from 1.5 to 2.2 million kg of active ingredient per year [12] (http://www.ncfap.org/pubs.htm). The annual use of DEET as an insect repellant also is comparable to the mass of the insecticide diazinon used annually (2.0 million kg) in outdoor urban settings by homeowners, professional lawn-care companies, and pest-control operators [13].

The repellant DEET is classified by the U.S. Environmental

* To whom correspondence may be addressed (sandstro@usgs.gov).

Any use of trade names is for descriptive purposes only and does not imply endorsement by the U.S. government.

Protection Agency (U.S. EPA) as an indoor, residential-use pesticide rather than as an outdoor-use pesticide, because it is applied directly only to the human body/clothing, cats, dogs, pet quarters, and household/domestic dwellings. Despite its use in quantities comparable to agricultural insecticides, a limited set of toxicity data for indoor-use pesticides is required for pesticide registration. For example, precautionary label statements are created, and environmental hazards in case of spills are assessed. However, ecological risk assessments are not conducted for such products [7].

The available toxicity data characterize DEET as being slightly toxic to birds, fish, and aquatic invertebrates and practically nontoxic to mammals [7]. As a result, the registration of DEET for pesticide use concluded that its application to the human body and clothing or to animals, according to label directions, was not likely to affect terrestrial wildlife or aquatic organisms adversely. However, the U.S. EPA required improved label warnings and restrictions for DEET products to be especially protective of children and other individuals who may be more sensitive to chemical substances, because DEET is so widely used among the U.S. population, including children, and is applied directly to the skin. The repellant DEET has been thought to be associated with incidents of seizure, especially when applied to the skin of young children [14].

The purpose of the present study paper is to present an expanded interpretation of the presence of DEET in 56 streams sampled in the year 2000 by the U.S Geological Survey's Toxics Substances Hydrology Program during the 1999 to 2000 reconnaissance study. Concentrations of DEET are compared to those of pesticides, personal care products, and other OWCs. In addition, the likelihood for detection of DEET degradates in the environment is considered.

MATERIALS AND METHODS

Site selection and sampling

The selection of sampling sites for the reconnaissance study focused primarily on areas that were considered likely to be contaminated by human, industrial, or agricultural wastewater [3]. The 56 stream sites sampled for DEET during the year 2000 represent a wide range of geography, hydrogeology, land use, climate, and basin size. Predominant land use for the stream sites where DEET was measured were as follows: agricultural (7 sites), urban (36 sites), mixed urban and agricultural (10 sites), and minimally developed (3 sites). A map with the distribution of sites in the United States is shown in Figure 1. The analytical schedule for samples collected during 1999 did not include DEET.

All samples were collected by U.S. Geological Survey personnel using nationally consistent protocols designed to obtain a water sample representative of the streams by using standard depth- and width-integrating techniques. At each site, a single, composite, unfiltered water sample was collected from four to six vertical profiles and split into appropriate containers for shipment to the laboratory. Water samples were stored in precleaned, amber-glass bottles. Following collection, samples were chilled immediately and sent to the National Water Quality Laboratory in Denver (CO, USA). Sample collection and processing protocols were designed to minimize contamination [15]. For the present study, uses of personal care items (e.g., DEET) were discouraged during sample collection and processing.

Each stream site was sampled once during the year 2000 study for DEET. That sampling was conducted over the course of a year provided an opportunity to observe potential seasonal patterns in DEET concentrations that might have been present if the seasonal signal was significantly more important than site-to-site variations.

Fig. 1. Location of sample collection sites. DEET = *N*,*N*-diethyl-*m*-toluamide.

Analytical methods

One-liter, whole-water samples were extracted with methylene chloride using continuous liquid–liquid extraction for analysis of DEET and 95 selected OWCs, including the pesticide diazinon. Samples were extracted for 3 h at ambient pH and for an additional 3 h at pH 2. The extracts were concentrated by solvent distillation in the extractor and by evaporation using nitrogen to 1 ml and then analyzed by capillary-column gas chromatography/mass spectrometry (GC/MS) operated in selected-ion monitoring mode. With this method, positive identification of DEET and other compounds required elution within the expected retention time and abundance of three characteristic ions in the same ratio as that of a reference standard. After these qualitative criteria were met, the concentration was calculated from a five-point calibration curve using internal-standard quantitation. Reporting levels were estimated by evaluation of instrument response and adjusted based on experience with the compounds in the method and possible interferences. The reporting level is equivalent to the lowest-concentration standard that could be quantitated reliably. The analytical reporting level for DEET initially was set at 0.04 μg/L and then revised to 0.08 μg/L, Estimated concentrations were reported below this level (as low as 0.02 μg/L) if the GC/MS identification criteria (retention time and abundance of three characteristic ions in the same ratio as that of a standard) were met. If qualitative criteria were not met, then the result was reported as less than the reporting level. For statistical analysis, nondetection results were set to zero. Additional method details have been provided elsewhere [3,16].

Quality assurance

At least one laboratory spike, fortified at a DEET concentration of 0.1 μg/L, and one laboratory blank were analyzed with each set of 10 to 16 environmental samples. Surrogate compounds were added to samples before extraction to monitor method performance. The average recovery of DEET in 18

Table 1. Detections and concentrations of *N,N*-diethyl-*m*-toluamide in stream sites in different land-use settings in the U.S. Geological Survey's national reconnaissance study in 2000

Land use	Sites (n)	Sites with detection (%)[a]	Median concentration (μg/L)	Maximum concentration (μg/L)
All sites	56	73.2	0.05	1.13
Agricultural	7	85.7A	0.036	0.55
Mixed	10	70.0A	0.032	0.19
Urban	36	77.8A	0.057	1.13
Minimally developed	3	0.0B	<0.04	<0.04

[a] Percentage detection values followed by the same uppercase letter are not significantly different ($p < 0.05$) as determined by the nonparametric Kruskal–Wallis test.

laboratory-spike samples was 74%, with a standard deviation of 10%.

The laboratory blanks were used to assess potential sample contamination, and DEET was reported in only 1 of the 18 laboratory blanks at a concentration of 0.03 μg/L. This result was inferred to represent random contamination, so the environmental sample data were not censored based on this detection.

A field quality-assurance protocol was used to determine the effect, if any, of field equipment and procedures on the concentrations of DEET and other compounds analyzed in water samples. Field blanks, prepared using high-performance liquid chromatography–grade water, were submitted for three (~5%) of the sites and analyzed for DEET (and the other 95 selected OWCs). The field blanks were obtained using the same sample processing procedures, handling methods, and equipment as used for the stream samples. No detections of DEET occurred in any of the field-blank samples submitted. After the original samples for the present study were analyzed, field blanks were collected for other U.S. Geological Survey studies using similar field protocols, although use of personal care items, such as insect repellents, could not always be avoided. In some cases, low concentrations of DEET were detected in these other field blanks. These results underscore the need to avoid use of DEET during sample collection to minimize the contamination of samples.

RESULTS AND DISCUSSION

Detections and observed concentrations of DEET

The repellant DEET was detected at levels of 0.02 μg/L or greater in 73% of the 56 sites sampled (Table 1). The compound was commonly detected in all land-use settings except those that were minimally developed (Fig. 2). Although few streams were sampled for DEET in some of the different land-use settings, these results suggest that DEET is commonly detected in streams that are subject to contamination by OWCs (i.e., downstream from intense urbanization or livestock production). The repellant DEET is not used in general livestock production, but it is used to control insect bites on horses. In addition, potential human uses associated with livestock production and with rural households and small urban settings within these agricultural basins might account for DEET in streams from agricultural land-use settings. Although DEET was detected in most of the streams that were sampled, the median concentration was low (0.05 μg/L). The highest concentrations were found in urban streams (Table 1). The range of concentrations appeared to be constant throughout the sampling period from March through October 2000 (Fig. 3). This result contrasts with those for other environmental contaminants, such as pesticides, that commonly show seasonal cycles of concentration in surface water, primarily in response to their cycles of application [17].

Correlation with other OWCs

The concentrations of DEET in streams were correlated significantly ($p < 0.05$) with those of other OWCs in the same water sample that are predominantly related to indoor use and to the percentage of streamflow represented by wastewater effluent (Table 2). This included compounds such as caffeine and coprostanol and personal care products such as triclosan and 4-nonylphenol. In addition, the concentration of the fire-

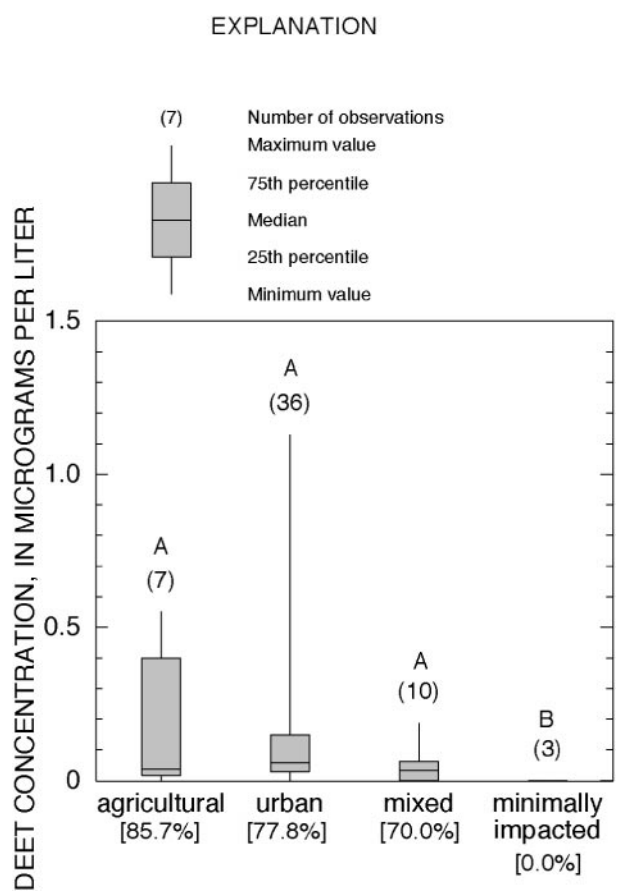

Fig. 2. Box-plot of *N,N*-diethyl-*m*-toluamide (DEET) concentrations in samples from streams in agricultural, urban, and mixed land-use basins in the national reconnaissance study of 2000. Concentration distributions in land-use settings denoted by the letter A were not significantly different from one another ($p > 0.05$) but were significantly different from that observed in minimally developed areas.

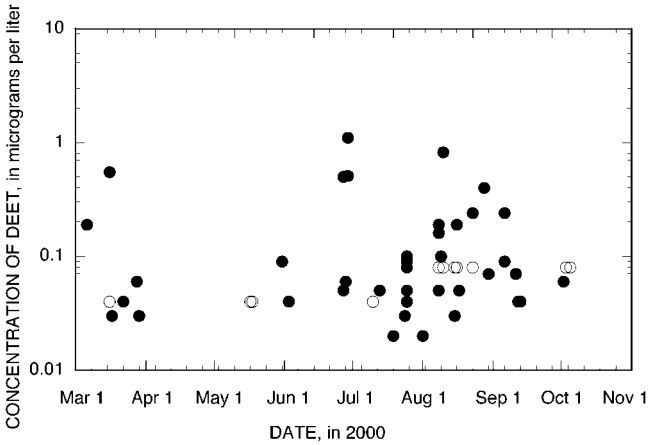

Fig. 3. Concentration of *N,N*-diethyl-*m*-toluamide (DEET) in samples from all 56 surface-water sites by sampling date in the year 2000. Open symbols indicate nondetections at the reporting levels shown. Reporting levels generally are equivalent to the lowest calibration standard that could be quantitated reliably at the time the samples were analyzed. Concentrations below this level were estimated if all qualitative gas chromatography/mass spectrometry criteria were met.

retardant tri(2-chloroethyl)-phosphate and of the plasticizers bisphenyl A and ethanol 2-butoxy-phosphate, commonly used in household products, also were significantly correlated with DEET concentrations in samples from urban streams (Table 2). These results support the hypothesis that DEET, like other household and indoor-use chemicals, can enter the hydrologic system as a consequence of discharge from wastewater-treatment systems.

Comparison with other pesticides

Concentrations of DEET were correlated significantly with concentrations of diazinon (Table 2), a pesticide commonly used on lawn and gardens in urban settings, and like other urban-use pesticides, it can enter streams directly from urban runoff [18]. In some urban areas, such pesticides can enter wastewater effluent where storm and sanitary sewers are combined. The concentrations of DEET are correlated less strongly with those of diazinon than with those of other OWCs (Table 2). This result might occur because the principal route of transport of diazinon to surface water is through runoff from outdoor application sites, whereas DEET more likely is introduced to streams by wastewater.

The percentage of sites with detections and maximum concentration of DEET determined in the present study are comparable to the results of previous investigations of pesticides in urban streams. In a study of eight urban streams from across the United States, diazinon was the most frequently detected insecticide (69% of samples) [18]. The maximum concentration was 1.4 μg/L, comparable to the maximum concentration of DEET in urban sites of the present study.

Metabolic fate of DEET

Numerous studies have examined the extent of adsorption and metabolism of dermally applied DEET [19–22], because the principal route of exposure of DEET to humans is adsorption through the skin. In human absorption studies, a small percentage (<20%) of dermally applied DEET is absorbed, and essentially all the adsorbed DEET is metabolized before elimination in the urine [23]. The human metabolites are the same as those identified in rat metabolism studies [24]. One major metabolite, *m*-(diethylaminocarbonyl)-benzoic acid, resulted from oxidation of the methyl moiety on the aromatic ring of DEET to carboxylic acid, whereas another, *m*-(ethylaminocarbonyl)-benzoic acid, was formed through *N*-dealkylation of an ethyl group from the amide moiety and oxidation of the methyl group on the ring, as shown in Figure 4 [24–26]. Other less oxidized metabolites, resulting from partial oxidation of the methyl moiety on the aromatic ring of DEET, also have been identified as metabolites in urine, including *N,N*-diethyl-3-(hydroxymethyl)-benzamide and *N*-ethyl-3-(hydroxymethyl)-benzamide. These metabolism studies suggest that wastewater-treatment facilities could receive oxidized metabolites excreted in urine. In addition, stream samples might have degradates formed by other, nonbiochemical transformation processes.

The present study of OWCs in streams did not include these DEET degradates as analytes in the original analytical methods [3]. The present authors subsequently made an attempt to identify some of these degradates in the stream samples by reanalysis of the sample extracts using full-scan GC/MS. The

Table 2. Spearman rank correlation coefficients (ρ) for relations of *N,N*-diethyl-*m*-toluamide concentrations with selected chemical concentrations and other variables for different land-use settings[a]

Chemical or variable	Use of chemical	Spearman rank correlation coefficients (ρ)			
		All sites	Urban	Agricultural	Mixed
Chemical concentration					
Tri(2-chloroethyl)-phosphate	Fire retardant	*+0.722*	*+0.744*	+0.741	+0.491
Caffeine	Stimulant	*+0.674*	*+0.668*	+0.612	+0.569
Cotinine	Nicotine metabolite	*+0.591*	*+0.671*	ND[b]	+0.534
Bisphenyl A	Plasticizer	*+0.535*	*+0.535*	+0.612	+0.560
Triclosan	Antimicrobial disinfectant	*+0.512*	*+0.653*	+0.148	+0.085
4-Nonylphenol	Nonionic detergent degradate	*+0.463*	*+0.408*	*+0.877*	*+0.739*
Coprostanol	Fecal sterol	*+0.439*	*+0.503*	+0.670	−0.411
Ethanol 2-butoxy-phosphate	Plasticizer	*+0.428*	*+0.425*	+0.612	−0.145
Diazinon	Pesticide	*+0.330*	+0.320	ND	ND
Lincomycin	Antibiotic	+0.138	+0.101	ND	ND
Water flow					
% Streamflow from municipal effluent		*+0.427*	*+0.536*	−0.030	0.0
Stream discharge		−0.033	+0.002	+0.714	+0.042

[a] Significant correlations ($p < 0.05$) are in italic.
[b] ND = not detected.

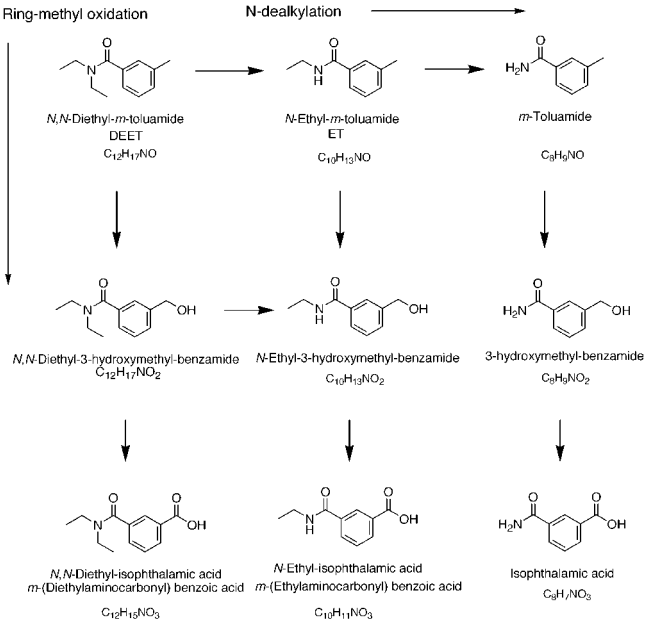

Fig. 4. Structures of *N*,*N*-diethyl-*m*-toluamide (DEET) and metabolites. Primary routes of degradation include *N*-dealkylation of nitrogen shown in the horizontal direction and ring-methyl oxidation shown in the vertical direction [6].

mass chromatograms were reviewed for characteristic ions of the neutral intermediate degradates (dealkylated-toluamides and hydroxymethyl-benzamides), which would be expected to be identified by electron-impact GC/MS without derivitization [24]. None of the degradates could be identified. However, this type of analysis would be successful only if the compounds were present at high concentrations, because retention times of the degradates were not known from authentic standards and the presence of other interfering chemicals can obscure the characteristic fragment ions in the mass chromatograms.

More accurate documentation of DEET degradates in the water will require the use of authentic standards and derivitization for GC/MS determination [25,26]. As of this writing (2005), only the fully deaklyated degradate of DEET, a metabolite thought to be of minor importance, has an authentic standard that is commercially available. This minor metabolite was not found in urine in a rat metabolism study [27].

Better knowledge concerning the amounts of DEET and major degradates is needed for improved exposure estimates and risk assessment of DEET transported to streams. The transformation of DEET in wastewater-treatment processes and the stability of DEET in surface water ultimately will affect the potential exposure to aquatic organisms; however, both are poorly understood processes.

Toxicological assessment

The health risk to users of insect repellant containing DEET was reviewed by the U.S. EPA during the reregistration of DEET [7]. It was decided that use of DEET as an insect repellant did not pose a significant health risk to the general U.S. population. This finding was based on the fact that DEET was not believed to be acutely toxic, carcinogenic, mutagenic, or likely to impair fetal development. However, it was noted that DEET is widely used by the general population, including children, and that in some cases, it has been thought to be associated with incidents of seizure. Therefore, the U.S. EPA recommended improved label warnings and restrictions for DEET products. Other reviews of the health risk of DEET similarly concluded that it generally is safe for topical use if applied as recommended, although it occasionally has been related to side effects, such as toxic encephalopathy, seizure, acute manic psychosis, cardiovascular toxicity, and dermatitis, along with a few cases of death caused by extensive skin absorption [14,28] (http://www.advisorybodies.doh.gov.uk/pdfs/reviewofdeet.pdf). These occasional side effects and incidents need to be considered in the context of the large proportion of the U.S. population using DEET annually. While the detection of DEET in a high percentage of sampled U.S. stream sites probably does not represent a substantial health risk to the general population, it might be necessary to assess the potential risk to children or individuals more sensitive to certain chemicals.

In contrast to the human risk assessment, only a limited set of ecological toxicity data are available for DEET. In part, this is because pesticides that have only indoor use, such as DEET, simply require a limited set of ecological toxicity studies for registration. During the reregistration of DEET, the ecological toxicity data for DEET were reviewed by the U.S. EPA [7]. From the few studies available, DEET was determined to be slightly toxic to birds (northern bobwhite, median lethal dose [LD50] = 1,375 mg/kg), fish (rainbow trout, LD50 = 75 mg/L), and freshwater invertebrates (*Daphnia magna*, median effective concentration = 75 mg/L) and to be nontoxic to small mammals. The DEET concentrations in streams reported in the present study are low compared to the concentrations determined to be slightly toxic. The results from this U.S. Geological Survey study show that personal care products and DEET may be transported to streams through wastewater-treatment systems, resulting in the potential exposure of aquatic organisms to these chemicals. Thus, the registration of indoor-use chemicals also needs to consider potential adverse effects on terrestrial wildlife or aquatic organisms as a result of the passage of the compound and its transformation products through wastewater-treatment systems. More ecological toxicity data are warranted for DEET and other personal care products based on the widespread detection of DEET in surface water and limited ecological toxicity data, which show that it is slightly toxic to some of the organisms tested.

CONCLUSIONS

In 56 streams sampled in the year 2000 across the United States during a reconnaissance study, DEET was one of the most commonly detected OWCs. The presence of DEET in streams was correlated significantly with that of other OWCs predominantly related to indoor and household use as well as with the percentage of streamflow contributed by wastewater effluent. The percentage of sites with detections and the maximum concentration of DEET determined in the present study are comparable to those from previous investigations of pesticides in urban streams, and the mass of DEET used annually is comparable to those of some widely used agricultural pesticides. The results from the present study show that the delivery of personal care products, including indoor-use pesticides such as DEET, to streams through wastewater-treatment systems and other pathways is likely to result in the potential exposure of aquatic organisms to these chemicals. These findings suggest that the toxicity of DEET and other indoor-use products to aquatic biota and other nonspecified organisms might need to be considered during the registration (or reregistration) of these compounds for indoor use.

REFERENCES

1. Heberer T. 2002. Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: A review of recent research data. *Toxicol Lett* 131:5–17.
2. Ternes TA, Meisenheimer M, McDowell D, Sacher F, Brauch HJ, Haist-Gulde B, Preuss G, Wilme U, Zulei-Seibert N. 2002. Removal of pharmaceuticals during drinking water treatment. *Environ Sci Technol* 36:3855–3863.
3. Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT. 2002. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: A national reconnaissance. *Environ Sci Technol* 36:1202–1211.
4. Hendriks AJ, Maas-Diepeveen JL, Noordsij A, Van der Gaag MA. 1994. Monitoring response of XAD-concentrated water in the Rhine delta: A major part of the toxic compounds remain unidentified. *Water Res* 28:581–598.
5. Barnes KK, Christenson SC, Focazio MJ, Kolpin DW, Furlong ET, Zaugg SD, Meyer MT, Barber LB. 2004. Pharmaceuticals and other organic wastewater contaminants within a leachate plume down-gradient of a municipal landfill. *Ground Water Monit Remediation* 24:119–26.
6. Weigel S, Kuhlmann J, Huhnerfuss H. 2002. Drugs and personal care products as ubiquitous pollutants: Occurrence and distribution of clofibric acid, caffeine, and DEET in the North Sea. *Sci Total Environ* 295:131–41.
7. U.S. Environmental Protection Agency. 1998. Reregistration eligibility decision (RED) for DEET. EPA 738-R-98-010. Washington, DC.
8. Abou-Donia MB, Wilmarth KR, Abdel-Rahman AA, Jensen KF, Oehme FW, Kurt TL. 1996. Increased neurotoxicity following concurrent exposure to pyridostigmine bromide, DEET, and chlorpyrifos. *Fundam Appl Toxicol* 34:201–22.
9. Chaney LA, Wineman RW, Rockhold RW, Hume AS. 2000. Acute effects of an insect repellent, *N,N*-diethyl-*m*-toluamide, on cholinesterase inhibition induced by pyridostigmine bromide in rats. *Toxicol Appl Pharmacol* 165:107–114.
10. Davis EE. 1985. Insect repellents: Concepts of their mode of action relative to potential sensory mechanisms in mosquitoes (Diptera: Culicidae). *J Med Entomol* 22:237–243.
11. Dogan EB, Ayres JW, Rossignol PA. 1999. Behavioral mode of action of DEET: Inhibition of lactic acid attraction. *Med Vet Entomol* 13:97–100.
12. Gianessi LP, Marcelli MB. 2000. Pesticide use in U.S. crop production: 1997. National Center for Food and Crop Protection, Washington, DC.
13. U.S. Environmental Protection Agency. 1999. Environmental risk assessment for diazinon. Reregistration Eligibility Decision (RED). Washington, DC.
14. Qiu H, Jun HW, McCall JW. 1998. Pharmacokinetics, formulation, and safety of insect repellent *N,N*-diethyl-3-methylbenzamide (DEET): A review. *J Am Mosq Control Assoc* 14:12–27.
15. Wilde FD, Radke DB, Gibs J, Iwatsubo RT, eds. 1999. *National Field Manual for the Collection of Water-Quality Data*, Book 9, Chapter A6. U.S. Geological Survey, Reston, VA.
16. Barber LB, Brown GK, Zaugg SD. 2000. Potential endocrine disrupting organic chemicals in treated municipal wastewater and river water. In Keith LH, Jones-Lepp TL, Needham LL, eds, *Analysis of Environmental Endocrine Disruptors.* STP 747. American Chemical Society, Washington, DC, pp 97–123.
17. Larson SJ, Gilliom RJ, Capel PD. 1999. Pesticides in streams of the United States: Initial results from the National Water-Quality Assessment Program. Water-Resources Investigations Report 98-4222. U.S. Geological Survey, Sacramento, CA.
18. Hoffman RS, Capel PD, Larson SJ. 2000. Comparison of pesticides in eight U.S. urban streams. *Environ Toxicol Chem* 19: 2249–2258.
19. Robbins PJ, Cherniack MG. 1986. Review of the biodistribution and toxicity of the insect repellent *N,N*-diethyl-*m*-toluamide (DEET). *J Toxicol Environ Health* 18:503–525.
20. Schoenig GP, Hartnagel RE Jr, Osimitz TG, Llanso S. 1996. Absorption, distribution, metabolism, and excretion of *N,N*-diethyl-*m*-toluamide in the rat. *Drug Metab Dispos* 24:156–163.
21. Stinecipher J, Shah J. 1997. Percutaneous permeation of *N,N*-diethyl-*m*-toluamide (DEET) from commercial mosquito repellents and the effect of solvent. *J Toxicol Environ Health* 52:119–135.
22. Usmani KA, Rose RL, Goldstein JA, Taylor WG, Brimfield AA, Hodgson E. 2002. In vitro human metabolism and interactions of repellent *N,N*-diethyl-*m*-toluamide. *Drug Metab Dispos* 30:289–294.
23. Selim S, Hartnagel RE Jr, Osimitz TG, Gabriel KL, Schoenig GP. 1995. Absorption, metabolism, and excretion of *N,N*-diethyl-*m*-toluamide following dermal application to human volunteers. *Fundam Appl Toxicol* 25:95–100.
24. Taylor WG, Spooner RW. 1990. Identification and gas chromatographic determination of some carboxylic acid metabolites of *N,N*-diethyl-*m*-toluamide in a rat urine. *J Agric Food Chem* 38:1422–1427.
25. Constantino L, Iley J. 1999. Microsomal metabolism of *N,N*-diethyl-*m*-toluamide (DEET, DET): The extended network of metabolites. *Xenobiotica* 29:409–16.
26. Taylor WG. 1986. Metabolism of *N,N*-diethyl-meta-toluamide by rat liver microsomes. *Drug Metab Dispos* 14:532–539.
27. Abu-Qare AW, Abou-Donia MB. 2001. Simultaneous determination of malathion, permethrin, DEET (*N,N*- diethyl-*m*-toluamide), and their metabolites in rat plasma and urine using high-performance liquid chromatography. *J Pharm Biomed Anal* 26: 291–299.
28. United Kingdom Department of Health. 2002. Review of the toxicology literature for the topical insect repellent diethyl-*m*-toluamide (DEET). COT/02/05-November 2002. Committee on Toxicity of Foods and Consumer Products and the Environment, London.