Octachlorodipropyl Ether (S-2) Mosquito Coils Are Inadequately Studied for Residential Use in Asia and Illegal in the United States

Robert I. Krieger, Travis M. Dinoff, and Xiaofei Zhang

Department of Entomology, Personal Chemical Exposure Program, Graduate Program in Environmental Toxicology, University of California, Riverside, California, USA

Children and their parents in residences are often protected by insecticides from nuisance and disease-bearing mosquitoes. The annual worldwide consumption of the four major types of residential insecticide products—aerosols, mosquito coils, liquid vaporizers, and vaporizing mats—is in the billions of units. Mosquito coils are burned indoors and outdoors in East Asia and to a limited extent in other parts of the world, including the United States. Coils consist of an insecticide/repellant, organic fillers capable of burning with smoldering, binder, and additives such as synergists, dyes, and fungicide. The number of coil users in China is in the millions. In Indonesia alone, an estimated seven billion coils are purchased annually. Coils containing pyrethroid insecticides, particularly *d*-allethrin, may contain octachlorodipropyl ether (S-2, S-421) as a synergist or active ingredient. Use of those coils likely exposes children and adults to some level of bis(chloromethyl)ether (BCME). BCME is formed from formaldehyde and hydrogen chloride, combustion products formed from the slow smoldering (about 8 hr/coil) of the mosquito coils. Because BCME is an extremely potent lung carcinogen, the nature and extent of prolonged exposures that recur in homes during the mosquito season in tropical regions must be evaluated with respect to health. In a small analytical study, coils purchased in Indonesia and in the United States contained highly variable amounts of S-2. Some coils that contained S-2 were not labeled, making it impossible for consumers to make an informed decision about coil contents. Mosquito coils containing S-2 are unregistered, and their use is illegal in the United States. Indoor air monitoring under conditions that represent conditions of use in tropical settings and epidemiology to assess health impacts of coil use are essential to permit responsible regulatory decisions regarding continuing S-2 use. *Key words:* bis(chloromethyl)ether, chloroalkyl ether, *d*-allethrin, lung carcinogen, mosquito coil, octachlorodipropyl ether, S-2. *Environ Health Perspect* 111:1439–1442 (2003). doi:10.1289/ehp.6177 available via *http://dx.doi.org/* [Online 28 May 2003]

Children and their parents in residences are often protected from nuisance and disease-bearing mosquitoes by insecticides. The annual worldwide consumption of the four major types of residential insecticide products—aerosols, mosquito coils, liquid vaporizers, and vaporizing mats—are listed by region in Table 1 [World Health Organization (WHO) 1998a]. Mosquito coils are burned indoors and outdoors in East Asia and to a limited extent in other parts of the world, including the United States. Coils consist of an insecticide/repellent, organic fillers capable of burning with smoldering, binder, and additives such as synergists, dyes, and fungicide. The number of coil users in China is in the millions (WHO 1998a). In Indonesia alone an estimated seven billion coils are purchased annually (Zainun Z. Personal communication). Mosquito coils are the preferred antimosquito products in low-income communities (Mulla et al. 2001).

Mosquito coils burn for about 8 hr without flame on a nonflammable stand or holder (Figure 1). Coils are often used overnight in sleeping quarters, where elevated exposure may occur as parents seek to protect their children from mosquitoes. The most common active ingredients in coils are various pyrethroids. Pyrethroid-based coils are effective against genera of mosquitoes including *Aedes*, *Anopheles*, and *Mansonia*. Children and their parents are exposed to a chemically complex mosquito-coil smoke containing small particles (< 1 μm), metal fumes, and vapors (Liu and Sun 1988) that may reach the alveolar region of the lung (Cheng et al. 1992). Chronic exposures occur during the summer use period; in Taiwan use was estimated to be 6–9 months each year (Cheng et al. 1992).

Frequently, mosquito coils contain octachlorodipropyl ether (S-2, S-421; Figure 2) as a synergist or active ingredient. S-2 was first prepared in 1959 by Becke and Sperber (1960). S-2 was soon discovered to have insecticide and synergistic activity (Adolphi 1958; Hayashi 1969). S-2 is a chloroalkyl ether used as both an insecticide and insecticide synergist in mosquito coils (Mrusek 1996; Spiller 1996) containing pyrethrin and *d*-allethrin as active ingredients. In 1998, an estimated 200 tons of bis-(chloromethyl)ether (BCME) were produced in China as an intermediate in the manufacture of about 700 tons of S-2 (WHO 1998a). Because the products are not registered in the United States, there is no record of sales or estimates of human exposure. Despite the fact that no pesticide can be sold legally in the United States without federal (and in many states also state) registration, unregistered products do find their way into channels of trade. Sales are likely to increase as concern about West Nile virus and other mosquito-borne disease mounts in the United States.

S-2 may be volatized from mosquito coils and may cause inhalation and contact exposures. The exposures are of uncertain significance because both clinical and epidemiologic studies of mosquito coil users are lacking. Considerable relevant experimental data have been collected. The degradation of S-2 to BCME and congeners, including bis-(chloromethylmethyl)ether (CMME), during the burning of mosquito coils is of particular health concern (WHO 1998a) because BCME may be the most potent lung carcinogen known (ATSDR 1989). BCME can be formed from hydrogen chloride and formaldehyde during resin manufacturing (Frankel et al. 1974; Tou and Kallos 1974). This observation was not supported by other experimental studies that used low concentrations (Tou and Kallos 1976) in settings that might be more similar to the indoor environments where mosquito coils are burned. Recently, using improvements of methods of Langelaan and Nielen (1989) for trace analysis of BCME in air, Pauluhn (2002) reported that BCME is released during combustion of mosquito coils. Quantitative data are not available at this time. Volatile constituents of S-2 include undefined genotoxic agents (Pauluhn and Mohr 2000). If BCME is formed, the potential long-term exposure of residents, including children, to unmeasured amounts of this potent lung carcinogen (Sittig 1981) and other combustion products must be evaluated as a proactive public health measure.

We conducted a preliminary survey and chemical analysis of mosquito coils sold in Indonesia and California labeled to contain *d*-allethrin and S-2. Sales of unregistered mosquito coils containing S-2 are illegal in the United States. The U.S. Environmental Protection Agency (U.S. EPA) does not register

S-2 for any use, so products containing S-2 as an active ingredient or synergist are not permitted.

Materials and Methods

Sources of mosquito coils. Mosquito coils were purchased in various retail outlets in Jakarta and Bandung, Indonesia. Coils manufactured in China were also purchased from several Asian markets in southern California. The samples were selected to represent a variety of products and by no means constituted a statistical sampling of retail outlets in either Indonesia or California. The coils were transported to the laboratory under ambient conditions and stored at room temperature (~21°C). Laboratory inventory numbers in Table 2 identify products tested. Fifty-three packages of coils were tested. Results of range-finding analyses and 14 quantitative analyses were intended to determine whether mosquito coils sold illegally in the United States contained S-2, an ingredient inadequately evaluated for safe use.

Sample preparation and extraction. A small piece of mosquito coil was broken off and weighed in an 8 mL vial. Samples ranged from 0.5 to 0.75 g. Three milliliters of ethyl acetate and two pellets (≈0.2 g) of potassium hydroxide were added. The vial was filled with distilled water, capped, and shaken vigorously. Each sample was shaken occasionally during the next several hours and then allowed to stand overnight on the bench top at room temperature. The next day, the sample was again shaken and then centrifuged, and a portion of the ethyl acetate phase was placed into an auto sampler vial. Samples were then analyzed by gas chromatographic/mass spectrometric (GC/MS) analysis for S-2 and other pesticides.

Standard. Authentic S-2 (> 97% pure) was obtained from a manufacturer in China and as S-421 Pestanal [99.2%; Chemical Abstracts Service (CAS) no. 127-90-2] from Sigma-Aldrich (St. Louis, MO). The colorless liquid was virtually odorless. GC/MS analysis of the authentic S-2 revealed numerous contaminants, including lower chlorinated dipropyl ethers. An arbitrary high, medium, and low scale was established to represent the amount of S-2 present in coil extracts.

Other pesticides or insecticide synergists found in extracts were identified based upon mass spectrometry. Each was reported but not quantified.

Analysis. Extracts were analyzed on a Hewlett-Packard 5973 GC/MS unit (Hewlett-Packard, Palo Alto, CA) in full-scan 70 electron volt electron impact (eV EI) mode equipped with a 30 m × 0.25 mm inner-diameter Hewlett-Packard HP-5MS capillary column. The temperature program used was 50°C for 1 min, and then ramped up at 15°C per min to 300°C, where the temperature was held for 1 min before returning to the starting conditions.

The recovery of S-2 at 0.1% (wt/vol) and 1.0% (wt/vol) from spiked coil samples was measured using pieces of coil from products previously shown to be free of S-2. At the lower level, S-2 recovery was 127 ± 4% (*n* = 5), and at the higher level, the S-2 recovery was 113 ± 2% (*n* = 5). Results were not corrected for recoveries.

Results

The mosquito coils purchased in Indonesia and California had the same general appearance and texture. Each sample was easily dispersed and extracted from an alkaline suspension with ethyl acetate. The S-2 standard was used to estimate micrograms and percentage of S-2 (Table 2), based on analysis of three samples of each coil. The selected data are not suitable for exposure assessment because of small sample size and uncertainty due to possible matrix effects on analysis that were not investigated.

Coil packages tested contained up to five double coils and listed either allethrin only or allethrin and S-2 at 1.5% (wt/wt) (Tables 3 and 4). Three samples obtained from Jakarta, each labeled 1.5% S-2, contained a remarkable range of S-2: < 0.001%, 0.03%, and 0.3% S-2, respectively. Three packages of coils labeled 1.5% S-2 that were purchased in Bandung had more similar levels of S-2 (mean = 0.7%).

The mosquito coils purchased in southern California contained allethrin (confirmed by analysis), but their packaging did not list S-2. The S-2 content of coils from three packages was 0.2–0.3%. Of samples from Jakarta that did not list S-2 as an ingredient, the coils contained from 0.007 to 0.2% (*n* = 5). Other coils (*n* = 7) did not contain detectable S-2, and one contained MGK-264 (CAS no. 113484; McLaugthlin Gormley and King Co., Bloomington, MN).

Discussion

Household insects that are nuisances and contribute to sanitary and health problems are ubiquitous throughout the world. The demand for insect control is on the increase, particularly in many tropical developing countries. The yearly worldwide residential insecticide market is estimated to be more than US$2 billion (WHO 1998a). Mosquito coils are prominent among pest management tools in Asia, as shown in Table 1 (WHO 1998a).

Shortly after its synthesis, S-2 was shown to be a synergist for pyrethroids and other insecticides. Later studies have demonstrated the inherent insecticide activity of S-2 (Mrusek 1996; Spiller 1996). International authorities have emphasized that S-2 possesses both mosquito knockdown and killing activity and that it should be classed as an insecticide (WHO 1998b). Because the registration requirements for active ingredients and synergists differ outside the United States, controversy concerning S-2 may distract attention from the need to more fully characterize the toxicology of S-2, synthetic by-products, and combustion products in mosquito coils.

Only *d*-allethrin products were used for this study. *d*-Allethrin products that listed S-2 and others that did not list S-2 on the label contained S-2 in highly variable amounts (0.001–0.7% wt/wt). This may reflect the fact that an estimated 30% of pesticides marketed in developing countries do not meet internationally accepted quality standards (WHO 2003). The chemical composition of mosquito coils included other unknown and unquantified chlorinated dialkyl ethers. S-2 from different sources has notable genotoxicity and irritancy (Pauluhn 1996). No other pyrethroids used in mosquito coils, including

Figure 1. A mosquito coil containing allethrin and S-2 burning to kill or repel mosquitoes in family living quarters. The coil is secured to a small metal stand, and it will burn about 8 hr. The plate retains segments of ash as the coil burns.

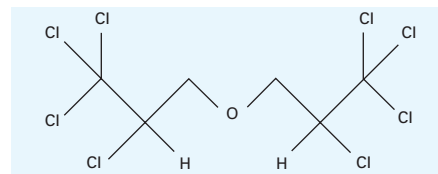**Figure 2.** Structural formula of S-2 (S-421).

Table 1. Consumption of household insecticide products in 1996 (region type and consumption, 10^8).

Region	Aerosols	Coils	Liquid vaporizers	Vaporizing mats
Asia	3	270	0.5	45
America	4	16	0.06	7
Europe	1	0.8	0.2	96
Middle East and Africa	2	3	0.01	93
Total	10	290	0.8	240

d-trans allethrin (75:25), prallethrin, and trans-fluthrin, were tested.

None of the products manufactured in China and purchased in southern California are registered with the U.S. EPA. Those containing S-2 would require additional toxicity testing and labeling by the Department of Pesticide Regulation, California Environmental Protection Agency (EPA). Proposition 65 would likely require additional labeling because BCME is a chemical known to the state to cause cancer (California EPA 1994). Without knowledge of human exposure potential and the hazards of S-2, product impurities, and combustion products, including BCME and CMME, the potential health impacts of continued use of the coils cannot be gauged.

Environmental persistence of S-2. S-2 use may result in environmental contamination. S-2 is a persistent, lipophilic chlorinated hydrocarbon that has been found in environmental and human samples in part-per-billion levels resulting from manufacturing or use. Residues of chlorinated bis-(propyl)ethers (BPEs) have been found as persistent environmental pollutants in Germany's Elbe River and its tributaries (Franke et al. 1995). Di-, tri-, and tetrachlorinated BPEs were detected by GC/MS analysis of water and sediments. The Cl_2- and Cl_3-BPEs were not noticeably affected by sewage treatment. Water and sediment may represent pathways of exposure to chlorinated impurities and transformation products associated with the manufacture and use of mosquito coils containing S-2.

S-2 is a bioavailable environmental contaminant. Because of the detection of S-2 during organochlorine analysis of human milk in Japan (Miyazaki et al. 1981), an analytical method was developed (Miyazaki 1982). Milk samples obtained in Tokyo on a milk fat basis contained 32 ± 27 ppb (9 positive of 12) and 14 ± 8 ppb (6 of 10). Knowledge of the use of S-2 as a pyrethroid synergist against mosquitoes, houseflies, and cockroaches in Tokyo prompted analysis of aerosol sprays, mosquito coils, and mosquito mats. Sprays (3 of 8) and coils (2 of 5) contained S-2, but none was detected in the mats. Miyazaki (1982) concluded that sprays and coils were the likely source of the S-2 residues in milk.

These findings demonstrate the potential bioavailability of S-2 used in mosquito coils.

The routes of exposure may include inhalation and contact transfer (dermal and hand to mouth) from surfaces in enclosed residential environments. Fishbein et al. (1968) performed a chromatographic study of the fate of intravenous S-2 in rats (150 mg/kg). Urine and bile were collected during an 8-hr period, and portions were applied directly to silica gel DF-5. Based upon the chromatographic behavior of metabolites, the authors speculated that dehydrohalogenation, ether cleavage, and hydrolysis were important metabolic transformations. Further characterization of S-2 metabolites has not been reported.

BCME. The possible formation of BCME and other toxic combustion products from mosquito coil use has not been adequately evaluated. Hydrogen chloride and formaldehyde are formed from combustion of S-2, but quantitative data corresponding to conditions of use are lacking. Under laboratory test conditions, hydrogen chloride and formaldehyde react in smoky air to form BCME (CAS no. 542-88-1) and other unknown toxic substances (Frankel et al. 1974; Tou and Kallos 1974). This β-chloroalkyl ether is colorless and volatile (30 mm Hg at 22°C) and has a characteristic "suffocating" odor (Sittig 1981).

Natural sources of BCME have not been identified, and it is an unlikely environmental contaminant. In air, the BCME is degraded by photo-oxidation and hydrolysis with a half-life of < 2.9 days (Cuppit 1980). Tou and Kallos (1974) reported that the half-life of BCME was < 1 day in humid air. In air, decomposition products of BCME include formaldehyde, hydrogen chloride, and chloromethylformate (Cuppit 1980). BCME is extremely rapidly hydrolyzed in water ($t_{1/2}$ = 38 sec at 20°C) to formaldehyde and hydrogen chloride. Because of the highly reactive nature of BCME in air and water, it will not persist in the outdoor environment because of the use of S-2 in mosquito coils.

Indoor BCME exposure potential. Similar data concerning the stability of BCME indoors are not available. Even BCME half-lives measured in periods as long as days would not prevent repeated short-term (8-hr) exposures

during times of the year when mosquito coils are burned indoors. Those environments are frequently sheltered from direct sunlight, thus reducing the extent of photolysis. BCME is likely to be more stable indoors than outdoors, and the pattern of use of mosquito coils may result in more prolonged human exposure to BCME and other combustion products. No quantitative data are available for the exposure of populations that use mosquito coils containing S-2.

Under workplace conditions, BCME forms upon reaction of formaldehyde and hydrogen chloride. The reaction may occur in air (Van Duuren et al. 1969). Measurable workplace concentrations of BCME have been found in atmospheric reaction mixtures containing formaldehyde and hydrogen chloride (Frankel et al. 1974; Kallos and Solomon 1973). Although BCME is an "intense, immediate irritant" (Nelson 1976), it provides insufficient warning to prevent human cancer from BCME exposure in the workplace (and even less warning from small amounts likely produced in residential settings).

Table 3. S-2 in mosquito coils purchased in Indonesia and the United States.

Sample code	Label % S-2	S-2 (µg/g)	Measured % S-2[a]
Jakarta			
JK-06	0	6.8	0.0068
JK-07	0	12.1	0.012
JK-08	0	200	0.20
JK-10	0	2.5	0.0025
JK-11	1.5	< 1	< 0.001
JK-12	1.5	2.5	0.0032
JK-14	1.5	320	0.32
JK-22	0	52	0.052
Bandung			
BD-01	1.5	780	0.78
BD-02	1.5	540	0.54
BD-03	1.5	620	0.62
California			
CA-01	0	290	0.29
CA-04	0	220	0.22
CA-09	0	200	0.20

[a]% S-2 = µg S-2/g coil × 100.

Table 4. Triplicate analyses of mosquito coils containing S-2.

Sample	S-2 (ug/g coil)	Mean ± SD	Coefficient of variation
JK-22			
1	3,748		
2	3,901		
3	3,841		
		3,830 ± 77	0.02
JK-07			
1	88		
2	108		
3	115		
		104 ± 14	0.14
CA-16			
1	4,276		
2	2,858		
3	4,044		
		3,726 ± 761	0.20

Abbreviations: CA, California; JK, Jakarta, Indonesia.

Table 2. Mosquito coils purchased in Indonesia and California screened for S-2.

Origin, label listed S-2	Analysis			
	S-2 Detected	No S-2[a]	Total	Range (µg/g)
Jakarta				
Yes	3	0	3	< 10–3,200
No	12	7	19	25–2,000
Bandung				
Yes	3	0	3	5,400–7,800
No	0	13	13	None
California				
Yes	0	0	0	None
No	10	6	16	2,000–4,300

[a]< 10 µg/g.

Quantitative data are not available to estimate the sensitivity of children and adults to the hazards. Air levels of BCME and knowledge of surface deposition of S-2 and other coil combustion product releases are important for evaluating exposure and for developing effective risk management strategies. False negatives due to matrix and analytical conditions may complicate verification of BCME in coil smoke (Langelaan and Nielen 1989).

Cancer. The status of BCME as a potent human lung carcinogen is established. Any solid or liquid containing more than 0.1% BCME by weight or volume is regulated by the U.S. Occupational Safety and Health Administration. Studies in rats and mice have shown that 0.1 ppm or 1 ppm of BCME in air, respectively, induced lung cancer. Oat cell carcinoma, a rare form of lung cancer (primarily small cell undifferentiated), occurred in 12 of 13 persons occupationally exposed to BCME and CMME. With one exception, the affected workers had been exposed only 3–14 years, and their average age was 45 years, well below the average age for lung cancer of 60 years. The potency of BCME was also evident in a small factory in China. There, 5 of 15 workers exposed to BCME during S-2 manufacture were diagnosed with lung cancer. Four of the workers were younger than 40 years (Xue et al. 1988). BCME is among those potent human carcinogens (U.S. DHHS 2002).

Other agencies offer similar classifications of BCME as a carcinogen. The Office of Environmental Health Hazard Assessment of the California EPA designated BCME a priority carcinogen (California EPA 1994). This classification is consistent with the group A (known human carcinogen) designation by the U.S. EPA (2003) and the group 1 (human carcinogen) categorization by the International Agency for Research on Cancer (IARC 1987).

Recommendations. In 1998, a WHO Pesticides Evaluation Scheme document, *Guideline Specifications for Household Insecticide Products* (WHO 1998a), reported informal consultations. Included among the recommendations were the needs to identify household insecticide products in use, to establish product specifications, and to encourage regulatory harmonization. A second document (WHO 1998b) sought further research to measure "the degree of exposure of the general public to BCME and CMME through the use of mosquito coils containing the S-2 synergist octachlorodipropyl ether." Additionally, the degree of contamination of S-2 with BCME and CMME should also be determined. To date, these actions have not occurred, and extensive use of S-2 continues.

With respect to the use of mosquito coils in the United States, these toxicologic issues concerning β-chloroalkyl ethers overlie the illegal sales of products containing an unregistered product, S-2. All users are entitled to the

benefit of toxicity testing and continuing product stewardship related to the manufacture and use of S-2 and to knowledge of the potential risk from likely combustion products that include BCME, a human lung carcinogen.

Household insecticide products are used under a variety of conditions by persons who rely upon their experience or label instructions to guide safe use. Children, the elderly, and the infirm may be continually exposed to these slow-release systems. The potential for a health impact is elevated by the recurring exposures of children and adults during the mosquito season each year. The WHO (1998b) emphasized that household insecticide should contain only well-defined active ingredients. The occurrence of uncharacterized combustion products and active ingredients in coil smoke creates potential for acute and chronic toxicity.

Existing knowledge is not adequate to support safe residential use of mosquito coils containing S-2, and it is unfortunate that the environmental data and experimental studies have not been more prominent in S-2 risk management. No quantitative data are available for the exposure of populations that use mosquito coils that contain S-2, but the number of exposed persons is extremely large given the extent of use of mosquito coils (WHO 1998a). Unreacted BCME in coils and the extent of BCME as a combustion product must be determined under conditions of coil use as part of well-formed epidemiologic studies. In many situations, it seems likely that the reality of mosquito-borne diseases (Mulla et al. 2001) may dominate determination of hypothetical risk:benefit ratios for mosquito insecticides delivered using devices such as coils. However, if BCME were an important environmental contaminant resulting from burning mosquito coils containing S-2, it would be impossible to maintain use given the well-established carcinogenicity of BCME in humans.

REFERENCES

Adolphi H. 1958. Examination of a pyrethrum synergist—preliminary information. Pyrethrum Post 4:3–5.

ATSDR. 1989. Toxicological Profile for Bis(chloromethyl)ether. Atlanta, GA:Agency for Toxic Substances and Disease Registry.

Becke F, Sperber H. 1960. Octachlorodipropyl ether. U.S. Patent 2,913,500. Chem Abstr 54:3203e.

California EPA. 1994. Office of Environmental Health Hazard Assessment. Safe Drinking Water and Toxic Enforcement Act of 1986. Status Report: No Significant Risk Levels for Carcinogens and Acceptable Intake Levels for Reproductive Toxicants. Sacramento, CA:California Environmental Protection Agency.

Cheng V, Lee HR, Chen CS. 1992. Morphological changes in the respiratory system of mice after inhalation of mosquito-coil smoke. Toxicol Lett 62:163–177.

Cuppit L. 1980. Fate of Toxic and Hazardous Materials in the Air Environment. Research Triangle Park, NC:Atmospheric Chemistry and Physics Laboratory, U.S. Environmental Protection Agency.

Fishbein L, Fawkes J, Falks HL, Thompson. 1968. Thin-layer chromatography of rat bile and urine following intravenous administration of the pesticidal synergist octachlorodipropyl ether. J Chromatogr 37:256–263.

Franke S, Hildebrandt S, Francke W. 1995. The occurrence of chlorinated bis-(propyl) ethers in the Elbe River and tributaries. Naturwissenshaften 82:80–83.

Frankel LS, McCallum K, Collier L. 1974. Formation of bis-(chloromethyl) ether from formaldehyde and hydrogen chloride. Environ Sci Technol 8:356–359.

Hayashi A. 1969. Synergistic effect of octachlorodipropylether (S-421). Botyu-Kagaku 34:189–192.

IARC. 1987. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. IARC Monogr Eval Carcinog Risks Hum 7(suppl):1–440.

Kallos GJ, Solomon RA. 1973. Investigations of the formation of bis-(chloromethyl)ether in simulated hydrogen chloride-formaldehyde atmospheric environments. Am Ind Hyg Assoc J 34:469-473.

Langelaan FCGM, Nielen MWF. 1989. Determination of trace levels of chloromethyl-methylether and bis(chloromethyl)ether in air. Int J Environ Anal Chem 36:27–34.

Liu WK, Sun SE. 1988. Ultrastructural changes of tracheal epithelium and alveolar macrophages of rats exposed to mosquito coil smoke. Toxicol Lett 41:145–147.

Miyazaki T. 1982. Residues of the synergist S-421 in human milk collected from the Tokyo metropolitan area. Bull Environ Contam Toxicol 29:566–569.

Miyazaki T, Kaneko S, Horii S, Yamagishi T. 1981. Identification of the synergist bis-(2,3,3,3-tetrachloropropyl)ether in human milk. Bull Environ Contam Toxicol 26: 421–423.

Mrusek K. 1996. The usage of S-2 in household insecticide products. In: Proceedings of the International Seminar on Recent Development of Mosquito Coils: Efficacy, Toxicology, Environmental Impact and Legislation, 5–7 December 1996, Penang, Malaysia. Penang, Malaysia:Vector Control Research Unit, Universiti Sains Malaysia, 29–32.

Mulla MS, Thavara U, Tawatsin A, Kong-Ngamsuk W, Chompoosri J. 2001. Mosquito burden and impact on the poor: measures and costs for personal protection in some communities in Thailand. J Am Mosquito Control Assoc 17:153–159.

Nelson N. 1976. The chloroethers—occupational carcinogens: a summary of laboratory and epidemiology studies. Ann NY Acad Sci 271:81–90.

NTP. 2002. Report on Carcinogens, 10th ed. Research Triangle Park, NC:National Toxicology Program.

Pauluhn J. 1996. Assessment of mosquito coil smoke for it's potential to induce irritation-related respiratory tract changes on nose-only exposed rats: a comparison of different methods. In: Proceedings of the International Seminar on Recent Development of Mosquito Coils: Efficacy, Toxicology, Environmental Impact and Legislation, 5–7 December 1996, Penang, Malaysia. Penang, Malaysia:Vector Control Research Unit, Universiti Sains Malaysia, 33–49.

———. 2002. Risk assessment of mosquito coil smoke—new critical evidence. Presented at the 11th Annual Workshop on Biology & Control of Vectors & Urban Pests, 6–8 May 2002, Penang, Malaysia.

Pauluhn J, Mohr U. 2000. Inhalation studies in laboratory animals—current concepts and alternatives. Toxicol Pathol 28:734–753.

Sittig M. 1981. Handbook of Toxic and Hazardous Chemicals. Park Ridge, NJ:Noyes Publications.

Spiller N. 1996. Are active ingredient cocktails of any value in mosquito coils? Proceedings of the International Seminar on Recent Development of Mosquito Coils: Efficacy, Toxicology, Environmental Impact and Legislation, 5–7 December 1996, Penang, Malaysia. Penang, Malaysia:Vector Control Research Unit, Universiti Sains Malaysia, 12–18.

Tou J, Kallos G. 1974. Kinetic study of the stabilities of chloromethyl methyl ether and bis(chloromethyl) ether in humid air. Anal Chem 46:1866–1869.

———. 1976. Possible formation of bis(chloromethyl ether) ether from the reactions of formaldehyde and chloride ion. Anal Chem 48:958–963.

U.S. EPA. 2003. Integrated Risk Information System. Washington, DC:U.S. Environmental Protection Agency. Available: http://www.epa.gov/iris/subst/0375.htm#top [accessed 13 May 2003].

Van Duuren BL, Sivak A, Goldschmidt BM, Katz C, Melchionne S. 1969. Carcinogenicity of halo-ethers. J Natl Cancer Inst 43:481–486 (1969).

WHO. 1998a. Pesticides Evaluation Scheme, Division of Control of Tropical Diseases, Guideline Specifications for Household Insecticide Products. Geneva:World Health Organization.

———. 1998b. Environmental Health Criteria 201, Selected Chloroalkyl Ethers. Geneva:World Health Organization.

———. 2003. Communicable Diseases 2002. In: Global Defense against the Infectious Disease Threat (Kindhauser MK, ed). Geneva:World Health Organization, 32–53.

Xue SZ, Quian C, Tang GF, Wang ZQ, Zhou DH, Deng J, et al. 1988. Epidemiological investigations on the lung cancer among chloro-methyl-ether exposures. In: Occupational Health in Industrialization and Modernization (Xue SZ, Liang Y, eds). Shanghai:Shanghai Medical University Press, 75–80.