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HEALTH EFFECTS OF HEXACHLOROETHANE (HC) SMOKE

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19. ABSTRACT (Continue on reverse if necessary and identify by block number) Grenades, smoke pots, and artillery shells are used to produce HC smoke. Soldier exposure to HC smoke and worker exposure to the volatile components of HC smoke munitions are reviewed. HC smoke is produced by the combustion of a mixture of hexachloroethane (HCE), zinc oxide and aluminum. The major component of the smoke is zinc chloride. There are also several chlorinated organic compounds in the smoke, some of which are documented potential human carcinogens. Exposure of unprotected soldiers to high concentrations of HC smoke for even a few minutes has resulted in injuries and fatalities. Therefore, it must be emphasized that this smoke should never be employed in enclosed areas and that all personnel must be compelled to mask when HC smokes are employed. In addition, HCE, the organic component of the smoke mixture, while it is not a major component of the smoke, has been recognized as a possible human carcinogen and has been shown to accumulate in the blood of exposed workers. HCE thus constitutes an occupational hazard to the workers in Army ammunition plants where smoke munitions are assembled, loaded, and packed.

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INTRODUCTION

Ever since smokeless powder came into common use, armies have sought means to create, for tactical advantage, a haze similar to that which blanketed the battlefield when black powder was the standard propellant for guns and rifles. An array of tactical smokes has been developed and used in wartime operations for obscuration, screening, and deception and for signalling or identification of targets. White smoke grenades are used to cover or screen individual vehicles, while colored smoke grenades are used to mark or spot specific locations. Obscuring smoke is used on enemy targets to degrade the enemy's vision, thereby hindering target acquisition as well as hampering the enemy's visual communication and inhibiting his movement. Screening smoke, used to conceal the location and activities of a force, is deployed in the area of friendly forces, or between the enemy and friendly forces (Department of the Army, 1978). Various chemical mixtures have been used to produce obscurant and screening smokes since the beginning of World War I. The effectiveness of each smoke depends on its ability to reflect, refract, and scatter light rays so as to obscure visibility. For this reason, all military smokes consist of aerosols with particle dimensions approximating the wavelength of the portion of the electromagnetic spectrum that they are designed to obscure (0.4 to 0.8 μm for visible light). Among the most widely used smoke munitions are those which produce smoke by burning a mixture of a chlorinated hydrocarbon and zinc oxide (ZnO). The hydrocarbon that is now generally employed in these smoke mixtures is hexachloroethane (HCE, chemical formula C_6Cl_6), and the generic name attached to HCE-ZnO smokes and the munitions that produce them is HC smoke. ("HC smoke," in this report always refers to the smoke mixture or the smoke produced from it, and "HCE" is the abbreviation used for the chemical compound hexachloroethane.)

The precursor to HC smoke was developed by Captain E.F. Berger of the French Army. Berger's mixture contained carbon tetrachloride, powdered zinc, and zinc oxide, which, when ignited, produced an aerosol of zinc chloride and sooty carbon particles. In the period between the world wars, several refinements of the Berger mixture were made by the U.S. Army Chemical Warfare Service, starting with replacement of the volatile liquid carbon tetrachloride with HCE, which is a solid at room temperature. Later changes in the chemical mixture were made to overcome difficulties caused by the limited availability of some of the chemical ingredients and the explosive nature of others, leading to the Type C composition (see Table 1) widely employed today in HC smoke producing devices. This composition, which is ignited manually or electrically by a pyrotechnic starter mixture, has been used in artillery shells, grenades, and bombs. Current type classified weapons used for deploying HC smoke are 105mm and 155mm shells, M8 grenades, and ABC-M5, M4A2, and M1 smoke pots (Taylor, 1993). Most of the HC mixture produced for the U.S. Army is used in smoke pots. These are cylindrical metal canisters containing the HC mixture along with a pyrotechnic charge, which, when ignited by the firing mechanism within the canister, provides the heat necessary to generate the HC smoke. The M1 ten pound HC smoke pot measures 9 in. by 5.5 in. diameter and produces smoke for 5 to 8 minutes. The M5 thirty pound HC smoke pot measures 9.5 in. by 8.5 in. diameter and produces smoke for 12 to 22 minutes. Smoke pots are ordinarily used to provide small area screens and to supplement other smoke sources by filling holes in screens and

helping to rapidly establish screens (Department of the Army, 1982). HC smoke pots were used extensively in World War II to provide preliminary screens during the approximately five minutes needed to set up large thermo-mechanical fog oil smoke generators. In addition, pots were used by the U.S. Army and Navy to cover harbors in Italy and North Africa and in both the European and Pacific theaters, on land and water, to screen supply routes, bridge construction, amphibious operations, tanks, ammunition dumps, troop concentrations, and ground operations and to hide mortar flash (Cichowicz, 1983). The AN M8 grenade produces smoke for about 2 minutes. This hand grenade is used, along with the M18 colored smoke grenade, for signalling and, by small units or individual soldiers, for creation of obscurant or screening smoke (Department of the Army, 1978).

COMPOSITION OF HC SMOKE GENERATING MIXTURES AND OF HC SMOKES

Materials

HC smoke mixtures may differ in composition depending on the manufacturer and use. Grenades, pots, and projectiles produced for use by the United States military forces contain Type C HC smoke mixture (Table 1), with some variation in the amount of aluminum. Many of the formulations used by other countries do not contain aluminum. Each type of American munition (grenade, artillery shell, and smoke pot) contains slightly different chemical mixes for producing HC smoke (Novak, 1983). Military smoke mixtures used by the British contain 46 percent HCE, 29-47 percent zinc oxide, and 7-25 percent calcium silicide (Jarvis, 1970). A Swedish mixture contains 40-48 percent zinc, 48-56 percent HCE, 3 percent magnesium oxide, and 1 percent potassium bichromate (Karlsson et al., 1986). HC smoke pots, bombs, grenades, and candles produced for non-military uses (e.g., for training fire fighters) may also differ in composition (Zey and Richardson, 1988). Marrs et al. (1983) used two pyrotechnic mixtures which differed in the quantities of HCE and zinc oxide; some minor components were present in one mixture but not in another.

Katz et al. (1980) sampled and analyzed the components and impurities at the top, middle, and bottom of each of ten M5 smoke pots (two each from five different manufacturers' lots). Their data are summarized in Table 2. The cadmium content of one of the lots of smoke pots exceeded the military specifications. Based upon a zinc oxide content of 46.7 percent (Table 1) and a maximum allowable content of 0.2 percent cadmium oxide in the zinc oxide (Department of the Army, 1988), the maximum cadmium content of the smoke mix should not exceed 0.082 percent. The 0.15 percent cadmium that was consistently found at all three levels of both representatives of one lot of M5 smoke pots was almost double the allowable content.

Products

The smoke mixture in the pot or grenade is initially ignited by a pyrotechnic starter mixture and is then self-perpetuating and exothermic. The overall reaction has been summarized by Cichowicz (1983):

$$2Al + C_2Cl_6 + 3\,ZnO \rightarrow 3\,ZnCl_2 + Al_2O_3 + 2\,C + \text{heat}$$

Type C smoke mix (Table 1) contains less than the proportion of aluminum required to balance the above equation. This causes the formation of carbon monoxide (CO) in place of a portion of the particulate carbon that would be produced by burning a mixture containing the stoichiometric proportion of aluminum. Zinc chloride ($ZnCl_2$) leaves the reaction zone as a hot vapor. On cooling beyond the condensation point, it nucleates to form an aerosol that rapidly absorbs water from the surrounding atmosphere (Cichowicz, 1983). These hydrated $ZnCl_2$ particles, which constitute the principal component of the aerosol, scatter light and thereby

obscure vision. (Katz, 1980). The alumina (Al_2O_3) and carbon particles also contribute to the obscurant effect, but these particles are not hygroscopic and do not grow in size.

Table 1. HC Mixture (Type C)

INGREDIENT (Cichowicz, 1983)	**Percent (approximate) in HC Mixture**
Grained aluminum[a]	6.7
Zinc oxide	46.7
Hexachloroethane	46.7
IMPURITIES (Department of the Army, 1988)[b]	**Percent (maximum)**
Lead as PbO	0.280
Cadmium as CdO	0.093
Arsenic as As_2O_3	0.047
Antimony as Sb_2O_3	0.047
Water soluble salts	0.233

a. The aluminum content is intentionally varied in different mixtures for different munitions, and even in different zones in the same munition, in order to control the rate of burning. b. Based upon maximum content permitted in technical grade zinc oxide, grade A (for manufacture of pyrotechnic mixtures).

Analysis

Katz et al. (1980) also characterized the smoke produced when the M5 smoke pot was fired out of doors in the normal manner and when miniature versions of the smoke pot were fired in the laboratory.

Field Study. One M5 smoke pot was ignited in the open. Samples of the aerosol were collected in evacuated flasks, four of which were about 15 cm downwind from the burning pot and one was 2 meters downwind. The flasks were analyzed for hydrogen chloride (HCl) and CO and for various chlorinated organic vapors: phosgene, tetrachloromethane, tetrachloroethylene, HCE, and hexachlorobenzene (HCB). The results are shown in Table 3. In all samples, CO was below the detection limit of 1 ppm. A mass

median diameter of 1.0 μm was measured, but this was not accurate because, as the investigators noted, the cascade impactors used were incapable of capturing particles smaller than 0.65 μm. A Royco particle counter was also used, but the particle concentration exceeded its upper limit of 1000 cm^{-3} (Katz et al., 1980).

Table 2. Analysis of Composition of 10 M5 HC Smoke Pots (Adapted from Katz et al., 1980)

INGREDIENTS	Percent in HC Mixture		
	Mean	Range	Standard Deviation
Aluminum[a]	5.4	4.4-7.7	0.66
Zinc oxide[a]	46.4	44.3-48.1	1.46
Hexachloroethane[b]	45.5	42-49	1.93
IMPURITIES	**Parts per million (ppm) in HC Mixture**		
	Mean	Range	Standard Deviation
Mercury[c]	0.48	0.44-0.6	0.095
Arsenic[c]	2.9	0.1.-5.0	2.1
Cadmium[d]	583 (0.06%)	50-1544 (0.005-0.15%)	498
Lead[d]	451 (0.045%)	26-926 (0.003-0.09%)	344

NOTES: a. Atomic absorption spectrophotometric (AAS) analysis of two samples each from three separate zones from two different smoke pots from each of 5 different lots: a total of 60 samples.

b. Gas chromatograph analysis of 30 samples, one from each layer of each of the 10 pots sampled.

c. Commercial laboratory analysis (method not given) of one sample each from 5 lots of M5 smoke pots.

d. AAS analysis of 54 samples (samples from one zone of one smoke pot were lost).

Table 3. Chemical Analysis of Vapor Products from Field Test of One M5 Smoke Pot (Adapted from Katz et al., 1980)

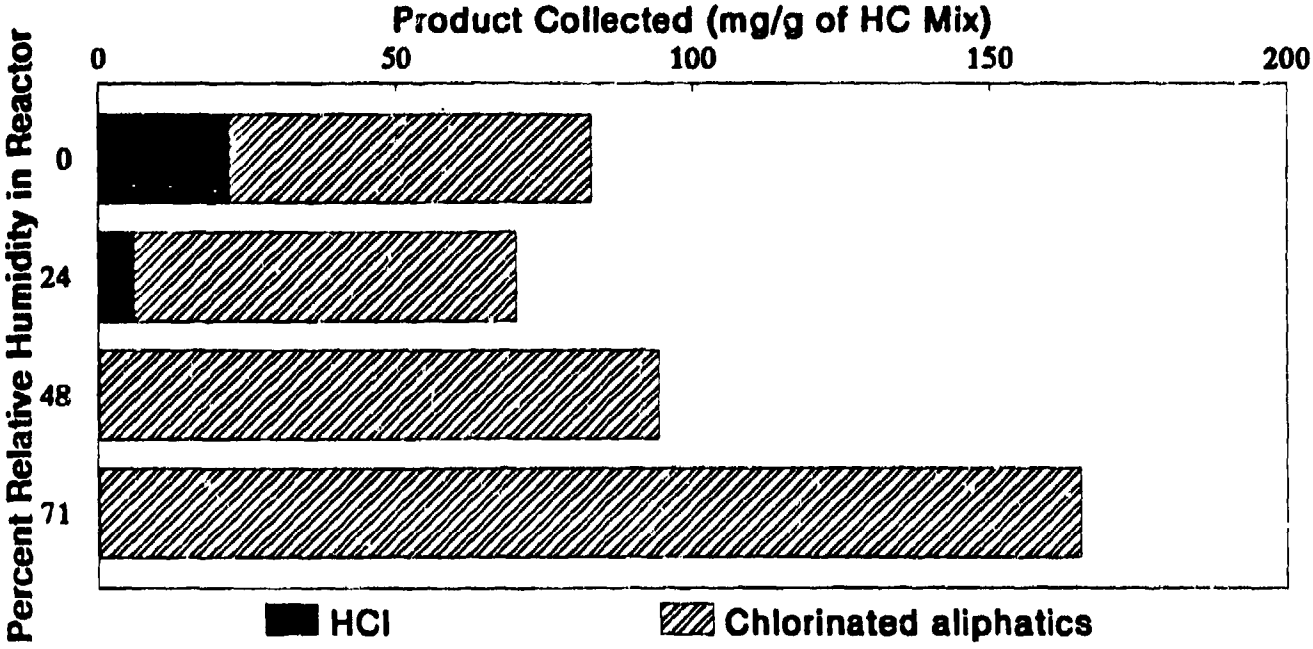
Distance from pot	HCl ppm	$COCl_2$ ppm	CCl_4 ppm	C_2Cl_4 ppm	C_2Cl_6 ppm	C_6Cl_6 ppm
15 cm	3875	24	33.5	79.5	40[a]	99[a]
Concentration Range	1128-6822	16-30	8-57	9-192	40-40	95-103
Standard Deviation	2805	7.1	20	81		
200 cm	1137	1	1	2	nd[b]	nd

NOTES: a. Two samples only. b. nd = not determined.

Laboratory Studies. Katz and his colleagues (1980) performed a series of experiments in glass and stainless steel vessels to determine the trace gases produced by burning the HC mix. The most closely-controlled of these experiments were conducted in restricted-opening steel reactors in which humidity was carefully measured and controlled. The same chemical species found in the field tests were also present in the vapor phase in the stainless steel reactor. In addition, 9 to 37 ppm CO was present in all samples. The results of these tests are summarized in Table 4. Variation in relative humidity had no apparent effect upon the CO concentration. However, relative humidity did have an effect upon the concentrations of HCl and the chlorinated hydrocarbons. As can be seen in Figure 1, HCl was not found in appreciable amounts at humidities greater than 24 percent. The chlorinated aliphatic hydrocarbons in Figure 1 represent the sum of the yields of tetrachloromethane, tetrachloroethane, and hexachlorethane in mg/g of original HC mixture (taken from an M5 smoke pot). Phosgene was also measured at yields between 0.6 and 11 mg/g HC mix, and HCE varied between 4 and 9 mg/kg HC mix in the reactor vapors. There are undoubtedly many more components present in the vapor phase of HC smoke. Henry et al. (1981) found hexachloro-1,3-butadiene, but did not provide quantitative data. Karlsson et al. (1986, 1991) analyzed the composition of the smoke from two Swedish HC smoke mixtures. HCB, hexachlorobutadiene, and HCE (in relative proportions of 20:2:1, respectively) were present in condensates from the combustion products of a smoke mixture containing 40-48 percent zinc and 48-56 percent HCE. A 30-second smoke candle used for firefighter smoke simulation was burned in a cardboard box and sampled for gases, vapors, metals, and inorganic acid (Zey and Richardson 1988). These analyses showed that the majority of the particles in the smoke cloud consisted of zinc compounds and HCl. There

were more than 50 chlorinated hydrocarbons in a gas chromatograph of the vapors, including carbon tetrachloride, trichloroethylene, perchloroethylene, hexachloroethane, and possibly hexachlorobutadiene.

Figure 1. Effect of Humidity on HCl and Chlorinated Aliphatics in HC Smoke



Data from stainless steel reactor measurements of Katz et al. (1980)

Table 4. Gaseous Products Generated by Burning Type C HC Mix in a Restricted-opening Steel Reactor
(Adapted from Katz et al., 1980)

Percent Relative Humidity	Product Collected, mg/g of HC Mixture						
	CO	HCl	$COCl_2$	CCl_4	C_2Cl_4	C_2Cl_6	C_6Cl_6
0	29	22	4	15	43	2	4
24	19	6	2	15	43	6	4
48	23	<0.3	2	21	56	17	6
71	21	<0.3	3	20	133	18	6

The aerosol particles were composed primarily of $ZnCl_2$, with 1-2 percent aluminum. Lead and cadmium were present in proportion to their content in the original HC mix. A

mass median particle diameter of about 0.3 μm was observed, 5 minutes after generation, for all aerosols in the chamber experiments. Aerosol concentrations at this time were 1 to 10×10^6 particles per cm^3. With aging, the number of particles decreased and the mean particle size increased. In the outdoors, where most smokes are generated, the process of particle growth by coagulation would not be as rapid, since it is attenuated due to dispersal of the particles over time and space, allowing for fewer collisions among the particles as the cloud expands.

Analysis of Smoke from Fire Training Devices. The National Institute of Occupational Safety and Health (NIOSH) conducted experiments with several HC smoke generating devices from smoke candles to white smoke pots (produced by Superior Signal Company, Inc., Spotswood, NJ) to aid in evaluating the health hazard to fire fighters exposed to these smokes during training exercises (Zey and Richardson, 1988). Smoke generating devices were burned in a 6000-ft^3 ground floor room with windows and doors closed (but floor and ceiling grilles were apparently open), and sampling was conducted for 25 minutes before the doors were opened and the building allowed to clear. In the preliminary set of tests, two 3C smoke bombs, which weighed less than one-half pound each and were capable of producing 40,000 ft^3 of smoke according to the manufacturer, were ignited simultaneously in one test; and one white smoke pot (shipping weight 4 lbs., 500,000 ft^3 of smoke) was ignited in another test. The final set of tests was conducted four months later. Smoke was produced in the presence of a firefighter trainer, upon whose advice the number of 3C smoke bombs was increased on the second day of the final set of tests in order to better approximate the smoke density in a typical training drill. Smoke candles and grenades were also combusted during this set of tests. In the first set of tests, chloroform, tetrachloromethane, perchloroethylene, HCE, and hexachlorobutadiene were detected from one or the other of the devices tested, and trace amounts of octachlorocyclohexadiene and HCB were found. Hexachlorobutadiene and carbon tetrachloride were detected in the smoke produced by the white smoke pot, but not in the other HC smokes. The results of sampling for the other components in the second set of tests are summarized in Table 5.

Table 5. Range of Airborne Concentrations of Smoke Cloud Components from Five Separate Smoke Generating Devices, April, 1986
Concentrations in mg · m^{-3}
(Adapted from Zey and Richardson, 1988)

SMOKE DEVICES TESTED:	Candles (6)	3C Bombs (6)	Grenades (2)	4-lb. Pot (1)
SMOKE COMPONENTS				
Hydrogen Chloride	2-17	27-36	38-110	12-421
Tetrachloromethane	ND[a]	ND	(4.8-5)	22-43
Perchloroethylene	19-29	80-96	145-163	282-596
Hexachloroethane	5-11	15-18	16-24	5-39
Zinc Chloride	34-75	120-143	133-134	99-498
Percent Zinc as $ZnCl_2$	50-70	80-90	60-70	90-95
Lead	0.05-0.07	0.22-0.25	0.09-0.1	0.12-0.54

a. ND = Not Determined.

The concentration of $ZnCl_2$ in the smoke varied with the smoke-generating device. Zinc chloride ranged from 50 percent with the one minute candle to 90-95 percent for the white smoke pot. The remaining zinc was present mostly as zinc oxide. The concentrations measured by Zey and Richardson (1988) are not typical of military smoke exercises, and the smoke munitions differ from those used by the U.S. Army. However, the results confirm the presence of components found in HC smoke by other investigators.

WORKPLACE EXPOSURE: CHEMICAL AND PHYSICAL PROPERTIES OF HEXACHLOROETHANE, ZINC OXIDE, AND GRAINED ALUMINUM

Hexachloroethane

While HCE is one of the two major components of the smoke mixtures used in munitions and in smoke devices used for firefighter training, it is present only as a minor contaminant in the smoke. Hexachloroethane is a white crystalline solid with a camphor-like odor. It has a high vapor pressure which allows for a maximum air concentration of about 770 ppm at 25°C. Because of this volatility, it constitutes the major industrial health problem associated with manufacture of HC smoke munitions in U.S. Army ammunition plants. With an odor threshold of 0.15 ppm, HCE has adequate warning properties (Santodonato, 1985).

Zinc oxide and aluminum

Metal fume fever has been associated with freshly formed zinc oxide in the workplace (Taylor, 1986), but the zinc oxide used in the HC mix is not freshly formed and is treated as a nuisance dust, with an 8-hr TWA-TLV of 10 mg · m^{-3} (ACGIH, 1992). Pulmonary aluminosis, a severe disease of the lung characterized by progressively worsening cough, dyspnea, and spontaneous pneumothorax, has been associated with inhalation of "pyropowder" aluminum flakes coated with an aliphatic oil, used in pyrotechnics for short periods of time in Germany and Great Britain. The etiology of the disease has been ascribed to the aliphatic oil coating, which prevented the initial oxidation of the surface of the aluminum flakes, but the oil coating was removed in the intracellular milieu, resulting in a vigorous exothermic reaction which was the cause of the tissue damage characterizing pulmonary aluminosis (Dinman, 1987). The "grained aluminum" in Type C HC smoke mix is of much greater size, is not coated with aliphatic oil, and is not associated with any occupational disease (Brooks, 1986). Granular aluminum has been shown to be "biologically inert" when instilled into the tracheas of rats (Corrin, 1963), and aluminum powers inhaled by hamsters and guinea pigs caused no pulmonary fibrosis (Gross et al., 1973). Thus, only the properties of HCE need be considered in evaluating the occupational health risks to workers involved in production of HC smoke munitions.

PHARMACOKINETICS OF MAJOR COMPONENTS OF HC SMOKE

No studies have dealt with the pharmacokinetics of HC smoke *per se* in animals or humans. The pharmacokinetics of many of the components identified in HC smoke have been studied after ingestion rather than after inhalation, the common route by which humans are exposed to HC smoke.

The largest part of the mass of HC smoke consists of suspended liquid droplets. Solid particles and vapor components are also found (Katz et al., 1980). The site and extent of deposition of particles in the human respiratory tract is dependent upon their size and shape. Fifty percent of particles with diameters of 4 μm (and greater proportions of smaller particles, e.g., 97 percent of 1 μm-diameter particles) enter into the alveoli (ACGIH, 1992), where their fate depends upon their solubility. Soluble particles that come into contact with alveolar walls are eventually dissolved into the bloodstream. Insoluble particles deposited upon alveolar walls are slowly removed by the action of macrophages. The particle-laden macrophages travel up the mucociliary escalator and may be expectorated and swallowed, thereby entering the body via the gastro-intestinal tract. The acidity of the HC smoke particles can be expected to inhibit the cleansing action of the cilia and the macrophages. Particles larger than 10 μm may be trapped in the nasal passages (Brain and Valberg, 1979; Hinds, 1982). Vapors enter into the alveoli, where, depending upon their solubility and other transport properties, they are partitioned between the bloodstream and the exhaled airstream.

Hexachloroethane

Chlorinated ethanes in general are rapidly absorbed following ingestion or inhalation. They are metabolized by dechlorination and/or oxidation to alcohol derivatives which are then excreted in the urine or expired air (Santodonato, 1985). In addition, Town and Leibman (1984) showed that *in vitro* metabolism of HCE by rat liver microsomes produced pentachloroethane and tetrachloroethylene. Olefin formation was attributed to "...a cytochrome P-450-mediated *vic*-bisdechlorination reaction, which may involve a free radical intermediate".

The U.S. Environmental Protection Agency (USEPA) Office of Water (Gordon et al., 1991) reviewed the pharmacokinetics of HCE and discussed absorption, distribution, excretion, and metabolism of HCE were discussed in detail. In summary, they noted that HCE can be absorbed following inhalation, ingestion or dermal contact and that it is preferentially accumulated in fat. Kidney levels are significantly higher in male rats than in females (Gorzinski et al., 1985). The main route of excretion is expired air; urinary excretion plays a minor role. In rats and mice, Mitoma et al. (1985) administered a single dose of 1,2-^{14}C-HCE after oral administration of the maximum tolerated dose (500 mg/kg for rats and 1000 mg/kg for mice) of unlabeled HCE for 4 weeks, 5 days/week. Recovery of the ^{14}C label in the expired air was 65 percent of in rats and 72 percent in mice. Only 2 percent of the recovered radiolabel was in the form of carbon dioxide; the remainder was assumed to be non-metabolized HCE. Several metabolites were demonstrated both *in vivo* and *in vitro*, and reductive dechlorination was proposed as the method of metabolism. Tetrachloroethylene was the principal metabolite found in extracts from the urine and feces of sheep fed 0.5 g/kg HCE (Fowler, 1969). Tetrachloroethylene was also the major metabolite formed under anaerobic conditions with liver microsomal fractions (Nastainczyk et al. 1982; Town and Leibman, 1984). Plasma levels of HCE in an exposed worker declined from 11.05 $\mu g \cdot m^{-3}$ to below detection limits ($< 0.02\ \mu g \cdot m^{-3}$) after approximately six weeks of non-exposure, consistent with a half-life of HCE in the plasma of less than one week (Seldén et al., 1993).

Hexachlorobenzene

The pharmacokinetics of HCB was reviewed by the International Agency for Research on Cancer (IARC, 1979). Hexachlorobenzene administered orally to rats was absorbed slowly from the gut, mainly via the lymphatic system, and after 48 hours, was stored extensively in the fat (Iatropoulos et al., 1975). In rats, more ^{14}C label from ^{14}C-HCB, administered orally or intraperitoneally, was recovered in the feces than in the urine. Unchanged HCB was found in both feces and urine. The major metabolites in the urine were pentachlorophenol, tetrachlorohydroquinone, and pentachlorothiophenol (Engst et al., 1976; Koss and Manz, 1976; Mehendale et al., 1975; Renner and Schuster, 1977). Radiolabeled HCB, given orally to monkeys for a year, was recovered mainly in the feces, and was 99 percent unchanged. Between 5 and 7 percent of the administered dose was

found in the urine: 50 percent of this as pentachlorophenol, 25 percent as pentachlorobenzene, the remainder as unchanged HCB and unidentified metabolites (Rozman et al., 1977).

Zinc Chloride

The toxicokinetics of ingested zinc have been studied in animals and humans, but the fate of inhaled $ZnCl_2$ particles has not been well studied (Donohue et al., 1992). Payton et al. (1982) measured intestinal uptake of oral doses of radiolabeled zinc chloride ($^{70}ZnCl_2$) in adult humans. Up to 55 percent of the radiolabeled compound was absorbed at low dose levels (90 μmol or less). Absorption decreased to 25 percent when 900 μmol of zinc was administered. Istfan et al. (1983) also found that reduction of dietary zinc resulted in a significant increase in absorption of a trace oral dose of $^{70}ZnCl_2$. In ostomy patients, Payton et al. (1982) showed that zinc is absorbed before it reaches the colon. They found that average absorption of zinc did not decrease in these patients, at a dose level of 92 μmol, while in patients with intestinal malabsorption, the average absorption was only 30 percent. In guinea pigs, skin absorption of $ZnCl_2$ was minimal: less than 1 percent of a percutaneous dose was absorbed in 5 hours (Skog and Wahlberg, 1964). In two soldiers who developed ultimately fatal adult respiratory distress syndrome (ARDS) after brief exposures, unmasked, to high concentrations of HC smoke, the plasma zinc concentrations slowly increased during the course of the illness. Intravenous infusion of acetylcysteine, a chelating agent, brought this concentration down to normal levels for a few days following treatment, with concurrent elevation of zinc concentration in the urine. On autopsy, the zinc levels in the lungs of one patient, and in the striated muscle tissue of both, were slightly higher than those of a control group of 10 males of a similar age who had died after trauma. Zinc levels in other organs and tissues from the HC smoke fatalities were within the range of those exhibited by the controls (Hjortsø et al., 1988). The roles of metallothionen and interleukin-1 in regulation of zinc homeostasis are discussed in Nutrition Reviews (1989).

HUMAN EXPOSURE

Human Exposure to HC Smoke

The effects of exposing humans and animals to HC smokes has been reviewed by Cichowicz (1983). He cautions that while the toxicity of each compound found in HC smokes is to some degree understood, little is known about the possible synergistic or antagonistic effects when the components are combined.

Military Exposure Incidents.

Pare and Sandler (1954) reported the symptoms of an 18-year-old man who was exposed for 10 minutes during an army exercise in which a smoke canister was set off in a staircase inside a house. Initial symptoms were a dry cough and lack of appetite, followed

by vomiting, shortness of breath, drowsiness, and nosebleed (on the second day). Breathing difficulties and lung sounds progressed for six days prior to his admission to the hospital. At this time, a chest x-ray showed patchy consolidation throughout both lungs. Three weeks later, there was only a diffuse fine mottling, which was also apparent after one month, when clinical symptoms in the chest had cleared. The mottling cleared after 6 weeks, and 10 months later the clinical and radiological picture was normal. The authors noted that in contrast to phosgene poisoning, where the radiological signs clear in less than a fortnight, the mottling in the lung resulting from exposure to Zn-HCE smokes persists much longer.

Lange and Kirk (1986) reported on two cases of bronchial asthma in elderly women precipitated by exposure to $ZnCl_2$ smoke for 75 minutes. One of the cases ended fatally. These cases were complicated by advanced age and pre-existing heart and lung disease. Pedersen et al. (1984) reviewed cases of $ZnCl_2$ smoke poisoning and summarized the symptoms as cough, sore throat, metallic taste, hoarseness, nausea, and vomiting. They noted complications in the form of bronchospasm and chemical pneumonitis which have been described following inhalation of nonhydrolized $ZnCl_2$ particles.

Evans (1945) reported an incident in Malta where 10 of 70 people died upon exposure to concentrated "$ZnCl_2$" smoke released in a confined space. The symptoms were a feeling of constriction in the chest, retrosternal and epigastric pain, laryngeal stridor, and red and running eyes. The majority had a paroxysmal cough, some with abundant blood-stained sputum. Other symptoms among members of the group were pale gray cyanosis, difficulty breathing and speaking, pain in the throat and nasopharynx, epigastric pain and nausea, with some retching and vomiting, and reddened conjunctiva or burns of the cornea. Some expectorated sloughs of bronchial mucous membrane.

"A striking feature was the absence of abnormal physical signs in the chest, only a few having scattered moist adventitious sounds." This was true even in four who developed bronchopneumonia, who finally displayed moist sounds over both lungs. Generally, Evans' findings confirmed the clinical impression that the effect of the smoke was primarily one of severe damage to the mucous membrane of the nasopharynx and respiratory tract. The air passages were far more damaged than the lung itself. The deaths occurring immediately or within a few hours after exposure were apparently the result of shock and profuse pulmonary edema. When death did not occur immediately, bronchopneumonia developed as a complication of the initial lesion.

Matarese and Matthews (1986) described a lung injury in a 20-year-old male exposed for an estimated five minutes to $ZnCl_2$ fumes from a military smoke grenade which was functioned inside a closed civilian vehicle. They reported the experience of their patient as unique in that he displayed pathologic conditions "...consistent with an acute respiratory distress-like syndrome" (laryngeal, tracheal, and bronchial mucosal edema and ulceration, interstitial edema, interstitial fibrosis, alveolar obliteration, and bronchiotis obliterans), but survived his high exposure to HC smoke without treatment.

In contrast, Milliken et al. (1963) reported on a fatal case of interstitial pulmonary fibrosis in a fireman exposed for "several minutes" to a smoke bomb during a fire prevention exercise. Another fireman who had withdrawn "almost immediately" from the scene was also treated. Both patients complained of nausea, sore throat, and chest tightness, especially upon deep breathing. The briefly-exposed patient was discharged two days after the incident. At this time, the severely-exposed patient still had elevated temperature and chest pain on deep breathing but was also apparently recovering. However, 30 hours after exposure he developed rapid breathing, then cyanosis, confusion, and coma. The symptoms progressed, and the patient died 18 days after his exposure. Chest radiographs on the first and 18th day showed the same patterns as other severe cases of $ZnCl_2$ poisoning. The prolonged period of survival allowed the patient to develop advanced pulmonary fibrosis, not seen in patients with shorter survival times.

Two soldiers exposed to smoke bombs at an estimated dose level of 3500 mg · min · m^{-3} were examined by Blom and Hven (1986). "Immediately after exposure, both of the patients developed respiratory insufficiency and lost consciousness. The patients were ventilated with oxygen and recovered consciousness after 24 hours."

Wang et al. (1987) reported the case of a 21-year-old Chinese man who activated a smoke grenade under a poncho in order to drive away attacking bees. Immediately upon exposure to the smoke (after only 4 breaths) he felt a burning sensation in his throat and became weak and severely dyspneic. His eyes began to water and copious amounts of thick, clear mucus discharged from the nose and mouth. After 2 weeks he still had a slight cough and was breathless on exertion but his condition began to improve. Chest x-rays showed diffuse fine nodulation in both lung fields, pneumomediastinum and subcutaneous emphysema. Pulmonary function was restrictive and this was consistent with increased pulmonary edema. Pulmonary function improved after 2 months, and was normal at 9 months after exposure. The smoke was produced by a mixture of zinc oxide, HCE and calcium silicide. Because analysis by the Singapore Armed forces showed that ignition of this mixture produces phosgene, acetylene and carbon dioxide, Wang et al. (1987) attributed the symptoms to phosgene. But this claim was disputed by Karlsson (1988), who stated that "...the concentration of phosgene in the smoke is generally very low and probably of limited importance from a toxicological point of view....A more plausible explanation of the symptoms described by Wang et al. is the presence of $ZnCl_2$ in the smoke."

Hjortsø et al. (1988) described an incident in which 5 soldiers were injured by inhalation of $ZnCl_2$ smoke during a training exercise which took place inside a 30 m long pipe, 1.75 m in diameter. Two of the soldiers, who were exposed, unmasked, for one or two minutes, developed severe ARDS over the course of the following two weeks, and died 25 and 32 days after exposure. These men had elevated temperatures, but there was no evidence of sepsis either during the course of the disease or upon autopsy. Lung vascular injury in these two soldiers was assessed at autopsy (Homma et al., 1992). The lungs showed fibrosis within the alveoli and within the outer elastic layer of the pleura. Pulmonary veins and arteries of the two fatal cases were significantly thicker than normal.

$ZnCl_2$ was recognized as the most toxic component of the smoke by Homma et al. (1992). They proposed that the hydrochloric acid released by $ZnCl_2$ was the trigger for the ARDS incidents. The rise in body temperature in these patients was attributed by Homma et al. (1992) to "metal fume fever." The three other soldiers, who were wearing "ill fitting gas masks" developed severe coughing and dyspnea immediately after exposure, but these individuals recovered, and their lung function was nearly normal after 12 months, although they still complained of slight dyspnea on exercise.

A U.S. Marine Corps lieutenant was exposed, unprotected, inside a building, to smoke from an M8 smoke grenade (Blount, 1990). He quickly developed dyspnea, cough, sore throat, and chest tightness. Two and one half hours later, he was admitted to a U.S. Army hospital with elevated pulse rate and body temperature, nausea, chills, and malaise. After being treated overnight with oxygen, antipyretics, and nebulized bronchodilators, he was asymptomatic and was released, diagnosed with metal fume fever. The evening of his discharge, he was readmitted with the same, but worsened symptoms as the previous day. Forced vital capacity was 80 percent of the predicted value. He was treated with oxygen, bronchodilators and, for the first evening, antibiotics. The next morning, the diagnosis was changed to "serious" metal fume fever, the antibiotics were discontinued, and corticosteroids begun. He improved rapidly and was discharged, without symptoms, on day 5.

Seven British soldiers were exposed for about 10 minutes to HC smoke in an enclosed environment. They were admitted to an army hospital, treated with oxygen therapy, and discharged the following day. Allen et al. (1992) treated one patient who was readmitted 60 hours after this exposure. This patient complained of a dry cough and low exercise tolerance. His body temperature and respiratory rate were elevated. Chest x-rays showed widespread alveolar shadowing. A restrictive defect in breathing was revealed by spirometry, and he suffered from hypoxemia. Treatment consisted of high flow oxygen, intravenous hydrocortisone, followed by prednisone, and twice daily doses of penicillamine. His condition deteriorated over the next 48 hours as shown by chest x-ray, but there was then a gradual improvement in symptoms, arterial oxygen, and chest x-ray. Breathlessness and subnormal lung function continued twelve months after his exposure, but his chest x-ray had returned to normal by that time—an unusual finding in this case—attributed by the authors to early administration of penicillamine.

Civilian Exposure Incident.

In 1979, approximately 163 people were exposed to a $ZnCl_2$ aerosol (generated by the ignition of equal quantities of ZnO and HCE with a small amount of calcium silicide) during an airport disaster drill (Schenker et al., 1981). The incident occurred out of doors and, although smoke concentrations were not measured, it was possible to categorize exposures. One group was heavily exposed because, when wind blew a dense cloud of smoke in their direction, they obeyed previous instructions not to move. Medical questionnaires given to a group of 82 "passengers" and 28 physician or nurse "attendants," all of whom were associated with a local health center, revealed that symptoms correlated

positively with the degree of exposure. No evidence of lower-airway abnormalities attributable to smoke exposure was found among the participants who submitted to spirometry. Early symptoms among those who reported adverse effects were cough and hoarseness or sore throat which declined with time. Eleven victims had symptoms of nausea, fatigue or headache beginning 2-20 hours after the exposure to smoke, and symptoms lasted a minimum of 6 hours. Three of these had light exposure to the smoke; the exposures of the remaining eight were categorized as "moderate to heavy."

The respiratory symptoms (metallic taste, hoarseness, sore throat and cough) reported in this incident are anatomically referable to the pharynx, larynx and upper airways. Wheezing, a symptom characteristic of middle and lower respiratory tract injury was reported in 30.2 percent of the victims with moderate to heavy exposures. "The predominance of upper respiratory tract symptoms correlate well with the physical properties of $ZnCl_2$ aerosol." Zinc chloride is extremely soluble. While the dry particles of $ZnCl_2$ are in a respirable size range, the aerosol is extremely hygroscopic and forms solution droplets that will increase in size in the high humidity of the respiratory tract. In the incident investigated by Schenker et al (1981), the pattern of injury is more consistent with the physiologic properties of $ZnCl_2$ than with the action of agents such as phosgene, which are relatively insoluble and tend to reach the alveoli before they begin to act. The high incidence of upper respiratory tract symptoms, some of which lasted 1 to 2 weeks, is consistent with the extreme toxicity of $ZnCl_2$ aerosol (Schenker et al., 1981). Milliken et al. (1963) suggested that the trachea and bronchi initially become more necrotic and inflamed than lung tissue because $ZnCl_2$ is soluble and is immediately absorbed in high concentrations in the upper respiratory tract. Lower concentrations reach the lung tissue.

Human Exposure to Components of HC Smoke

Hexachloroethane.

Hexachlorethane is the component that presents the greatest hazard to workers involved in the manufacture, loading, and packing of munitions containing the HC mixture. Five weeks after commencing loading and packing operations, plasma levels of HCE in workers rose from 0.08 $\pm$ 0.14 μg/L to 7.30 $\pm$ 6.04 μg/L (Seldén et al., 1993). Air concentrations of HCE in the rooms where HC munitions were milled, pressed, and assembled were generally in excess of the accepted occupational exposure limit of 9.7 mg $\cdot$ m^{-3} (ACGIH, 1992), but workers were provided with compressed-air-fed visors at permanent work stations and with full-piece face masks equipped with a gas and respirable dust filter. Controls, made up of assembly line workers in the same plant and formerly exposed workers, showed no detectable plasma HCE. There are no data linking specific plasma levels of HCE to the occurrence of ill effects in either humans or animals.

Gordon et al. (1991) found no data on the acute or chronic effects of exposure to HCE in the English literature. Santodonato et al. (1985) examined reported cases of

occupational exposure to HCE for the National Cancer Institute (NCI) and reported no evidence for carcinogenicity in humans. Approximately 1500 workers were occupationally exposed to HCE in 1972-1974 (Parker et al., 1979). No ill effects have been reported among workers handling this chemical in the production of HC smoke devices (ACGIH, 1980). However, Saric and Knezevic (1957), Irish (1967), and Fischer (1969) reported that workers in dry cleaning and drug factories complained that HCE caused irritation, but serious symptoms were rare. The serum albumin:globulin ratio changed, but no other sign of liver injury was apparent (Saric and Knezevic, 1957). Liver injury (Sax, 1975) and effects on the central nervous system (Gleason, et al., 1976) have been attributed to exposure. Mild neurologic effects have been reported, usually an inability to close the eyelid. Direct effects upon the eye include conjunctivitis, photophobia and blepharospasm (Grant, 1986). Liver or kidney injury, pulmonary irritation, and damage to blood forming systems are associated with the chloroethanes in general, according to Parker et al. (1979). In the course of their work with HCE, the chemists N. N. Plotnikov and L. N. Sokolov (1947) ingested 30 g of HCE in 3 days and 48 g in 4 days, respectively; they reported only diminished skin sensitivity (Dacre et al., 1979).

Zinc Chloride.

A recent review of the toxicity of $ZnCl_2$ was performed by the Office of Water, USEPA, (Donohue et al., 1992). Acute oral exposures of humans to $ZnCl_2$ have produced vomiting, diarrhea, lethargy, and irritation of the mouth, throat, and stomach. Ingestion can also cause corrosive gastritis and liver necrosis (Hill et al., 1978). Concentrations of 225-450 mg of zinc salts are emetic and produce immediate vomiting. In two reported cases of ingestion of multi-gram quantities of soldering flux containing $ZnCl_2$, the emetic properties of the compound were presumed to have limited the amount absorbed, thereby preventing serious systemic effects (Potter, 1981; Chobanian, 1981). Brown et al.(1964) investigated two incidents of mass food poisoning caused by zinc contamination from galvanized containers which were used to store foodstuffs in one case and punch in the other. In the case of the zinc-contaminated food, symptoms occurred 3 to 10 hours after eating among 300 to 350 of the 400 people who were present where the food was served. Effects included severe diarrhea with abdominal cramping, some tenesmus, and only occasional cases of nausea or vomiting. Half the people with diarrhea had gross blood in their stool. Dry mouth, nausea, vomiting, and diarrhea appeared within 20 minutes among the people who drank the punch. Subsequent effects were general discomfort, muscular pain, and, in one case, double vision. All of the patients in both incidents recovered rapidly after the cessation of acute symptoms. Laboratory tests showed that the emetic dose (as zinc sulfate) was exceeded in both incidents, but where the zinc was ingested with food, the symptoms were delayed and developed in the intestinal tract; whereas in the absence of solid food, symptoms were immediate and were primarily gastric.

The acute toxic effects from inhaling HC smoke are essentially those of its primary component, $ZnCl_2$. Zinc chloride is hygroscopic and astringent and causes severe burns when in contact with moist body surfaces including the respiratory and gastrointestinal tract.

It damages nerve endings in the nasal passages and thereby may cause a permanent loss in the sense of smell. Contact with the eye causes burns and permanently impaired vision. Skin contact with aqueous $ZnCl_2$ solutions causes severe burns especially when contacting a pre-existing wound (Hill et al., 1978). Because of these effects, $ZnCl_2$ is a potential hazard to personnel involved in testing or training (Cichowicz, 1983).

Single exposures to airborne $ZnCl_2$ produce signs and symptoms related to the hygroscopic nature of the compound and its hydrolysis to hydrochloric acid when combined with moisture from the atmosphere or from mucous membranes. All of the effects summarized in the section above, "Human Exposure to HC Smoke," have been attributed to the $ZnCl_2$ component of the smoke. These effects include "dyspnea, chest constriction, retrosternal and epigastric pain, hoarseness, stridor, cough, lacrimation, expectoration, and an occasional hemoptysis" (Donohue et al., 1992). Sequelae include cyanosis, elevated pulse, fever, and widespread edema. Death, when it occurs, is usually attributed to respiratory insufficiency due to the edema in the lungs (Donohue et al., 1992) or to ARDS (Hjortsø et al., 1988; Homma et al., 1992). Prolonged exposure to low concentrations causes temperature elevation, moderate inflammation of the pharynx and conjunctivae, pain in the chest on deep inspiration, headache, slight cough, malaise, and muscular pains. (Cichowicz, 1983). Table 6, reproduced from Donohue et al. (1992), summarizes the effects of inhalation of $ZnCl_2$ smoke at various concentration-time combinations (C · T products).

Table 6. Effects of Exposure to $ZnCl_2$ Smoke Related to C · T Product [a]
(From Donohue et al., 1992)

C · T Product [b] ($mg \cdot min \cdot m^{-3}$)	EFFECT
< 160	Essentially no effect; some awareness of presence.
160-240	Noticeable irritation of nose, throat, and chest.
1700-2000	Marked irritation: Hospitalization and treatment required.
20,000	Severe irritation; chemical pneumonia: Hospitalization and treatment required.
50,000	Massive injury: May be fatal.

a. Effects compiled by Stocum and Hamilton, 1976. b. Concentration x Exposure Time.

The lethal dose of $ZnCl_2$ in humans has been estimated as 50,000 $mg \cdot min \cdot m^{-3}$., which is not likely to be encountered under ordinary field exercise conditions, but "...would be achieved by one generator in a 100 cu. ft. room in 2-3 minutes." (Cullumbine, 1957). At lower concentrations such as 80 $mg \cdot min \cdot m^{-3}$ for 2 minutes, volunteers experienced

slight nausea and cough; at 120 mg · min · m^{-3} for 2 minutes irritation of the nose, throat and chest, with cough and nausea was evident (Cullumbine, 1957).

Hexachlorobenzene (HCB).

An incident involving HCB ingestion by humans in Turkey was reviewed in the IARC (1979) monograph on chlorinated hydrocarbons. Between 1955-59, grain that had been treated with HCB was consumed as food. The estimated daily human intake was 50-200 mg/day; this was associated with 4000 cases of porphyria cutanea tarda. (Mazzei and Mazzei, 1973; Peters, 1976; Peters et al., 1966, 1978). The disease caused 14 percent mortality in children; most affected were boys ages 4-14 years. (Children under 4 rarely develop this disease, but breast fed children developed a condition called "Pink sore", which had a 95 percent mortality (Cam 1960; Peters, 1976).

In a population living near HCB manufacturing plants (but not exposed occupationally), average plasma HCB levels were 3.6 $\mu g \cdot L^{-1}$. There was no evidence of porphyria in these individuals, but plasma coproporphyrin levels were abnormally high (Burns and Miller, 1975). Farm workers exposed occupationally to HCB had average blood HCB concentrations of 0.04 mg · L^{-1} with no evidence of porphyria (Burns et al., 1974).

Seldén et al. (1989) attributed a case of a highly differentiated hepatocellular carcinoma in a 65 year-old male aluminum foundry worker to occupational exposures to HCB or other chlorinated aromatic hydrocarbons, including HCE. The patient had worked in a foundry since the age of 14. During the last 14 years of his employment, he spent part of his time in aluminum smelting, which involved adding a degassing agent containing 30 percent HCE to the melting pots. This activity generated heavy chlorinated hydrocarbon smoke emissions (later found to contain 96 percent HCB) to which the patient was exposed. The authors concluded that the hepatocellular carcinoma may have resulted from exposure to HCB or other chlorinated hydrocarbons formed from the HCE charge used in the aluminum smelting process. The authors also noted that the patient was a moderated consumer of alcoholic beverages, that synergism between alcohol and acute carbon tetrachloride toxicity has been reported, and that there may be a similar mechanism of interaction with regard to HCB and structurally related chlorinated hydrocarbons.

ANIMAL STUDIES

Exposure of Laboratory Animals to HC Smoke

The effects of exposing animals and aquatic organisms to HC smokes and HC smoke components have been reviewed by Cichowicz (1983). The animal studies considered in this document primarily address the acute effects of $ZnCl_2$ following ocular and percutaneous application, intraperitoneal and subcutaneous injection, oral administration, and in drinking water. Only the results of the animal studies which may be useful for assessing the human risk from exposure to HC smokes are addressed below.

Marrs et al. (1983) exposed rabbits and rats to smoke produced by two chemically different mixtures of HCE and ZnO. They observed respiratory tract changes including acute inflammation and in some cases necrosis of the laryngeal and tracheal mucosa. Pulmonary edema and pneumonitis were also observed.

Another study by Marrs et al. (1988) determined the effect on female mice, rats and guinea-pigs of repeated doses of smoke produced by ignition of mixtures containing 44 percent HCE and 32 to 47 percent ZnO. The animals experienced a total of 100 exposures to three dose levels (0, 1.3, 12.8, or 121.7 mg $\cdot$ m^{-3}) distributed at 1 hour/day, 5 days/week for 20 weeks. High-dose guinea-pigs were taken off the study after 3 weeks because of a high mortality rate. The highest dose also caused a significant excess of early deaths in mice. Even so, Marrs noted that the toxicity of the smoke was not as great as might be expected, in view of the results of acute animal studies. The middle and low dose groups appeared to have normal survival rates and there was little or no affect on growth at any dose level. On the basis of survival and growth, the no-effect dose was 12.8 mg $\cdot$ m^{-3}. Marrs also found it surprising, in view of previous studies, that lung damage was not greater in the survivors, particularly those in the higher dose groups. This may be attributed to the long period of observation after exposures had ceased which allowed considerable time for repair. The major histopathological finding was a statistically significant increase in the incidence of alveologenic carcinomas in mice exposed to 121.7 mg $\cdot$ m^{-3} smoke. Inflammatory changes such as edema, emphysema, and macrophage infiltration were seen in the lungs of rats and guinea-pigs. Alveolar macrophage infiltration was a consistent finding in high dose mice (Marrs et al. 1988).

Brown et al. (1990) compared the effects of inhalation of smoke from burning the British mixture of HCE (46 percent), zinc oxide (40 percent), and calcium silicide (14 percent) with those from intratracheal instillation of $ZnCl_2$ in 200-250 g male Porton Wistar-derived rats. Forty rats were subjected to a single 60-minute exposure to a mean smoke concentration of 193 $\mu g \cdot L^{-1}$, giving a C $\cdot$ T of 11,580 mg $\cdot$ min $\cdot$ m^{-3}. Another group of 40 rats was instilled with aqueous $ZnCl_2$ at a dose of 2.5 mg/kg body weight. All treated animals showed respiratory distress, but the smoke-exposed animals seemed to recover by one hour after exposure. However, 11 of the 40 smoke-exposed animals died during the first 3 days following exposure, and gross pathology indicated severe pulmonary

edema. Respiratory distress developed more slowly and lasted longer in the case of the animals instilled with aqueous $ZnCl_2$, but only 2 of the 40 animals died, and that occurred within the first 48 hours. The lungs of these animals also showed edema. The main changes observed among the surviving animals after both treatments were similar, consisting of edema, destructive alveolitis, and macrophage infiltration, followed by the development of fibrosis. The sequence of changes for the animals exposed to HC smoke or instilled with aqueous $ZnCl_2$ is shown in Table 7.

Table 7. Effects of HC Smoke Inhalation or Intratracheal Instillation of $ZnCl_2$ in Male Porton-Wistar Derived Rats
(Adapted from Brown et al., 1990)

3 Days After Treatment	14 Days After Treatment	28 Days After Treatment
Pulmonary edema. Isolated macrophage infiltration.	Pulmonary edema absent. Some interstitial fibrosis. Macrophage infiltration.	Widespread fibrosis. Widespread macrophage infiltration.

Brown et al. (1990) compared their studies with the earlier work of Marrs et. al. (1983) and noted that the histological effects seen by Marrs et al. were more pronounced, suggesting the differences were due to the 10 times higher exposure used by Marrs. Marrs did not see fibrosis, probably because his observations were over a briefer time span (Brown 1990).

Toxicity of Components of HC Smoke in Animals

Lethal Concentrations.

The toxic inorganic compounds identified in HC smoke are $ZnCl_2$ (with associated toxic impurities, cadmium and arsenic) and HCl. These components are found in the particle phase of the smoke. In the vapor phase are the chlorinated hydrocarbons: HCE, HCB, hexachlorobutadiene (C_4Cl_6), tetrachloromethane (CCl_4, carbon tetrachloride), perchloroethylene (C_2Cl_4, tetrachloroethylene), and trichloroethylene (C_2HCl_3). The concentrations producing lethality from a single inhalation exposure to these components are summarized in Table 8 (where inhalation data were not available, acute lethal oral doses were substituted). Cadmium and arsenic are represented as the respective chlorides since chloride is the major anion found in the smoke. In the case of HCE, there were no data on acute inhalation exposures. Except for the chlorides of arsenic and cadmium, which are present in minute concentrations, the acute lethal concentrations fall within a narrow

range for most of the HC smoke components. Therefore, on the basis of concentration alone, $ZnCl_2$ and HCl are the components which appear to pose the greatest acute threat.

Table 8. Concentrations or Doses of Components of HC Smoke Causing Lethality in Animals After Single Exposures
(Compiled from RTECS, 1987, 1993)

COMPONENT (CAS Registry No.)	SPECIES	EFFECT[a]	DOSE or Concentration
$ZnCl_2$ (7646-85-7)	Rat	LCLo[b]	2 $g \cdot m^{-3}$ (10 min)
HCl (7647-01-0)	Rat Mouse	LC50[c] LC50	4.6 $g \cdot m^{-3}$ (1 hr) 1.65 $g \cdot m^{-3}$ (1 hr)
Arsenic chloride (7784-34-1)	Cat Mouse	LCLo LCLo	200 $mg \cdot m^{-3}$ (20 min) 2.5 $g \cdot m^{-3}$ (10 min)
$CdCl_2$ (10108-64-2)	Dog Mouse	LC90[d] LC50	420 $mg \cdot m^{-3}$ (30 min) 2.3 $g \cdot m^{-3}$
Hexachloroethane (67-72-1)	Rodents	Oral LD50	4.5-5 g/kg
Hexachlorobenzene (118-74-1)	Rat and mouse Cat	LC50 LC50	3.6-4 $g \cdot m^{-3}$ [e] 1.7 $g \cdot m^{-3}$ [e]
Hexachlorobutadiene (87-68-3)	Mouse Rat	LC50 Oral LD50	370 $mg \cdot m^{-3}$ [e] 82-175 mg/kg
Tetrachloroethylene (127-18-4)	Rat Mouse	LC50 LC50	34 $g \cdot m^{-3}$ (8 hr) 35 $g \cdot m^{-3}$ (4 hr)
Trichloroethylene (79-01-6)	Rat Mouse Cat	LCLo LC50 LCLo	43 $g \cdot m^{-3}$ (4 hr) 45 $g \cdot m^{-3}$ (4 hr) 32.5 $g \cdot m^{-3}$ (2 hr)
Tetrachloromethane (56-23-5)	Mouse Rodents	LC50 Oral LD50	59 $g \cdot m^{-3}$ (8 hr) 2.3-8 mg/kg

NOTES: a. Effects are from inhalation exposure except where "Oral" is indicated. b. LCLo is the lowest concentration producing fatalities. c. LC50 = Concentration determined to be lethal to 50% of the exposed animals. d. LC90 = Concentration determined to be lethal to 90% of the exposed animals. e. Exposure time not stated.

Noncarcinogenic Toxic Effects of HC Smoke Components.

Hexachloroethane. Investigators who have studied the composition of HCE-ZnO smokes (Marrs et al., 1983; Karlsson, 1991) have noted that HCE is largely consumed in the combustion reaction in which the smoke is produced, and its concentration in the smoke is likely to be below the TLV of 100 $mg \cdot m^{-3}$. However, as noted in the discussion of human exposures, HCE, because of its volatility, is the component of the HC smoke mixture most

likely to be a hazard to workers engaged in preparing the smoke mixture and in loading and packing HC smoke munitions. The toxic hazards of HCE are therefore examined in detail in the following paragraphs.

All of the chloroethane compounds, including HCE, cause central nervous system depression in laboratory animals. This is usually expressed as abnormal weakness, intoxication, restlessness, irregular respiration, muscle incoordination, and unconsciousness. Chloroethanes are generally irritating to the eyes and skin. Damage to the liver and/or kidney has been demonstrated in various animal species (cattle, mouse, rat, and sheep) following exposure to these compounds and there is a significant association in rats between increased dose and accelerated mortality (Parker et al., 1979).

Dacre et al. (1979) reviewed the foreign-language literature concerned with the toxicity of HCE in animals; references are as cited in their review. Cats and dogs surviving the minimal lethal subcutaneous or oral doses of HCE exhibited central nervous system effects, narcosis and fatty liver degeneration. (Plotnikov and Sokolov, 1947). The narcotic effect was also seen by C. Binz (1894). K. Steindorff (1923) observed that HCE has paralytic effects on the nervous system of the dog, and Binz (1894) found that oral doses of about 1 g/kg caused depression of the central nervous system characterized by weakness, staggering gait, and twitching of muscles. Barsoum and Saad (1934) found that dogs died from respiratory failure within 30 minutes after intravenous injection of 10 mg HCE per kg. Postmortem examination revealed fatty degeneration of the liver. Maloff (1928) found that the fat content of the liver of an 11.6 kg dog was unchanged by administration of 82 g of HCE in 1 or 2 g daily oral doses and 10 g in 1 g daily subcutaneous doses. Schwander (1937) and Burgi (1936) found that HCE applied to rabbit abdominal skin is exhaled 40 minutes after application.

Weeks et. al. (1979) administered HCE to several laboratory animals by inhalation and gavage. Lethal oral doses in rats and guinea pigs were as reported in Table 8. Daily oral doses of 1000, 320, and 100 mg/kg were given to male rabbits for 12 days. Results are summarized in Table 9. Acute (6-8 hour) range-finding inhalation exposures were followed by subchronic exposure (6 hours/day, 5 days/week for 6 weeks) of male and female rats, male guinea pigs, quail, and dogs. Observations were made up to 12 weeks following exposure. The results of the inhalation exposures are summarized in Tables 10 and 11

Table 9. Effects of Twelve Daily Oral Doses of Hexachloroethane in Rabbits (From Weeks et al., 1979)

DOSAGE	EFFECTS
100 mg/kg	No change compared with controls.
320 mg/kg	Reduced body weight gain beginning day 10. Liver degeneration and necrosis (i.e. fatty degeneration, coagulation necrosis, hemorrhage, ballooning degeneration, eosinophilic change, and hemosiderin-laden macrophages and giant cells). Toxic tubular nephrosis of the convoluted tubules in the corticomedulary region of the kidney. Tubular nephrocalcinosis (minimal). Decreased blood levels of potassium and glucose
1000 mg/kg	Reduced body weight gain beginning at day 7. Increases in kidney and liver weights relative to body weight. Liver degeneration and necrosis (as at 320 mg/kg, but more severe). Other effects reported at 320 mg/kg were the same at 1000 mg/kg.

Table 10. Effects in Male Rats of Single 8-hr Inhalation Exposures to HCE (From Weeks et al., 1979)

EXPOSURE CONCENTRATION	EFFECTS
2.5 $g \cdot m^{-3}$	No signs of toxicity during exposure or for 14 days thereafter.
57 $g \cdot m^{-3}$	2/6 rats died within 8 hrs. Survivors had reduced body weight gain over 14-day observation period. No gross lesions were observed. Minimally to moderately severe subacute diffuse interstitial pneumonitis in 2/4 survivors.

Table 11. Effects of 12-Week Inhalation Exposure to Hexachloroethane on Male and Female Rats, Male Dogs and Guinea Pigs, Quail, and Pregnant Rats
(From Weeks et al., 1979)

ENDPOINT	CONCEN-TRATION	SPECIES	EFFECTS
Weight Gain/ Clinical Observations	2.5 g · m^{-3}	♂ Dog	No body weight effects or significant changes in blood parameters. Tremors, ataxia, hypersalivation, severe head bobbing, facial muscular fasciculations; held eyelids closed. 1/4 dogs convulsed and died after 5 hrs exposure; cause of death not grossly evident. Signs recurred throughout exposures; disappeared overnight.
		♂ Guinea pig	Reduced weight gain beginning at week 2. 2/10 guinea pigs died in week 4, and 2/8 died in week 5. No sensitization to HCE.
		♂, ♀ Rats	Reduced weight gain in ♂ at week 3. All rats showed tremors, ruffled pelt, red exudate around eyes during week 3. 1/25 ♂ and 1/25 ♀ found dead during week 4. Recovery period: All signs disappeared; weight gain same as controls. Necropsy: no gross changes.
		Quail	No signs; no weight effects; no gross changes at necropsy.
	145-465 mg · m^{-3}	All species	No signs; no weight effects; no gross changes at necropsy. No sensitization in guinea pigs.
Behavior	145 mg-2.5 g · m^{-3}	♂ Rats	No measurable effects on avoidance performance or spontaneous motor activity.
Pulmonary Function	145 mg-2.5 g · m^{-3}	♂ Dogs	No measurable effects on compliance or resistance.
Oxygen Consumption	145 mg-2.5 g · m^{-3}	♂ Rats	No significant changes at 145 or 465 mg-2.5 g · m^{-3}. Significant decrease ($p < .05$) at 2.5 g · m^{-3}, indicative of lowered basal metabolism rate.
Teratogenesis	145 mg-2.5 g · m^{-3}	Pregnant ♀ Rats	Tremors observed in dams in 2.5 g · m^{-3} group. Maternal and fetal parameters appeared normal in all treated groups.
	Oral: 500 mg/kg daily		Tremors. Body weight gain in dams significantly lower than controls. No skeletal abnormalities in fetuses. Lower gestation index and lowered number of live fetuses/dam compared to corn oil controls.
Histopathology	145 mg-2.5 g · m^{-3}	♂ Dogs and Guinea pigs	No exposure-related lesions.
	2.5 g · m^{-3}	Quail	Excess mucus without inflammatory cells in 2/10 nasal turbinates.
	465 mg-2.5 g · m^{-3}	Rats	Increased incidence of mucopurulent nasal exudate. Upper respiratory tract irritation (70%); subclinical pneumonitis (20%).
	2.5 g · m^{-3}		Increased incidence and severity of mycoplasma-related lesions in nasal turbinates, trachea, and lung. No exposure-related lesions were observed at 12 weeks post exposure.

Weeks et al. (1979) demonstrated dose-dependent, species-specific systemic toxic effects resulting from exposures of animals to HCE vapor (Table 11). The major physiological effect of HCE were stimulation of the central nervous system and upper respiratory tract irritation. Results in rats were confounded by an intercurrent mycoplasia infection. Histopathological findings (respiratory lesions) in rats were likely from HCE exposure potentiation of an endemic mycoplasia infection, and they appeared to be transient." The authors concluded that HCE vapor may be less toxic than is suggested in the literature and implied by the OSHA PEL of 1 ppm with a skin notation.

Teratological studies were also conducted by Weeks et al. (1979). Pregnant female rats were exposed from day 6-16 of gestation to vapor concentrations of 15, 48, and 260 ppm by inhalation or to daily oral doses of 50, 100, and 500 mg/kg. Exposed pregnant females were sacrificed on day 20. Doses that were toxic to the dams were not teratogenic. However, they resulted in a slight retardation of fetal development (Table 11).

Eastin (1980) administered HCE in corn oil by gavage to F344/N rats for 16 days, 13 weeks, or 2 years. Animals were dosed 5 days/week (12 doses for the 16 day study) at levels shown in Table 12. The major non-neoplastic effects were kidney lesions in males and females and liver lesions in males. The neoplastic effects are discussed in a later section of this report.

Gorzinski et al. (1980) conducted a 2-week tolerance study of HCE in the diet of Fischer 344 rats. The doses, 0,10, 50, 200, and 500 mg/kg/day may not, according to the authors, have been accurate because HCE sublimes. The authors concluded that the kidney is the primary target organ in male rats. Relative liver weights were increased in female rats treated with 500 mg/kg/day. The results at each concentration are summarized in Table 13.

Table 12. Hexachloroethane Gavage Studies in F344/N Rats (Eastin, 1989: Animals were dosed 5 days/week)

DOSAGE mg/kg	EFFECTS
16-DAY STUDY (Dose range: 187-3000 mg/day	
187 and 375	♂: hyaline droplet formation in tubular epithelial cells; tubular cell regeneration. Granular casts in the tubule at the corticomedullary junction.
750	1/5 ♂ and 2/5 ♀ died before the end of the study. Dyspnea, ataxia, prostration, excess lacrimation; 25-37% lower mean body weight compared with controls.
1500	All rats died before the end of the study.
3000	All rats died before the end of the study.
13-WEEK STUDY (Dose Range: 47-750 mg/kg)	
94 or higher	Hyperactivity
188 or higher	Foci of hepatocellular necrosis observed in several rats.
375 and 750	Convulsions. Relative weight of liver, heart, and kidney increased. Kidney lesions.
<750	Hyaline droplets, tubular regeneration, and granular casts in kidney.
750	5/10 ♂ and 2/10 ♀ died before the study ended. Final mean body weight (♂): 19% lower than controls; (♀): 4% lower than controls. 5 ♂ rats which died before the end of the study had kidney lesions: renal papillary necrosis, tubular cell necrosis, and degeneration and hemorrhagic necrosis of the urinary bladder.
General observations:	Relative weight of liver, heart, and kidney increased. Kidney lesions in all dosed males; severity increased with dose.
2-YEAR STUDY (Dose Range: 10-20 mg/kg)	
General observations:	There were no survival differences between experimental and control groups. Increased nephropathy in male and female rats.
Specific observations:	Male rats had lesions characteristic of hyaline droplet nephropathy that is associated with accumulation of liver-generated α2μ-globulin in the cytoplasm of tubular epithelial cells (i.e. kidney mineralization; hyperplasia of the pelvic transitional epithelium; renal tubule hyperplasia). The severity of nephropathy was increased in dosed male rats. The severity and incidence of nephropathy was increased in dosed female rats. The incidences of adenomas and carcinomas of the renal tubule were increased in high dose male groups. The incidence of pheochromocytomas of the adrenal gland in low-dosed males was significantly higher than in controls.

Table 13. 2-Week Tolerance Study of HCE in Diet of F344 Rats
(Gorzinski et al., 1980)

HCE Dose in Diet (mg/kg/day)	EFFECTS IN RATS	
	Males	Females
50 and 200	Increased absolute and relative kidney weight. Diffuse paleness in kidney.	Kidney not affected.
500	Decreased body weight gain. Kidney swelling. Low incidence of liver color. Liver size alteration.	Decreased body weight gain. Increase of liver weight relative to body weight.

Zinc chloride. Zinc chloride, the major component of HC smoke, has been implicated by numerous investigators as the cause of acute distress, sometimes leading to death, in humans exposed to the smoke in high concentrations. Corresponding effects have been seen in animals (Basman et al., 1944; Evans, 1945; Johnson and Stonehill, 1961; Macaulay and Mant, 1964; Stocum and Hamilton, 1976; Schenker et al., 1981; Speizer and Taylor, 1981; Pedersen et al., 1984; Lange and Kirk, 1986; Matarese and Matthews, 1986; Hjortsø et al., 1988; Zey and Richardson, 1988; Brown et al., 1990; Homma et al., 1992).

Inhalation Exposures. In order to determine if $ZnCl_2$ is the primary toxicant in HC smokes, Karlsson et al. (1986) compared the acute inhalation toxicity of smoke generated from titanium dioxide (TiO_2)-HCE pyrotechnic mixtures, which generate titanium tetrachloride ($TiCl_4$) and ZnO-HCE pyrotechnic mixtures (which generate $ZnCl_2$) in female Sprague-Dawley rats. It should be noted that the comparison of the Zn and titanium containing smokes is inexact since the compositions of the smoke generating mixtures were not qualitatively or quantitatively equivalent for any of the components.

The toxicity of the TiO_2-HCE smoke proved to be much lower than the Zn-HCE smoke. TiO_2-HCE smoke caused no gross changes in the lungs but did cause minor acute inflammation of lung tissue (Karlsson provides detailed findings of his microscopic observations). All animals survived the highest exposures to TiO_2-HCE smoke. In contrast, even relatively low concentrations of ZnO-HCE smokes were lethal, causing extensive gross pathological pulmonary injuries with death due to blood congestion and pulmonary edema. The animals exhibited signs of dyspnea within 10-15 minutes after removal from the inhalation chamber. At 1 hour after exposure, most animals showed decreased locomotor activity, labored breathing, rhonchi and rales. In animals subjected to lethal exposure, death occurred within 2-5 days after exposure and was attributed to blood congestion in the lung with edema and hemorrhages, together with interstitial emphysema.

On the assumption that $TiCl_4$ and $ZnCl_2$ are the most toxic components of ZnO-HCE and TiO_2-HCE generated smokes, Karlsson et al. (1986) exposed rats to $TiCl_4$ gas or $ZnCl_2$ aerosol. No animals died from exposure to $TiCl_4$ at concentrations up to 2900 mg $\cdot$ m^{-3} for 10 minutes. Zinc chloride however was lethal, with an LC50 of 2000 mg $\cdot$ m^{-3} during a 10 minute exposure. The authors concluded that the difference between the two types of smoke is explained by the difference in toxicity between $TiCl_4$ and $ZnCl_2$.

Karlsson et al. (1986) compared their LC $\cdot$ T50 (concentration-time product producing 50 percent lethality) for $ZnCl_2$ aerosol in rats of 20,000 mg $\cdot$ min $\cdot$ m^{-3} (10 minute exposure), with LC $\cdot$ T50 of 11,800 mg $\cdot$ min $\cdot$ m^{-3} (exposure period not given) observed by Cullumbine (1957) in mice. Karlsson et al. (1986) concluded that this difference indicates that the acute inhalation toxicity of ZnO-HCE smoke used in the Carlson study is higher than the toxicity of $ZnCl_2$ aerosol. Richards et al. (1989) suggested that the difference implies "...that other, more toxic, minor components are present in the ZnO-HCE smoke and contribute to its overall toxicity". This comparison of time-weighted average toxic doses is suggestive that HC smoke is more toxic than $ZnCl_2$, its major component. But such a comparison cannot be conclusive, since the exposed species differed, the exposure conditions were not duplicated, and the C $\cdot$ T product is not an exact measure of dose. Karlsson et al. (1986) also compared their studies on $TiCl_4$ with those of Kelly et al. (1981) who found $TiCl_4$ to be 4 times more toxic than would be expected from its HCl formation and a 10-minute LC50 for $TiCl_4$ of around 10 g $\cdot$ m^{-3}, whereas Karlsson et al. (1986) found only minor inflammatory changes in animals exposed to a C $\cdot$ T product of 11.6 g $\cdot$ m^{-3}. They noted that by comparing their own data with that of Kelley, $TiCl_4$ is shown to be at least 5 times less toxic than $ZnCl_2$ upon inhalation, and suggest that this explains why the acute inhalation toxicity of TiO_2-HCE smoke is much lower than that of ZnO-HCE smoke.

Richards et al. (1989) conducted studies of the effects of $ZnCl_2$ and of ZnO in the lungs of Porton Wistar rats. Zinc chloride and ZnO dissolved or suspended in 0.5 Ml distilled water ($ZnCl_2$ is soluble and ZnO is not) were administered once to rats by intratracheal instillation. Doses ranged from 0.25 to 15 mg/kg body weight. Zinc chloride produced a dose-dependent edematous reaction, as assessed by histopathology and measurements of alveolar surfactant protein in lavage fluid. Zinc oxide did not produce these effects. The authors concluded that the effects of $ZnCl_2$ closely resembled the effects of inhaled HC smoke in experimental animals.

Zinc chloride is toxic to mammalian tissues; the toxic concentration for cultured human lymphocytes in is $3x10^{-3}$ mol $\cdot$ L^{-1} (Deknudt and Deminatti, 1978). Marrs et al 1983) speculated that necrosis observed in the upper respiratory tract is a direct cytotoxic effect of $ZnCl_2$ in a smoke aerosol.

Contact exposure to $ZnCl_2$ According to the review by Donohue et al. (1992), $ZnCl_2$ "...causes both skin and eye irritation, and percutaneous toxicity has been demonstrated." Zinc chloride caused severe edema and necrotic erythema in the test area when applied to the skin of male albino rabbits. Instillation of 0.1 mL of 10 percent $ZnCl_2$ into the lower

conjunctival sac of rabbits produced conjunctivitis and a moderate, penetrating corneal opacity. The animals recovered from these effects in one to two weeks (Williams, 1984). Percutaneous application of aqueous $ZnCl_2$ to the skin of guinea pigs resulted in no mortality in a 4-week study, but a cessation of weight gain was observed after the first week (Wahlberg, 1965).

Hexachlorobenzene. The following synopsis of the non-carcinogenic toxic effects of HCB is abstracted from the review by the IARC (1979: literature references are as noted in the IARC publication). The acute oral LD50 for HCB in rats varies from 3,500-10,000 mg/kg. Death is due to neurotoxic effects (Booth and McDowell, 1975). The LD50 in female rats given repeated doses over 4 months was 500 mg/kg diet. Effects observed in this chronic feeding study included hepatocellular hypertrophy and necrosis, spleen enlargement, and porphyria (Kimbrough and Linder, 1974). Porphyrins accumulated in urine, liver, kidney, and spleen, suggesting an effect on the activity of uroporphyrinogen decarboxylase (Doss et al., 1976; Goerz et al., 1978; Kuiper-Goodman et al., 1977). Mice given 167 mg/kg diet for 6 weeks were immunosupressed (Loose et al., 1977). This was indicated by decreased serum globulin levels and decreased response of spleen lymphocytes to sheep red blood cells. Administration of 50 mg/kg to pigs for 90 days caused porphyria and death. 100 mg/kg of HCB caused cleft palate and some kidney malformations in offspring of exposed pregnant mice (Courtney et al. 1976). Many of the nursing pups of female Sprague-Dawley rats, which had been administered concentrations of 320 or 640 mg/kg, died prior to weaning.

Carcinogenic Effects.

The carcinogenic potential of most of the compounds found in HC smoke has been evaluated by the IARC. Table 14 lists the IARC evaluations for the HC smoke components. Some of the studies of carcinogenicity of specific components of HC smoke are summarized in the following paragraphs.

Table 14. HC Smoke Components Suspected or Known to Be Human or Animal Carcinogens
(After Novak et al. 1987)

COMPOUND	EVIDENCE OF CARCINOGENICITY[a]		OVERALL IARC EVALUATION IN HUMANS[b]
	HUMAN	ANIMAL	
Arsenic and Arsenic Chloride	Sufficient	Limited	1
Cadmium and $CdCl_2$	Limited	Sufficient	2A
Hexachlorobenzene	Insufficient	Sufficient	2B
Hexachlorobutadiene	No adequate data	Limited	3
Hexachloroethane	No adequate data	Limited	3
Hydrogen Chloride[c] (Sulfuric acid mist)	Insufficient (Sufficient)	Insufficient	3 (1)
Perchloroethylene	Insufficient	Sufficient	2B
Tetrachloromethane	Insufficient	Sufficient	2B
Trichloroethylene	Insufficient	Limited	3
Zinc Chloride	Not Evaluated	Not Evaluated	Not Evaluated

NOTES: a. Evidence of carcinogenicity as tabulated in IARC, 1987, except as noted. b. IARC determinations, based upon the total body of evidence concerning the carcinogenicity of a substance: *Group 1 – The agent is carcinogenic to humans; Group 2A – The agent is probably carcinogenic to humans; Group 2B – The agent is possibly carcinogenic to humans; Group 3 – The agent is not classifiable as to its carcinogenicity to humans; Group 4 – The agent is probably not carcinogenic to humans.* c. Evidence and evaluation of HCl and sulfuric acid mist are from IARC, 1992.

Hexachloroethane. Inadequate evidence of carcinogenicity in humans according to the IARC (1987). The NCI (1978) conducted chronic bioassays of HCE in male and female Osborne-Mendel Rats and B6C3F1 mice. HCE was administered by gavage, 5 days/week, for 78 weeks, at doses of 212 and 423 mg/kg/day for rats and 590 or 1179 mg/kg/day for mice. In rats, treatments were discontinued for 1 week at week 23, and then followed by

4 weeks of treatment. This pattern of cyclic administration was maintained for the remainder of the dosing period. These experiments resulted in a significant dose-related association between HCE exposure and mortality in rats but not mice. Toxic tubular nephropathy was observed in all animals. Male and female mice developed hepatocellular carcinoma after receiving doses of 1179 mg/kg/day. There was no excess incidence of tumors in male or female rats. (National Cancer Institute, 1978; Weisburger, 1977). Eastin et al. (1989) conducted a 2-year gavage study of HCE in F344/N rats. Females were given 0, 80, or 160 mg/kg HCE in corn oil, 5 days/week. Males were given 0, 10, or 20 mg/kg HCE on the same schedule. In males, renal neoplasms were found in 1/50, 2/50, and 7/50 in the respective treatment groups; and adrenal gland pheochromocytomas were found in 15/50, 28/45, and 21/49. There were no neoplastic effects in the females. The National Toxicology Program Board of Scientific Counselors' Technical Review Subcommittee concluded that there was clear evidence for carcinogenicity of HCE in male rats and no evidence of carcinogenicity in female rats (Eastin et al., 1989).

Zinc Chloride. Not evaluated by the IARC. Furst and Haro (1969) reviewed the studies of their time and concluded that there was no adequate evidence that zinc salts are carcinogenic. Murray and Flessel (1976) noted that zinc is not a reported carcinogen.

Hexachlorobenzene: Possibly carcinogenic to humans according to the IARC (1987) evaluation. Cabral et al. (1977) found this chemical to be carcinogenic in a long-term oral study of HCB in mice and hamsters. Male and female Swiss mice, given HCB in the feed for 82 weeks, evidenced liver cell tumors at concentrations of 12-24 mg/kg/day. Male and female Syrian Golden hamsters given HCB in concentrations of 0, 4, 8, and 16 mg/kg/day in the diet from age 6 weeks for their lifespan evidenced increased incidences of hepatomas, liver hemangioendotheliomas and thyroid adenomas. HCB enhanced the hepatocarcinogenicity of polychlorinated terphenyls (PCT) in ICR mice at dietary doses of 250 mg/kg PCT, and 50 mg/kg HCB (Shirai et al., 1978)

Perchloroethylene: Possibly carcinogenic to humans according to the IARC (1987) evaluation. The NCI (National Cancer Institute, 1977) sponsored a 78-week study in which perchloroethylene was administered 5 days/week by gavage to Osborne-Mendel rats and B6C3F1 mice. The high and low time-weighted average doses were 941 and 471 mg/kg/day for male rats and 949 and 474 mg/kg/day for female rats. The doses for male mice were 1072 and 536 mg/kg/day, and 772 and 386 mg/kg/day for female mice. Hepatocellular carcinomas developed in mice but not rats. There was a positive association between dose and tumor incidence in mice. The NCI concluded that tetrachloroethylene is a liver carcinogen in B6C3F1 mice of both sexes.

Cadmium and Cadmium Chloride: Probably carcinogenic to humans according to the IARC (1987) evaluation. Takenaka et al. (1983) induced cancers in male Wistar rats exposed to cadmium chloride aerosols at concentrations ranging from 12.5 to 50 $\mu g \cdot m^{-3}$.

A review of mortality statistics among cadmium production workers (Thun et al., 1985) showed mortality rates of death from respiratory cancer and from nonmalignant gastrointestinal disease that were significantly greater than would be expected from United States workers. A statistically significant dose-response relationship was observed between lung cancer mortality and cumulative exposure to cadmium.

Mutagenicity.

HC Smoke. Yanders et al. (1985) and Schaeffer et al. (1987) tested the effects of HC, fog oil and diesel smokes on the plant Tradescantia, and native flora (Ambrosia dumosa) and fauna (Dipodomys merriami) in field studies at Fort Irwin, California. Exposures were for 30 minutes at distances of 15 to 150 meters from the smoke source. Exposure was dependent upon atmospheric conditions, and therefore was not well-controlled, according to the investigators. Tradescantia clones were examined for mutagenic effects indicated by micronuclei induction in developing pollen and pink somatic mutations in stamen hairs. Native rodents (Dipodomys merriami) were examined for sister chromatid exchanges and chromosome aberrations. HC smoke was found to be weakly mutagenic. Lower et al. (1983) also reported on experiments with HC smokes at Fort Irwin California. They noted that HC smoke was mutagenic to Tradescantia and that the mutagenic effects were more pronounced closer to the smoke source, usually within 50 meters. The combination of fog oil and HC smoke were mutagenic to Tradescantia up to 100 meters. Their animal mutagenicity studies were not conclusive.

Hexachloroethane. Mutagenicity tests in Salmonella typhimurium (Ames assay) and in yeast were negative (Weeks et al., 1979). Eastin et al. (1989) also found that HCE was not mutagenic in S. typhimurium when tested with and without exogenous metabolic activation.

Zinc Chloride: There is no evidence that $ZnCl_2$ is mutagenic, and teratogenic effects have been demonstrated only in chicken eggs. No tumors have been produced by oral or intraperitoneal administration to animals (Hill et al. 1978). The mutagenicity of $ZnCl_2$ has been evaluated in at least two *in vitro* assays. The infidelity of DNA synthesis was determined in a reaction mixture containing a DNA polymerase, a template-primer of restricted base composition and complementary and noncomplementary deoxynucleoside triphosphates each labeled with different radioactive isotopes. From the ratio of radioactive substrates incorporated, the error frequency was calculated. Zinc chloride had no effect on error frequency, whereas eight metal compounds shown to be mutagens or carcinogens enhanced the infidelity of DNA synthesis (Sirover and Lowb, 1976). In another test, 38 metal salts were examined for their capacity to enhance transformation of Syrian hamster embryo cells by a simian adenovirus. Metal salts that are carcinogenic or mutagenic increased the frequency of adenovirus transformation. Zinc chloride and ZnSO4 were only weakly positive in this assay, and the authors concluded that the results were inconclusive (Casto et al., 1979)

Hydrogen Chloride. The mutagenicity of HCl was examined in a microsuspension assay utilizing E. coli indicator strains for the detection of chemically-induced preferential kill of repair-deficient strains (McCarroll et al. 1981). This technique measures primary DNA damage, as indicated by inhibition of the growth of bacteria which are DNA repair deficient. (Generally carcinogens induce selective inhibition of repair deficient Escherichia coli. The experiment therefore was inconclusive with regard to HCl.

CURRENT STANDARDS

The American Conference of Governmental Industrial Hygienists (ACGIH) has proposed changes in the exposure standards for many of the components of HC smoke. The current standards and the proposed changes are given in Table 15.

Table 15. Time-Weighted Average and Short-Term Exposure Limits for Components of HC Smoke
(ACGIH, 1992)

COMPONENT	8-hr TWA – mg · m^{-3} (ppm)	15-min STEL – mg · m^{-3} (ppm)	ACGIH Designations (Carcinogen[a], Skin[b])
Zinc chloride	1	2	
Cadmium and cadmium salts	Present: 0.05 Proposed: 0.01 total 0.005 respirable		Proposed: A2
Arsenic and soluble compounds	Present: 0.2 Proposed: 0.01		Present: A2 (As_2O_3) Proposed: A1
Hydrogen chloride	Ceiling: 5 (7.5)		
Carbon monoxide	25 (29)		
Hexachloroethane	9		A2; Skin
Hexachlorobenzene	Proposed: 0.025		Proposed: A2; Skin
Hexachlorobutadiene	0.02 (0.21)		A2; Skin
Perchloroethylene (tetrachloroethylene)	Present: 50 (339) Proposed: 25 (140)	Present: 200 (137) Proposed: 100 (685)	Proposed: A3
Trichloroethylene	50 (269)	Present: 200 (1070) Proposed: 100 (537)	Proposed: A5
Tetrachloromethane (carbon tetrachloride)	5 (31)	Proposed: 10 (63)	Present: A2; Skin Proposed: A3; Skin

NOTES (ACGIH, 1992): a. A1 – *Confirmed Human Carcinogen*, A2 – *Suspected Human Carcinogen*; A3 – *Animal Carcinogen*; A4 – *Not Classifiable as a Human Carcinogen*; A5 – *Not Suspected as a Human Carcinogen*.
b. "Skin" Notation: There is a potentially significant contribution to the overall exposure by the cutaneous route.

DISCUSSION

Workplace hazards

The hazard to workers in Army munitions plants who process, load, and pack HC munitions is principally related to exposure to HCE vapors. Even when efforts are made to eliminate HCE from the workplace atmosphere, concentrations of HCE may routinely exceed the ACGIH TLV-TWA of 9.7 mg · m^{-3}. Seldén et al. (1993) showed that workers provided with face masks or air-fed visors had elevated levels of plasma after working with HCE-containing munitions for 5 weeks. Since there are no data on the relationship between plasma levels in animals or humans to the occurrence of adverse effects, there is no way of knowing if the plasma HCE levels measured by Seldén et al. (1993) are cause for concern. Seldén et al. (1993) postulated that HCE particles which have settled on warm surfaces such as fluorescent tubes may, because of the volatility of HCE, be a secondary source of HCE vapors in the workplace, even in the presence of ventilation controls. Similarly, sedimentation on the shoes and clothing of workers could also be a source of exposure to their families.

Gordon et al. (1991) developed a Reference Dose (RfD) based upon the 16-week study of Gorzinski et al. (1980), in which rats developed kidney lesions when fed dietary levels of HCE in excess of 1.3 mg/kg/day. Based upon this no-observed-adverse-effects level (NOAEL), the RfD for HCE was calculated to be 1 μg/kg/day, using an uncertainty factor of 1000 (for a less-than-lifetime animal study). At this level of consumption, the predicted level of human cancer (from a linearized multistage model) is 10^{-5}, i.e., there would be an expected increase of one cancer for each 100,000 persons consuming HCE in water at a concentration equivalent to the RfD of 1 μg/kg/day for a 70-year lifetime. The dose received by a worker breathing HCE vapors is dependent upon the concentration and duration of the exposure and upon the pharmacokinetics of absorption, distribution, accumulation, clearance, metabolism, and excretion of HCE. A worker exposed to HCE at the TLV (9.7 mg · m^{-3}) would inhale about 50 mg of HCE vapor each working day, so that, even with minimal absorption, the internal dose would be many times the RfD calculated by Gordon et al. (1991).

Exposure to HC smoke

In no aspect is the information necessary to assess the risks to soldiers of exposure to HC complete. Toxic effects of HC smoke and its components have been carefully measured in some animal studies. The effects have also been carefully studied in a few cases of accidental human exposure to HC smoke, but the exposure conditions that elicited these effects in humans can only be approximated. Little information is available concerning exposures encountered by soldiers. Smoke pots and grenades are the source of troop exposures. The amount of smoke generated by these munitions can be estimated with sufficient accuracy for the purpose of risk assessment, and the relative concentrations of the smoke components can be calculated with confidence from the measurements of Katz et al.

(1980). But, except for the case of exposure in an enclosed space, there are too many uncontrollable variables to allow the range of individual exposures to be described by statistical parameters. Local wind and weather conditions determine the concentration of smoke particles and vapors within the plume. The humidity determines the extent and rate of growth of the hygroscopic $ZnCl_2$ particles. The positions of the individual soldiers relative to the smoke cloud may be determined by events during the training scenario and personal choices of the soldiers and their leaders in the field. And the number of smoke munitions that will be needed to provide the required screening effect depends upon the degree of dispersion provided by the local meteorological conditions

In view of the lack of knowledge concerning the distribution of exposure among the soldier population in any particuiar scenario, risk assessment must be based upon average exposure, a worst-case scenario, or one designed to protect some large percentage of the exposed population from adverse effects. Two such efforts at risk assessment or minimization have been published in recent years (Cichowicz, 1983). In the first (Cichowicz, 1983) concentrated on the acute hazards of inhalation of $ZnCl_2$. He estimated minimum distances downwind from a M5 smoke pot to limit exposures to stated concentrations and concentration-time profiles under various atmospheric conditions. Cichowicz' estimates are summarized in Table 16.

Table 16. Downwind Distances from One M5 Smoke Pot (HC) Necessary to Limit Exposure to Designated $ZnCl_2$ Concentrations and Concentration-Time Products (Adapted from Cichowicz, 1983)

Condition	Wind speed $m \cdot s^{-1}$	Plume rise meters	Peak Conc. $\leq 2\ mg \cdot m^{-3}$	$C \cdot T^a \leq 30$ $mg \cdot min \cdot m^{-3}$	$C \cdot T \leq 2000$ $mg \cdot min \cdot m^{-3}$	$C \cdot T \leq 4800$ $mg \cdot min \cdot m^{-3}$
NIGHT (F Stability)[b]	1	0	3900 m[c]	3700 m	190 m	100 m
	3	0	2000 m	1720 m	80 m	40 m
	1	18	3600 m	3200 m	-	-
DAY (D Stability)[b]	1	0	1100 m	950 m	80 m	50 m

NOTES: a. C · T = Concentration-time product. b. F = Very Stable, D = Neutral. c. Minimum distance from smoke pot necessary to limit $ZnCl_2$ concentration or C · T product to value at top of column.

The Threshold Limit Value–Short-term Exposure Limit (TLV-STEL) adopted by the ACGIH (1992) for $ZnCl_2$ is 2 $mg \cdot m^{-3}$. The STEL is defined as a 15-minute time-weighted average concentration which should not be exceeded at any time during a workday (ACGIH, 1992). It is used only for those substances for which effects have been reported for short-term, high-level exposures in either humans or animals. The STEL for $ZnCl_2$ is designed to prevent irritation or chronic or irreversible tissue damage (ACGIH, 1992). In Table 16, the minimum distances downwind from one M5 smoke pot are listed under "Peak

Conc. ≤ 2 mg·m^{-3}." Similarly, distances are shown which are calculated to yield the concentration-time (C · T) products ranging from the STEL (2 mg · m^{-3} x 15 min = 30 mg · min · m^{-3}) to the reported lowest toxic dose of 4800 mg · min · m^{-3}.

Inhalation of high concentrations of HC smoke produces effects similar to those from inhalation of strong mineral acid. This is not surprising, since the $ZnCl_2$ which makes up the bulk of the smoke is known to dissociate in water to form hydrogen chloride. But the acute effects of HC smoke inhalation cannot be attributed solely to those of the associated HCl. The toxic effects of inhaling $ZnCl_2$ aerosols occur at lower concentrations than the equivalent concentrations of HCl. This is recognized by the ACGIH in assigning a lower TLV to $ZnCl_2$ than to HCl. Evidence for the implication of zinc in the development of ARDS from inhalation of HC smoke lies in the reported success of chelating agents such as penicillamine in preventing the progress of the disease (Allen et al., 1992). The chelating agents are effective in removing metals such as zinc, but do not ameliorate the effects of the reduced pH caused by the presence of mineral acids. Zinc may also play a part by substituting for calcium in calmodulin and thereby disturbing enzymes in cell processes, including cell proliferation (Cheung, 1984).

All of the reported cases where soldiers were seriously injured or killed by exposure to HC smoke have occurred when the smoke was deployed in an enclosed space and the personnel were inadequately protected. In none of the reports of cases of severe and fatal injury to personnel by HC smoke was there any attempt to estimate the smoke concentration. From descriptions of the smoke cloud in many of these cases, it can be assumed that visibility was less than 10 meters and was probably closer to 2 meters. Based upon the extinction coefficient of HC smoke determined at a wavelength of 0.6 μm by Milham and Anderson (1983), the $ZnCl_2$ concentration that corresponds to a visibility of 2 meters is 134 mg · m^{-3}. Concentrations corresponding to other visibility conditions are shown in Table 17. The extinction coefficients were measured at 85 percent relative humidity; at lower humidities, the yield of smoke would be less, and greater concentrations of $ZnCl_2$ would be required to achieve the light attenuation equivalent to the visibilities listed in Table 17. The extinction coefficients were also smaller at wavelengths longer than 0.6 μm but still within the visible range, and the concentrations of $ZnCl_2$ necessary to achieve the stated visibilities would be correspondingly greater.

Table 17. Zinc Chloride Concentrations in HC Smoke Corresponding to Various Visibility Conditions

Visibility (m)	200	50	10	5	2
$ZnCl_2$ Concentration ($mg \cdot m^{-3}$)	1.3	5.4	27	54	134

BASIS: The extinction coefficient measured by Milham and Anderson (1983) for HC smoke at 85% relative humidity at a wavelength of 0.6 μm was 4.09 $m^2 \cdot g^{-1}$, based on the starting material. The $ZnCl_2$ concentration was calculated on the basis of 76% yield of $ZnCl_2$ and is the concentration that will reduce the intensity of light transmitted through the path by 90%.

Novak et al. (1987) considered the health hazards of chronic exposure to the carcinogens that were found in HC smoke by Katz et al. (1980). These are perchloroethylene, tetrachloromethane, HCE, HCB, arsenic, and cadmium and cadmium chloride. A "worst-believable-case military exposure" was developed for soldiers in the opposing forces (OPFOR) who engage in battle scenarios with troops training at the U.S. Army National Training Center, Fort Irwin, CA. Using data on smoke pot expenditures at Fort Irwin and the maximum concentrations of each of the identified carcinogens in the HC smoke, Novak et al. (1987) applied the concept of maximum allowable body dose, used by the USEPA to calculate maximum doses of the carcinogens over a 70-year lifetime. Under the worst-case conditions, exposures of OPFOR cadre to the identified carcinogenic components during a two-year tour at Fort Irwin would subject them to a total risk of 17.5 excess cancers per 100,000 individuals experiencing 2-year exposures to these 6 components of HC smoke. Since there is no evidence of tumor inhibition by any of the 6 substances, the combined effect would probably not be less, and could exceed the simple sum of the carcinogenic potential of these three components of HC smoke. The cancer risks predicted by Novak et al. (1987) are summarized in Table 18. The "worst-practicable-case" exposure conditions used by Novak et al. (1987) to calculate cancer potentials are based upon the highest concentrations of each of the listed organochlorine compounds found in laboratory-generated smoke (Table 3) or upon the highest concentrations of cadmium and arsenic found in the uncombusted HC smoke mix (Table 2), assuming 100 percent completion of the combustion reactions and 100 percent aerosolization of the products. In addition to the predicted cancer rate from HC smoke exposure, Novak et al. (1980) calculated the number of exposures to a single M5 smoke pot that would result in an additional risk of cancer of one in 100,000. These are listed in Table 18 for each of the 6 identified carcinogens. The summation of these effects was made in the manner recommended by the ACGIH (1992) for arriving at TLVs for mixtures when effects can be assumed to be additive. Thus at D Stability conditions (daytime, with a wind speed of 6 $m \cdot s^{-1}$), exposure to 15 M5 smoke pots is predicted to result in a 1/100,000 (10^{-5}) additional incidence of cancer. The calculations for F Stability conditions indicate that for nighttime exercises with wind speeds of 2 $m \cdot s^{-1}$, exposures of personnel within 50 meters of the smoke pot would be greater, resulting in a

higher predicted incidence of excess cancers and a much smaller number of smoke pots to achieve a one in 100,000 increase in cancer expectation.

Table 18. Carcinogenic Potential of 6 Chemical Substances in HC Smoke
(Adapted from Novak et al., 1987)

CHEMICAL SUBSTANCE	Carcinogenic Potential [a]		Maximum No. of M5 Smoke Pots [b]	
	D Stability [c] Conditions	F Stability Conditions	D Stability Conditions	F Stability Conditions
Hexachlorobenzene	7.34×10^{-5}	65.5×10^{-5}	36	4
Hexachloroethane	0.34×10^{-5}	3.06×10^{-5}	760	86
Perchloroethylene	3.32×10^{-5}	29.5×10^{-5}	79	9
Tetrachloromethane	1.21×10^{-5}	10.8×10^{-5}	216	24
Cadmium and $CdCl_2$	4.88×10^{-5}	43.9×10^{-5}	54	6
Arsenic and soluble salts	0.41×10^{-5}	3.07×10^{-5}	640	85
TOTALS [d]	17.5×10^{-5}	156×10^{-5}	15	2

NOTES: a. Probability of developing cancer as a result of 2-year exposure to the chemical substance at the worst-case level for smoke generator personnel at Fort Irwin. b. Total number of M5 smoke pots projected to yield an exposure which would result in a 10^{-5} probability of developing cancer. c. D stability: day, wind=6 $m \cdot s^{-1}$; F stability: night, wind=2 $m \cdot s^{-1}$. d. Cancer risk totals are simple sums; totals for number of pots are reciprocals of sum of reciprocals.

There are hazards from both long-term and short-term exposure to HC smoke. The acute effects present themselves most dramatically, causing severe lung disease and even death from the most severe exposures. Long-term exposure to low concentrations of HC smoke may be a greater health threat because of the larger population so exposed. The consensus among those who have studied the effects of inhaled HC smoke in humans and in animals is that the causative agent of the severe acute effects is the major component, $ZnCl_2$. The components of the smoke that have been identified as potential human carcinogens will, with the exception of cadmium and arsenic compounds, always be produced in trace amounts when the ZnO-HCE mixture is combusted to form the smoke. (Cadmium and arsenic are present as impurities in the ZnO component of the smoke, and they could be eliminated, at some cost, by requiring a high purity grade of ZnO.) Thus, as long as HC smoke is employed, there is the danger of ARDS and its sequelae from exposure of unprotected individuals to high concentrations and the danger of increased risk of cancer among those exposed to lower concentrations for long periods of time. The only way to prevent these dangers, short of a complete ban on HC smoke, is to obey the strictures of Cichowicz (1983): "(a) enforce the Army directive to mask in the presence of HC smoke: (b) closely regulate the deployment of HC smoke on all...installations; (c) restrict HC deployment to areas of the installation as far as practically possible from cantonments and

other populated areas; (d) take special precautions to protect higher risk individuals such as those highly allergic, children and the aged and; (e) under no conditions should HC be deployed indoors or in confined quarters." In an evaluation of the effectiveness of the military protective mask in smoke, it was concluded that the filtration provided by the M40 or the M17 protective mask is sufficient to protect the soldier, even in the case of very dense smokes (visibliity of 10 meters). In the case of exceptionally high concentrations, such as when smoke is employed in enclosed areas, the protection afforded by the mask will be quickly overwhelmed, and the mask should be used only as a device to offer protection while escaping from the concentrated smoke (Eaton and Young, 1989).

Despite the Army policy, as reiterated by the U.S. Army Surgeon General in 1985 (Department of the Army, 1985), that the military protective mask is to be worn whenever exposure to HC smoke is anticipated, training episodes continue to be conducted in which soldiers are exposed, unmasked, to potentially high concentrations of HC smoke. Such an incident is illustrated in Figure 2. These training exercises are known as military operations in urban terrain (MOUT).

FIGURE 2. Use of HC Smoke in Enclosed Space.

This photograph, reproduced from *Arctic Soldier*, Spring 1990, shows soldiers inside a two-story building in the "Splinter Village" complex at Fort Richardson, AK. The room is filled with smoke, and the soldier in the foreground is apparently about to toss another smoke grenade. In the exercise, the attacking soldiers fight their way through the smoke-filled building and exit through a window and down a rope. (U.S. Army Photograph by SFC Elroy Garcia, used with permission of the Public Affairs Officer, Fort Richardson.)

REFERENCES

1. ACGIH. 1980. Documentation of the Threshold Limit Values. Fourth Edition. Cincinnati, OH, American Conference of Governmental Industrial Hygienists.

ACGIH. 1992. 1992-1993 Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH, American Conference of Governmental Industrial Hygienists.

Allen, M.B., A. Crisp, N. Snook, and R.L. Page. 1992. "Smoke-bomb" pneumonitis. Respir. Med. 86(2):165-166

Barsoum, G.S. and K. Saad. 1934. Relative Toxicities of Certain Chlorine Derivatives of the Aliphatic Series. Q. J. Pharm. Pharmacol. 7:205-214.

Basman, J. and Silver, S.D. MDR No. 14. The Toxicity of Screening Smokes-IV. Hexachlorethane Type (HC) Field Tests. Dec. 8, 1944. Unclassified report.

Binz, C. 1894. Contribution to the knowledge of halogen pharmacology, Arch. Exp. Pathol Pharmakol. 34:199-200.

Blom, L., and P.E. Hven. 1986. Poisoning with hexite smoke ammunition. Ugeskr. Laeger 148(8):454-455.

Blount, B.W. 1990. Two types of metal fume fever: mild vs. serious. Military Med. 155:372-377.

Booth, N.H., and J.R. McDowell. 1975. Toxicity of hexachlorobenzene and associated residues in edible animal tissues. J. Am. Vet. Med. Assoc. 166(6):591-595.

Brain, J.D., and P.A. Valberg. 1979. Deposition of aerosol in the respiratory tract. Am. Rev. Respir. Dis. 120:1325-1373.

Brooks, S.M. 1986. Pulmonary Reactions to Miscellaneous Mineral Dusts, Man-made Mineral Fibers, and Miscellaneous Pneumoconioses. In: Merchant, J.A., B. A. Boehlecke, G. Taylor, and M. Pickett-Harner, eds. Occupational Respiratory Diseases. DHHS (NIOSH) Publication No. 86-102. Washington, DC, U.S. Government Printing Office, pp. 401-410.

Brown, R.F.R., T.C. Marrs, P. Rice, and L.C. Masek. 1990. The histopathology of rat lung following exposure to zinc chloride followed by treatment with 70% oxygen. Environ. Health Perspect. 85:81-87.

Brown, M.A., Thom, J.V., Orth, G.L., Cova, P., and J. Juarez. 1964. Food poisoning involving zinc contamination. Arch. Environ. Health. 87(5):657-660.

Burgi, E. 1936. Permeability of skin to drugs and poisons. Bruxelles-Med. 16:1481-1489.

Burns, J.E., and F.M. Miller. 1975. Hexachlorobenzene contamination: its effects in a Lousiana population. Arch. Environ. Health 30:44-48.

Cabral, J.R.P., P Shubik, T. Mollner, and F. Raitano. 1977. Carcinogenic activity of hexachlorobenzene in hamsters. Nature (Lond.) 269:510-511.

Cam, C. 1960. A new epidemic dermatosis of children (French). Ann. Derm. Syph. (Paris) 87:393-397.

Casto, B.C., J. Meyers, and J.A. DiPaolo. 1979. Enhancement of viral transformation for evaluation of the carcinogenic or mutagenic potential of inorganic metal salts. Cancer Res. 39:193-198.

Cheung, W.Y. 1984. Calmodulin: its potential role in cell profliferation and heavy metal toxicity. Fed. Proc. 43:2995-2999.

Chobanian, S.K. 1981. Accidental ingestion of liquid zinc chloride: local and systemic effects. Ann. Emerg. Med. 10(2):91-93.

Cichowicz, J.J. 1983. Environmental Assessment, Programmatic Life Cycle Environmental Assessment for Smoke/Obscurants (Vol 4), HC Smoke. ARCSL-EA-83007. Chemical Research and Development Center, US Army Armament, Munitions and Chemical Command, Aberdeen Proving Ground Maryland.

Corrin, B. 1963. Aluminium pneumoconiosis II. Effects on the rat lung of intratracheal injections of stamped alumimium powders containing different lubricating agents and a granular alumimium powder. Br. J. Ind. Med. 20:264-267.

Courtney, K.D., M.F. Copeland, and A. Robbins. 1976. The effects of pentachloro-nitrobenzene, hexachlorobenzene, and related compounds on fetal development. Toxicol. Appl. Pharmacol. 35:239-256.

Cullumbine, H. The toxicity of screening smokes. 1957. J. Royal Army Med. Corps 103:119-122.

Dacre, J.C. , W.D. Burrows, C.W.R. Wade, A.F. Hegyeli, T.A. Miller, and D.R. Cogley. 1979. Problem Definition Studies on Potential Environmental Pollutants. V. Physical , Chemical Toxicological, and Biological Properties of Seven Substances used in Pyrotechnic Compositions. Technical Report 7704. Fort Detrick, Frederick, MD, U.S. Army Biomedical Research and Develomment Laboratory. NTIS: AD A090631.

Deknudt, G. and M. Deminatti. 1978. Chromosome studies in human lymphocytes after in vitro exposure to metal salts. Toxicology, 10:67-75.

Department of the Army. 1978. Small Unit Smoke Operations. Training Circular No 3-50-2. Washington, DC, Department of the Army.

Department of the Army. 1982. Deliberate Smoke Operations. FM 3-50-1. Washington, DC, Headquarters, Department of the Army.

Department of the Army. 1985. Letter, HQDA, OTSG, DASG-PSP-E, dated 27 Feb 85, subject: Issuance of Updated DA Policy for Use of Respiratory Protection when Using Large Area SMOKES/Obscurants. Alexandria, VA, Headquarters, Department of the Army, Office of the Surgeon General.

Department of the Army. 1988. Zinc Oxide, Technical. Military Specification No. MIL-Z-291F. Rock Island, IL, U.S. Army Armament, Munitions and Chemical Command.

Dinman, E.D. 1987. Aluminum in the lung: the pyropowder conundrum. J. Occup. Med. 29(11):869-876.

Donohue, J.M., L. Gordon, C. Kirman, and W.C. Roberts. 1992. Zinc Chloride Health Advisory. Washington, DC, U.S. Environmental Protection Agency.

Doss, M., E. Schermuly, and G. Koss. 1976. Hexachlorobenzene porphyria in rats as a model for human chronic hepatic porphyrias. Ann. Clin. Res. 8:171-181.

Dvizhkov, P.P. and I.N. Potapova. 1968. Blastomogenic Properties of Metal Zinc and Zinc Chlorides. Grg. Tr. Prof. Zabol. 12(1):23-27.

Eastin, WC. 1989. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Hexachloroethane (CAS No. 67-72-1) in F344/N Rats (Gavage Studies). NTP TR 361. NIH Publication No. 89-2816. Research Triangle Park, NC, National Toxicology Program.

Eaton, J.C., and J.Y. Young. 1989. Medical Criteria for Respiratory Protection in Smoke: the Effectiveness of the Military Protective Mask. Technical Report 8902. Fort Detrick, Frederick, MD, U.S. Army Biomedical Research and Development Laboratory. NTIS: AD A204303.

Engst, R., R.M. Macholz, and M. Kujawa. 1976. The metabolism of hexachlorobenzene (HCB) in rats. Bull. Environ. Contam. Toxicol. 16(2):248-252.

Evans, E.H. 1945. Casualties following exposure to zinc chloride smoke. Lancet, Sept. 23, pp. 368-370.

Fischer, H. 1969. [Accidents caused by combat and smoke chemicals, and their sequelae.] Wehrmed. Monatosschr. 13(12):355-359.

Fowler, J.S.L., 1969. Some hepatotoxic actions of hexachloroethane and its metabolites in sheep. Br. J. Pharmacol. 35:530-542.

Furst, A., and R.T. Haro. 1969. A survey of metal carcinogenesis. Prog. Exp. Tumor Res. 12:102-133.

Gleason, M.N., R.E. Gosselin, H.C. Hodge, and R.P. Smith. 1976. Clinical Toxicology of Commercial Products, 4th Ed. Baltimore, MD, The Williams and Wilkens Co., p. 112.

Goerz, G., W. Vizethum, K. Bolsen, T. Krieg, and R. Lissner. 1978. Hexachlorobenzene (HCB) induced porphyria in rats. Influence of HCB-metabolites on the biosynthesis of heme (Ger.). Arch. Dermatol. Res. 263:189-196.

Gordon, L., W.R. Hartley, and W.C. Roberts. 1991. Hexachloroethane Health Advisory. Washington, DC, U.S. Environmental Protection Agency. NTIS: PB91-159657.

Gorzinski, S.J., R.J. Nolan, S.B. McCollister, R.J. Kociba, and J.L. Mattsson. 1985. Subchronic oral toxicity, tissue distribution and clearance of hexachloroethane in the rat. Drug Chem. Toxicol. 8(3):155-169.

Gorzinski, S.J., C.E. Wade, S.B. McCollister, D.C. Morden, E.A. Hermann, and R.J. Kociba. 1980. Hexachloroethane: Results of a 2-week Tolerance Study in the Diet of Rats. Document from the Toxicology Research Laboratory, Health and Environmental Sciences, Midland, MI 48649, Dow Chemical USA.

Grant, W.M., ed. 1986. Toxicology of the Eye, 3d ed. Springfield, IL, Charles C. Thomas, p. 479.

Gross, P., Harley, R.A., and R.T.P. deTreville. 1973. Pulmonary reaction to metallic aluminum powders. Arch. Environ. Health 26:227-236.

Henry, M.C., J.J. Barkley, and C.D. Rowlett. 1981. Mammalian Toxicological Evaluation of Hexachlorethane Smoke Mixture and Red Phosphorus. Fort Detrick, Frederick, MD, US Army Medical Bioengineering Research and Development Laboratory. DTIC: AD A109593.

Hill, H.G., K. Wasti, and J.E. Villaume. 1978. A Literature Review, Volume 5 of 8, Occupational Health and Safety and Environmental Aspects of Zinc Chloride. Final Report, Contract No. DAMD17-77-C-7020. Philadelphia, PA, Franklin Research Institute.

Hinds, W.C. 1982. Aerosol Technology, Properties, Behavior, and Measurement of Airborne Particles. New York, John Wiley & Sons. pp. 211-232.

Hjortsø, E., J. Qvist, M.I Bud, J.L. Thomsen, J.B. Andersen, F. Wiberg-Jørgensen, N.K. Jensen, R. Jones, L.M. Reid, and W.M. Zapol. 1988. ARDS after accidental inhalation of zinc chloride smoke. Intensive Care Med. 14:17-24.

Homma, S., R. Jones, J. Qvist, W.M. Zapol, and L. Reid. 1992. Pulmonary vascular lesions in the adult respiratory distress syndrome caused by inhalation of zinc chloride smoke: a morphometric study. Hum. Pathol. 23(1):45-50.

IARC. 1979. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man, vol. 20. Some Halogenated Hydrocarbons. Lyon France, International Agency for Research on Cancer.

IARC. 1987. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Supplement 7, Overall Evaluations of Carcinogenicity: an Updating of IARC Monographs Volumes 1 to 42. Lyon, France, International Agency for Research on Cancer.

IARC. 1992. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man, vol. 54. Occupational Exposure to Mists and Vapours from Strong Inorganic Acids; and Other Industrial Chemicals. Lyon France, International Agency for Research on Cancer, pp. 155-178.

Iatropolous, M.J., A. Milling, W.F. Müller, G. Nohynek, K. Rozman, F. Coulston, and F. Korte. 1975. Absorption, transport and organotropism of dichlorobiphenyl (DCB), dieldrin, and hexachlorobenzene (HCB) in rats. Environ. Res. 10:384-389.

Irish, D.D. 1967. Aliphatic Halogenated Hydrocarbons. In: Patty, ed,. Industrial Hygiene and Toxicology, 2nd ed., Vol. II, Toxicology, New York, John Wiley & Sons, pp. 1297-1299.

Istfan, N.W., M. Janghorbani, and V.R. Young. 1983. Absorption of stable ^{70}Zn in healthy young men in relation to zinc intake. Am. J. Clin. Nutr. 38:187-194.

Jarvis, A. 1970. The combustion reactions of a pyrotechnic white smoke composition. Combustion and Flame 14:314-320.

Johnson, F.A. and R.B. Stonehill. 1961. Chemical pneumonitis from inhalation of zinc chloride. Chest 40:619-624.

Karlsson, N., G. Cassel, I. Fangmark, and F. Bergman. 1986. A comparative study of the acute inhalation toxicity of smoke from TiO_2-hexachloroethane and Zn-hexachloroethane pyrotechnic mixtures. Arch. Toxicol. 59(3):160-166.

Karlsson, N. 1988. Poisoning from smoke grenades in not due to phosgene [letter]. Eur. Respir. J. 1(6):575.

Karlsson, N., I. Fangmark, I. Haggqvist, L. Karlsson, L. Rittfelt, and H. Marchner. 1991. Mutagenicity testing of condensates of smoke from titanium dioxide/hexachloroethane and zinc/hexachloroethane pyrotechnic mixtures. Mutation Res. 260:39-46.

Katz, S.A., R. Snelson, R. Farlow, R. Welker, and S. Mainer. 1980. Physical and Chemical Characterization of Fog Oil Smoke and Hexachloroethane Smoke. Final report, Contract DAMD17-78-C-8085. NTIS: AD A080936.

Kelly, DP, Lee KP, and BA Burgess 1981. Inhalation toxicity of titanium tetrachloride atmospheric hydrolysis products. Toxicologist 1:76.

Kimbrough, R.D. and Linder, R.E. 1974. The toxicity of technical hexachlorobenzene in the Sherman strain rat. A preliminary study. Res. Commun. Chem. Path. Pharmacol. 8:653-654.

Kitchens, J.F., W.E. Harward, D.M. Lauter, R.S. Wentsel, R.S., and R.S. Valentine. 1978. Preliminary Problem Definition Study of 48 Munitions-Related Chemicals. Alexandria, VA, Atlantic Research Corporation. NTIS: A066309. April 1978.

Koss, G., and D. Manz. 1976. Residues of hexachlorobenzene in wild mammals of Germany. Bull. Environ. Contam. Toxicol. 15(2):189-191.

Kuiper-Goodman, T., D.L. Grant, C.A. Moodie, G.O Korsrud, and I.C. Munro. 1977. Subacute toxicity of hexachlorobenzene in the rat. Toxicol. Appl. Pharmacol. 40:529-549.

Lange, B., and N.U. Kirk, 1986. Bronchial asthma precipitated by zinc chloride smoke. Ugeskr. Laeger 148(8):455.

Loose, L.D., K.A. Pitman, K.-F. Benitz, and J.B. Silkworth. 1977. Polychlorinated biphenyl and hexachlorobenzene induced humoral immunosuppression. J. Reticuloendothel. Soc. 22:253-271.

Lower, W.R., R.J. Wang, S. Kapila, A.G. Underbrink, and A.F. Yanders. 1983. A Biological and Chemical Field Study of Obscurant Smokes at Fort Irwin, California. Technical Report, July 1983. Champagne IL, U.S. Army Corps of Engineers, Construction Engineering Research Laboratory.

Macaulay, M.B., and A.K. Mant. 1964. Smoke bomb poisoning: a fatal case following the inhalation of zinc chloride smoke. J. Royal Army Med. Corps 110:27-32.

Maloff, G.A. 1928. Toxicology of some chlorine derivatives of methane and ethane. Arch. Exp. Pathol. Pharmakol. 134:168-172

Marrs, T.C., W.E. Clifford, and H.F. Colgrave. 1983. Pathological changes produced by exposure of rabbits and rats to smokes from mixtures of hexachloroethane and zinc oxide. Toxicol. Lett. 19:247-252.

Marrs, T.C., H.F. Colgrave, J.A.G. Edginton, R.F.P. Brown, and N.L. Cross. 1988. The repeated dose toxicity of a zinc oxide/hexachloroethane smoke. Arch. Toxicol. 62(2/3):123-132

Matarese, S.L., and J.I. Matthews. 1986. Zinc chloride smoke bomb inhalation lung injury. Chest 89(2):308-309.

Mazzei, E.S., and C.M. Mazzei. 1973. Intoxication by a fungicide, hexachlorobenzene, contaminating wheat grains (French). Sem. Hôp. Paris 49:63-67.

McCarroll, N.E., C.E. Piper, and B.H. Keech. 1981. An *E. coli* microsuspension assay for the detection of DNA damage induced by direct- acting agents and promutagens. Environ. Mut. 3:429-444.

Mehendale, H.M., M. Fields, and H.B. Matthews. 1975. Metabolism and effects of hexachlorobenzene on hepatic microsomal enzymes in the rat. J. Agr. Food Chem. 23(2):261-265.

Milham, M.E., and D.H. Anderson. Obscuration Sciences Smoke Data Compendium: Standard Smokes. 1983. Special Publication ARCSL-SP-82024. Aberdeen Proving Ground, MD, U.S. Army Chemical Systems Laboratory.

Milliken, J.A., W. Douglas, and M.E. Kadish. 1963. Acute interstitial pulmonary fibrosis caused by a smoke bomb. Canad. Med. Assoc. J. 88:36-39.

Mitoma, C., T. Steeger, S.E. Jackson, K.P. Wheeler, J.H. Rogers, and H.A. Milman. 1985. Metabolic disposition study of chlorinated hydrocarbons in rats and mice. Drug Chem Toxicol. 8(3):183-194.

Montgomery, A.B., M.A. Stager, C.J. Carrico, and L.D. Hudson. 1985. Causes of mortality in patients with the adult respiratory distress syndrome. Am. Rev. Respir. Dis. 132:485-489.

Murray, M.J., and C.P. Flessel. 1976. A comparison of carcinogenic and noncarcinogenic metals *in vitro*. Biochemica et Biophysica Acta. 425:256-261.

Nastainczyk, W., H. Ahr, and V. Ulrich. 1982. The mechanism of the reductive dehalogenation of polyhalogenated compounds by microsomal cytochrome P450. Adv. Exp. Med. Biol. 136A:799-808.

National Cancer Institute. 1978. Carcinogenesis, Technical Report Series No. 68. Bioassay of Hexachloroethane for Possible Carcinogenicity. Publication No. NCI-CG-TR-68, CAS no. 67-72-1. Research Triangle Park, NC, National Toxicology Program.

National Cancer Institute. 1977. Carcinogenesis, Technical Report Series, No 13 Bioassay of Tetrachloroethylene for Possible Carcinogenicity. CAS No. 127-18-4. Publication No. NCI-CG-TR-13. Research Triangle Park, NC, National Toxicology Program.

Nemery, B. 1990. Metal toxicity and the respiratory tract. Eur. Respir. J. 3(2):202-219.

Novak, E.W., L.B. Lave, J.J. Stukel, and S. Miller. 1983. A health risk assessment for the use of hexachloroethane smoke on an army training area. U.S. Army Corps of Engineers, CERL Technical Report N-164, Dec, 1983. (Distribution limited to government agencies only.)

Novak, E.W., L.B. Lave, J.J. Stukel, and D.J. Schaeffer. 1987. A revised health Risk Assessment for the use of hexachlorethane smoke on an army training area. U.S. Army Corps of Engineers, CERL Technical report N-87/26, Sept 1987.

Nutrition Reviews. 1989. Interleukin-1 regulates zinc matabolism and metallothionein gene expression. Nutrition Rev. 47(9):285-287.

Pare, C.M.B, and M. Sandler. 1954. Smoke bomb pneumonitis: description of a case. J. Royal Army Med. Corps 100:320-322.

Parker, J.C., G.E. Casey, L.J. Bahlman, N.A. Leidel, P. Rose, H.P. Stein, A.W. Thomas, and J.M. Lane. 1979. Chloroethanes: review of toxicity. NIOSH Bulletin No. 27. J. Am. Ind. Hyg. Assoc. 40:A-46, A-48, A-50, A-52-60.

Payton, K.B., P.R. Glanagan, E.A. Stinson, D.P. Chordirker, M.J. Chamberlain, and L.S. Valberg. 1982. Technique for determination of human zinc absorption from measurement of radioactivity in a fecal sample or the body. Gastroenterol. 83:1264-1270.

Pedersen, C., C.P. Hansen, and W. Gronfeldt. 1984. Zinc chloride smoke poisoning following employment of smoke ammunition. Ugeskr. Laeger 146(32):2397-2399.

Peters, H.A. 1976. Hexachlorobenzene poisoning in Turkey. Fed. Proc. 35:2400-2403.

Peters, H.A., S.A.M. Johnson, S. Cam, S. Oral, Y Müftü, and T. Ergene. 1966. Hexachlorobenzene-induced porphyria: effect of chelation on the disease, porphyrin and metal metabolism. Am. J. Med. Sci. 251:314-322.

Peters, H.A., D.J. Cripps, and A. Gocmen. 1978. Porphyria 20 uears after hexachlorobenzene exosure (Abstract No. PP 10). Neurology 28:333.

Plotnikov, N.N., and L.N. Sokolov, 1947. Pharmacological Properties of Hexachloroethane. Farmakol. Toksikol. 10(2):47-51. (Chem. Abstr. 41:7535f, 1947)

Potter, J.L. 1981. Acute zinc chloride ingestion in a young child. Ann. Emerg. Med. 10(5):341-363.

Renner, G., and K.P. Schuster. 1977. 2,4,5-Trichlorophenol, a new metabolite of hexachlorobenzene. Toxicol. Appl. Pharmacol. 39:355-356.

Richards, R.J., J. Atkins, T.C. Marrs, R.F.R. Brown, and L. Masek. 1989. The biochemical and pathological changes produced by the intratracheal instillation of certain components of zinc-hexachloroethane smoke. Toxicology 54(1):79-88.

Rozman, K., W. Mueller, F. Coulston, and F. Korte. 1977. Long-term feeding study of hexachlorobenzene in Rhesus monkeys. Chemosphere 6:81-84.

RTECS. 1987. Registry of Toxic Effects of Chemical Substances, 1985-86 Edition. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Insittute for Occupational Safety and Health. Washington, DC, U.S. Government Printing Office.

RTECS. 1993. Registry of Toxic Effects of Chemical Substances, On-line database. Bethesda, MD. National Library of Medicine.

Santodonato, J., S. Bosch, W. Meylan, J. Becker, and M. Neal. 1985. Monograph on Human Exposure to Chemicals in the Workplace: Hexachloroethane. Syracuse Research Corporation, Syracuse, NY. NTIS: PB86-149317.

Saric and Knezevic. 1957. Industrial toxicology of some chlorinated hydrocarbons, Arg. Hig. Rada 8:251-269.

Sax, I.N. 1975. Dangerous Properties of Industrial Materials, 4th ed. New York, Van Nostrand Reinhold Company, p. 804.

Schaeffer, D.J., E.W. Novak, W.R. Lower, A. Yanders, S. Kapila, and R. Wang. 1987. Effects of chemical smokes on flora and fauna under field and laboratory exposures. Ecotoxicol. Environ. Safety 13(3):301-315.

Schenker, M.B., F.E. Speizer, and J.O. Taylor. 1981. Acute upper respiratory symptoms resulting from exposure to zinc chloride aerosol. Environ. Res. 25(2):317-324.

Schwander, P. 1937. Diffusion of halogenated hydrocarbons through the skin. Int. Arch. Gewerbepathol. Gewerbehyg. 76:109-116 (C.A. 31, 7520, 1937)

Seldén, A., G. Jacobson, P. Berg, and O. Axelson. 1989. Hepatocellular carcinoma and exposure to hexachlorobenzene: A case report. Br. J. Ind. Med. 46(2):138-140.

Seldén, A., M. Nygren, A. Kvarnlöf, K. Sundell, and O. Spångberg. 1993. Biological monitoring of hexachloroethane. Int. Arch. Environ. Health 65:S111-S114.

Shirai, T., Y. Miyata, K. Nakanishi, G. Murasaki, and N. Ito. 1978. Hepatocarcinogenicity of polychlorinated terphenyl (PCT) in ICR mice and its enhancement by hexachlorobenzene (HCB). Cancer Lett. 4:271-275.

Skog, E., and J.E. Wahlberg. 1964. A comparative investigation of the percutaneous absorption of metal compounds in the guinea pig by means of the radioactive isotopes: ^{51}Cr, ^{58}Co, ^{65}Zn, ^{110m}Ag, ^{115m}Cd, ^{203}Hg. J. Invest. Dermatol. 43:187-192.

Speizer, and J.O. Taylor. 1981. Acute upper respiratory symptoms resulting from exposure to zinc chloride aerosol. Environ. Res. 25:317-24.

Steindorff, K. 1923. Action of some chlorine derivatives of methane, ethane and ethylene upon the cornea. Arch Ophthalmol. 109:252-264.

Stocum, W.E., and R.G. Hamilton. 1976. A Risk Analysis of Exposure to High Concentration of Zinc Chloride Smoke. Report No. SAND76-0386. Albuqerque, NM, Sandia Laboratories.

Taylor, G. 1986. Acute Systemic Effects of Inhaled Occupational Agents. In Merchant, J.A., B. A. Boehlecke, G. Taylor, and M. Pickett-Hamer, eds. Occupational Respiratory Diseases. DHHS (NIOSH) Publication No. 86-102. Washington, DC, U.S. Government Printing Office, pp. 609-610.

Taylor, G.D. 1993. Chemical Agents, Weapons, and Defense Materiel Type Classified, Adopted, or Obsolete. Report No. ERDEC-SP-001. Aberdeen Proving Ground, MD, U.S. Army Edgewood Research, Development and Engineering Center.

Thun, M.J., T.M Schnorr, A.B. Smith, W.E. Halperin, and R.A. Lemen. 1985. Mortality among a cohort of U.S. cadmium production workers—an update. J. Nat. Cancer Inst. 74:325-333.

Town, C. and K.C. Leibman. 1979. In vitro dechlorination of polychlorinated ethanes by rat homogenates. Fed. Proc. 38: 538.

Town, C. and K.C. Leibman. 1984. The in vitro dechlorination of some polychlorinated ethanes. Drug Metab. Disp. 12(1):4-8.

Wahlberg, J.E. 1965. Percutaneous toxicity of metal compounds. A comparative investigation in guinea pigs. Arch. Environ. Health 11:201-204.

Wang, Y.-T., L.K.H. Lee, and S.-C. Poh. 1987. Phosgene poisoning from a smoke grenade. Eur. J. Respir. Dis. 70(2):126-128.

Weeks, M.H., R.A. Angerhofer, R. Bishop, J. Thomasino, and C.R. Pope. 1979. The toxicity of hexachloroethane in laboratory animals. Am. Ind. Hyg. Assoc. J. 40(3):187-206.

Weisburger, E.K. 1977. Carcinogenicity studies on halogenated hydrocarbons. Environ. Health. Perspect. 21:7-16

Williams, S.J. 1984. Prediction of ocular irritancy potential form dermal irritation test results. Food Chem. Toxicol. 22(2):157-161.

Yanders, A.F, E.W. Novak, W.R. Lower, A.G. Underbrink, and R. Wang. 1985. Mutagenic testing of obscurant smokes. Environmental Trace Substances Research Center, University of Missouri, Columbia, MO. 16th Annual Meeting of the Environmental Mutagen Society, Las Vegas, NV., USA, Feb. 25-March 1, Environ. Mutagen. 7, Suppl. 3.

Zey, J.N, and F. Richardson. 1988. Evaluation of Zinc Chloride Smoke Generating Devices, International Association of Fire Fighters, Washington, DC. U.S. Department of Health and Human Services, Cincinnati, OH, Report No. HETA-85-274-1879.

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