APPENDIX NN

INDEPENDENT CONSULTANT REPORT

BY

MELISSA MCDIARMID, M.D., M.P.H.

(REPORT ON CARCINOGENS)

DECONTAMINATING

AGENTS

Carcinogens in the Persian Gulf Conflict

Carcinogens

Introduction

The complexity and range of environmental hazards to which deployed Desert Storm/Desert Shield personnel had exposure opportunity include members of every known hazard class: biologic agents, chemicals and physical agents as well as those of warfare itself. Beyond identifying the presence of potential environmental hazards however, to assess the health risk of exposed personnel, the exposure circumstances, duration and dose of these agents is also crucial. The absence of these data severely limit the ability of public health professionals to make assessments about potential future health risk. This is generally true about most chronic outcomes, including cancer risk, although the relatively short duration of exposure in the Gulf (months) and our current understanding of the mechanism of cancer development, make determinations of cancer risk perhaps a bit easier to elucidate than some other disease outcome.

Mechanisms of Carcinogenesis

Over the last fifty years, the process of cancer development resulting from exposure to an environmental cancer causing chemical has been elucidated. While there are intricate molecular processes involved, there are several unifying and fairly straight-forward concepts which assist in understanding the process of cancer development.

The first concept is that cancer results from a multi-stage process, rather than a single insult or exposure. This process commences with exposure to a carcinogen- a substance which can cause cancers. This carcinogen interacts with DNA-the genetic material of a cell-and critically alters it, usually by covalently binding with it causing a mutation, this is termed " initiation." This process is not in itself sufficient to result in tumor formation. Rather it is the first in a series of events, the subsequent events and timing of which are also critical in advancing the likelihood of cancer development.

A subsequent exposure to usually a second agent, termed a "promoter", possibly in multiple doses, over the right time frame, may result in tumor formation. This " promotion" stage is likely composed of a number of steps. It is believed that part of the promotion stage involves a second critical mutational event in the cell's DNA.

The final stage of the process, " progression", then begins. It appears that there are chemicals that both enhance and inhibit this stage and that progression occurs over a prolonged period of time, with the type of tumor, its invasiveness and metastic properties being modulated by chemicals encountered during this later stage. [Frumkin, 1995]

Another important feature of the carcinogenic process is the concept of " latency". Latency is defined as the time span between the initiating event and the development of the recognizable tumor. The latency period for human cancer development tends to be quite long as we have observed in epidemiologic studies. According to Doll and Peto, world renowned cancer

epidemiologists, " It must be born in mind that cancer in humans seldom develops until one or more decades after beginning exposure to a carcinogen.." [Doll and Peto, 1981]

Risk Assessment

Risk Assessment is a process adopted by governmental public health agencies (EPA,OSHA), to characterize the magnitude and severity of population exposure to carcinogens. This is a four step process which involves:

(a) Hazard Identification- the collection of data to determine whether a substance is carcinogenic to humans. Data sources include epidemiologic studies, animal studies, short term bioassays and structure activity relationships (SARS) of the chemicals in question.

(b) Exposure Assessment- determines the population exposed to the putative carcinogen, at what concentration or exposure dose, for what duration and through what exposure route (inhalation, ingestion or skin absorption).

(c) Dose Response Assessment- involves applying information in the first two steps to construct a qualitative estimate of cancer risk at various exposure doses. This may involve extrapolation of data using mathematical models from higher dose exposures down to lower exposure concentrations, where cancer outcomes might be more difficult to identify.

(d) Risk Characterization- is the outcome of the above process. It yields a quantitative estimate of human cancer risk. It also considers measures of uncertainty for each of the above steps.
[Frumkin, 1995]

Epidemiologic Evidence

In examining the case for deployment-related cancer excess, we must look to epidemiologic studies. Two mortality studies of PGW veterans have been conducted (Kang and Bullman, 1995; Write et al, 1996). Neither found excess mortality for cancer when compared to that experienced by troops deployed elsewhere during the same period.

Another study of hospitalized PGW veterans reported in preliminary findings (Coate et al, 1995) pre-war versus post-war hospitalization rates for active duty troops deployed to the PG between August 1990 and July 1991 with those of un-deployed veterans. The study found no increase of hospitalization for any cause among PGW veterans compared to control veterans. Examination of 14 broad diagnostic categories in each of three past war periods elicited four instances of possible increased risk of hospitalization, one for neoplasms. The authors point out these were largely benign, but the time frame of 1991, would not allow for any latency after some presumed environmental exposure making any putative association biologically implausible.

The Cancer experience of active duty PGW service members is similar to that reflected in

the epidemologic studies. "Cancer is rare among CCEP enrollees. " (PAC Report pg.61) The types of cancer found most frequently (lymphomas, skin cancer and testicular cancer) are among the most commonly found in males of the deployed age group. These are the same findings involved in the DVA experience. "Cancer also is rare among individuals in VA's Registry. There does not appear to be an unusual incidence of any specific type of cancer in this population." (PAC Report pg. 61) The same three most common cancer types seen in the CCEP population were reported in the VA registry cohort. Thus both epidemologic evidence and registry data sources are corroborating no Cancer excesses in the PGW exposed cohort.

Exposure Assessment

Exposure Assessment in Reproductive Health Studies

Most of the studies of reproductive health of Persian Gulf War veterans, whether they be those that have been completed, or those that are ongoing, suffer from extremely weak exposure assessment. A majority of the studies use exposure assessment definitions as simple as those deployed being exposed, and those non-deployed being unexposed for controls. This is clearly inadequate. The most seriously flawed in this regard are the birth defects studies which generally use birth defects reporting data bases, and compare outcome with Persian Gulf deployed versus non-deployed members, and there is absolutely no discussion of exposure assessment. In exception to this, however, is the Iowa study of regular military and National Guard deployed versus non-Persian Gulf deployed regular and National Guard service members. Here, although the only reproductive outcome that is surveyed for are symptoms of sexual discomfort, there is a much greater emphasis in a fairly detailed environmental exposure history. Of the studies that are ongoing, again the very large hospital based medical record studies, such as the Cowan and Calderon studies, as well as the Aronetta studies 3, 4 and 7, referred to in Dr. Swan's report, all have this significant weakness of having no address of exposure assessment, except deployment status. The other studies that are ongoing, several do, however, address environmental exposures. These include the National Health Survey performed by the Department of Veterans Affairs, which is going to include a detailed self report of a number of environmental exposures, as well as the University of Oregon's evaluation of infertility, menstrual abnormalities, fetal loss and genital tract symptoms, where they are also going to include a quite detailed environmental history of physical, biological and chemical agents. The planned study by the KLEMM group of 10,000 Persian Gulf War deployed women compared to non-deployed woman, looking at infertility, pre-term birth, still birth and birth defects, has a very detailed environmental exposure history proposed, and includes duration of exposure before, during and after deployment to the same environmental hazards. This is an added strength that is not seen in any of the other studies heretofore. Also of interest, we should mention that the clinical study at the University of Cincinnati, looking at seminal plasma hypersensitivity reactions plans to address in a research format some of the environmental agents which may be active here by introducing some of these environmental substances in an in vitro system during the assessment of seminal plasma hypersensitivity. This type of inclusion of environmental effectors in a research protocol is something that we should like to see in future research studies.

Epidemology of Self-Reported Environmental Exposures

The 1996 summary of the Department of Defense's (DOD) Comprehensive Clinical Evaluation Program (CCEP) for Persian Gulf War Veterans included data for more than 18,000 returned service members who requested a complete health evaluation. Part of the health evaluation involved questionnaire completion of a self-reported environmental history. The questions elicited information about food and water intake, and personal habits, such as smoking and exposure to passive smoke, as well as questions regarding the more uncommon chemical environmental exposures. Obviously, the circumstances of exposure, and what determines the individual service member's positive response, are variable. Frequency of exposure is also not obtained by this method. Nonetheless, it gives a sketch of what individual soldiers reported.

A similar battery of questions were included in the Department of Veterans Affairs (DVA) Persian Gulf Registry questionnaire. Responses elicited are displayed in Table X. Of interest is the close agreement between the two sources on frequency of environmental exposures. Passive cigarette smoke, diesel exposure, oil fire smoke and tent heater fumes were most commonly reported.

The detail of the questions in both the DOD's CCEP assessment, and the DVA's assessment are problematic. While a fairly complete "laundry list" of potential exposures is elicited, information regarding crucial aspects of the exposure are lost because of the way the question is worded. Most of the questions from both sources are worded like: "While in the Persian Gulf, do you believe you were exposed to any of the following?" It is not clear to the service member what constitutes a positive answer. For example, exposure to diesel fumes, the most common affirmative response reported (90% of veterans and 88% of active duty service members) could like have been elicited by anyone riding in a vehicle. More discriminating information could have been elicited, such as attempting to determine more intense exposure, that is occupational diesel exposure arising from, say assignment to vehicle maintenance or transport. This compared to a "environmental" exposure opportunity of any vehicle rider, which is what is suggested by an open ended question like "Have you ever been exposed?" This simple discrimination would lend some semi-quantitative information about exposure intensity. The DVA questionnaire gives a good example of a simple improvement in questioning, which refines the information elicited. When asking about diesel or petrochemical exposure, it asked about skin contact. While it is understood that only so much detail can be captured, some simple refinement of questions could enhance the value of the information obtained without increasing the number of questions. Tightening up the overall summary questions from "were you ever" to "were you, as part of your job duties working with"; or "did you have skin exposure to..."; or "other than bystander exposure, did you work with or regularly (define time frequency appropriate to the substance in question) handle substance X ?"

There are some substances for which we are more interested in chronic exposure, such as petrochemicals, diesel and particulates, and discriminating phrases could be added to those questions to enhance response value. For other substances, we are interested in only one time exposure, such as mustard agent, but even then, we are interested in whether there was skin contact or true breathing of fumes, such as in a fire or explosion.

To summarize, without adding to the number of questions either health assessment battery currently includes, more refinement of the language used in crafting questions, and some guidance given to participants about what type of exposure constitutes a clinically important "yes" to the question, could

greatly enhance the value of this information.

Candidate Carcinogens

A number of carcinogens or potentially carcinogenic substances have been referred to as present in the Gulf War theater both by the IOM Committee and the PAC. I have attempted to include those substances and also have reviewed the GAO Report on Reproductive hazards to identify possible carcinogens on that list. A discussion on those agents' toxicology and evidence of carcinogencity is displayed in an appendix. In addition, several examples of each type of hazard class will be reviewed in the text and are summarized in Tables 2-4.

Pesticides

There is documentation that the DOD shipped large volumes of one OC-Lindane to the Gulf. A commonly encountered organochlorine insecticide, it is the agent used to treat head lice. (PAC p.106)

According to the National Toxicology Program (NTP), there is sufficient evidence for the carcinogenicity of various isomers of hexacholorocyclohexane (a substituent of lidane) in animals. There is inadequate human evidence for cacinogenicity however.

Sarin (O- isopropyl methylphosphonic acid)

Sarin is a chemical Warfare agent which is a potentially lethal cholinesterase inhibitor. It is not listed on the IARC or NTP carcinogen list (Sidell, 1992).

Possible exposure to sarin or other Chemical Biological Warfare (CBW) agents from atomospheric dispersion after bombing and destruction of Iraqi CBW facilities have been raised in PAC reports and IOM discussions. While atomospheric models of such an exposure are controversial at best, the IOM Committee counsels ".... There is no available evidence in human or animal studies to date that exposure to nerve agents at low levels that do not produce any detectable acute clinical or physiological manifestations results in any chronic or long-term adverse health effects."[u] IOM Report page 50.

While the committee went on to make recommendations of some issues which required further research (e.g. long-term, low level exposure effects), they stated that they "..relied heavily on known toxicological and pathological effects and existing knowledge regarding short and long-term health effects of CBW agents and on findings reported from extensive DOD and DVA clinical evaluations of veterans. "As well there has been no confirmed report of clinical manifestations of acute nerve agent exposure." (IOM report pg. 50).

As has been discussed throughout this document, while a number of toxic agents were present in the GW theater, the duration and chronicity as well as intensity of exposure figure into the likelihood of adverse health effects development. This is especially true of carcinogen exposure. While some of the commonly used pesticides are animal carcinogens, they are not

recognized human carcinogens and the expected exposure scenarios make cancer development unlikely.

Oil Fire and Soil Contaminants

Volatile Organic Compounds

A health study of Army personnel deployed from Germany to Kuwait in June-September 1991 included an assessment of blood concentrations of several commonly encountered volatile organic compounds (VOCs). Concern about VOC exposure from possible oil well fires suggested this component of the comprehensive health study.

Subjects were assessed in three phases, in Germany prior to deployment; several weeks after deployment in Kuwait; and upon return to Germany. Generally, there were not significant differences in findings in the three phases and VOC results were considered within the range of levels determined to be normal U.S. reference levels.

Investigators have reported only one significant elevation in VOCs among a large number of Kuwait-deployed servicemen and that was to the compound tetrachloroethelene (PCE). This compound is not usually associated with oil fires, but was also found to be higher in some firefighters in Kuwait. One suspicion is that these elevations are due to PCE exposure during weapons cleaning. (Personal Communication, D. Ashley, NCEH, CDC, Atlanta)

The compounds sampled for in this study can be found in the table below.

Table: Volatile Organic Compounds Sampled in Army Health Risk Assessment

1,1,1 - Trichloroethane
1,4 - Dicholorobenzene
Benzene
Chlorobenzene
Chloroform
Ethylbenzene
m-/p- Xylene
Xylene
Styrene
Tetrachloroethene
Toluene

It must be kept in mind that the time frame of sampling in Kuwait was summer 1991 and therefore not necessarily representative of VOCs exposure earlier in the deployment. None-the-less, the data are valuable in the context of excursions observed in Germany and as compared to expected levels in the U.S.

Particulate Matter/Air Pollutants

Dr. Leibowitz's report on air pollutants summarizes the work of a number of different investigators regarding air pollutants of different classes including particulate matter (PM), some metals and oxides of Nitrogen (NO_x) and sulfur dioxide (SO_2). He feels there is evidence for " likely acute health hazards and potential for some chronic health hazards" (Lebowitz draft,p. 12). I believe that this broad statement is about as precise as anyone can get given the exposure assessment limitations. For some of the air pollutants Dr. Lebowitz discusses, the data are better than they are for some other toxicant classes found in the theater. I don't think the duration of exposure to the air pollutant concentrations discussed here would significantly contribute to cancer risk of the a deployed service member.

Diesel Exhaust

Diesel exhaust is a complex made up of gases and particulate produced as a waste product from diesel-powered equipment. Its major components include carbon dioxide, carbon monoxide, oxides of nitrogen and particulates. Animal studies have consistently demonstrated significant increases in lung tumors in chronically exposed (at least 24 months) animals. (IARC, 1989). Also numerous epidemologic studies in humans demonstrate excess cancer risk (NIOSH 1988, IARC 1989). The International Agency for Research on Cancer (IARC) classifies diesel exhaust as a probable human carcinogen (Group 2A).

Benzo (a) pyrene

A number of toxic constituents characterize oil fire exposures, with much attention given to the polycyclic aromatic hydrocarbon benzo (a) pyrene.

Environmental characterization of Kuwait oil-well fires indicated the likely presence of numerous genotoxic contaminants. Mutagenic products of combustion including polycyclic aromatic hydrocarbons (PAH) such as benzo (a) pyrene (BAP) were a concern in performing a health risk assessment for troops deployed to Kuwait in June - September, 1991. As part of a larger health assessment of these troops, the U.S. Army Environment Hygiene Agency (USAEHA) assessed the potential for mutagenic exposure. The study employed a generic measure of mutagen exposure, sister chromatid exchange (SCE).

Elevations of baseline SCE frequencies have been employed as indicators of human genotoxic exposure to a number of environmental agents (Hansteen, 1982; Sorsa and Yager, 1987) including polycyclic aromatic hydrocarbons (PAHs) (Rudiger et al., 1976; Dosaka et al., 1987).

Frequencies of sister chromatid exchange (SCE), a measure of genotoxic exposure, were assessed in military troops deployed to Kuwait in 1991. Soldiers completed health questionnaires and had blood collected prior to, during and following deployment to Kuwait. Frequency of spontaneous SCE was determined on blood samples as a measure of mutagenic exposure and are displayed below in Table 1. Compared to pre-deployment baseline SCE frequency means, levels obtained two months into the Kuwaiti deployment were significantly increased ($P < 0.001$) and persisted for at least one month after return to Germany. Outcome was unaffected by known personal SCE effect modifiers including smoking, age, and diet.

Table 1.

Comparisons of SCE frequencies for soldiers prior to, during and post deployment to Kuwait

n	Prior	During	Post
50[a]	4.33[b] ± 0.07[c]	5.12 ± 0.09	
35	4.38[c] ± 0.09		5.28 ± 0.12
26	4.41[c,d] ± 0.11[c,d]	5.11 ± 0.16	5.29 ± 0.15

[a]The number n varies due to differences in soldiers available for phlebotomy during each collection mission.
[b]$p < 0.0001$ comparing 'Prior' to 'During', paired t-test; [c]$p < 0.0001$ comparing 'Prior' to 'Post', paired t-test.
[d]$p < 0.001$ comparing 'Prior' to "During' paired t-test; [e]Mean ± SE of individual means of SCEs per cell.

This study reveals a highly significant increase in mean SCE for a population of soldiers serving in Kuwait while oil-well fires burned. This increase persisted for at least one month following return to their pre-deployment assignment in Germany.

The genotoxicity of air particulates isolated during the Kuwait oil well fires was demonstrated by Kelsey et al. (1994) who reported a dose-response relationship for SCE induced in vitro with air particulate collected in Kuwait. However, a particulate sample collected in Washington, DC showed similar results, although not with the same intensity as the Kuwaiti sample. Kelsey also reported slight increases in the mutation frequency of the hprt locus induced by both particulate samples, with the Kuwaiti sample being more mutagenic. This study failed to demonstrate PAH-DNA adducts through ^{32}P-post-labelling experiments in a human lyphoblastoid cell line treated with the particulate samples. Darcey and colleagues also failed to show differences in levels of PAH-DNA adducts in lymphocytes of nine workers fighting oil fires in Kuwait (Darcey et al., 1992). These observations suggest that other constituents of combustion products rather than PAHs may be responsible for the genotoxicity reported by Kelsey et al. Environmental exposures not due to burning oil fires may have also caused the observed increases in SCE.

The authors concluded that although a statistical increase in SCE frequency has been demonstrated in troops deployed to Kuwait, implying a genotoxic exposure, multiple candidates exist as the potential cause of this observation. At present, SCE elevations are thought to measure exposure to some genotoxic agent, but the long-term health consequences of this phenomenon have not been determined in this or other populations' exposure to genotoxicants. (McDiarmid, et al., 1995).

Another aspect of the Army's larger health risk assessment determined environmental PAH

exposure which revealed low ambient levels of PAHs in the areas where soldiers were working in Kuwait. As well, measures of PAH interactions with human blood lymphocyte DNA (PAH-DNA adducts) and aromatic-DNA adducts were at their lowest levels in Kuwait compared to levels in Germany. (Poirier M. et al., in preparation). These results suggest that the SCE elevations observed by McDiarmid's group in this same cohort of soldiers are not due to environmental PAH exposure. It is important to realize however, that this group of soldiers were deployed in the June-September, 1991 time frame, and their duties did not involve oil well fire suppression, thus their proximity to the burning wells was not a likely risk factor, nor can these exposure circumstances be widely attributed to other deployed units. There is limited evidence, however, that environmental PAHs and BAP may not have played as significant a role as anticipated in potential health risks to soldiers during deployment.

Other Toxicants

Depleted Uranium (DU)

Uranium is a naturally occurring heavy metal found in the earth's crust which is an alpha-emitting radioactive nuclide. It occurs in several isotopic combinations. Naturally occurring uranium is an isotopic mixture of U^{234} (0.005%), U^{235} (0.711%) and U^{238} (99.284%).

Depleted uranium is a byproduct of the uranium enrichment process which increases the percentage of U^{235} in the isotopic mix of natural uranium. This enriched uranium has various nuclear power and nuclear weapons applications. The product remaining is a uranium compound "depleted" of U^{235} and U^{234}. Thus DU possess a radioactive activity about 60% that of naturally uranium. By weight percentage, naturally occurring uranium posses a radioactivity of 0.7 uCi/gm versus 0.4 uCi/gm for DU. [Daxon, 1995]. When alloyed with other metals to enhance its physical characteristics, DU is used in weapons systems.

The Nuclear Regulatory Commission's (NRC) standard for public exposure to "man-made" sources of radiation is 100 mrem/year above background (10.CFR 20.1301).

Uranium is an alpha particle emitter. An alpha particle is a positively charged (+2) ion composed of two protons and two neutrons. Alpha particles cannot penetrate the skin's outer layers and normally therefore don't pose a health risk unless they are internalized. Beta particles (an electron emitted during radioactive decay of a neutron) is more penetrating. A gamma ray, a discrete packet of electromagnetic energy with no mass or charge, is extremely penetrating and thus poses a health hazard externally and internally.

Potential radiologic health effects from external DU exposure are thought to be small. " The primary external hazards from DU are β and γ radiation. These emissions are generated by the radioactive decay of trace-levels of uranium daughter (decay) products. The radiation exposure that Army personnel receive depends on the amount of DU present, the DU component or piece of equipment in question, (kinetic energy penetrator, DU armor, etc.), the configuration (in manufacture, in storage, uploaded on a vehicle, bare penetrator, etc.) and the exposure time. All DU weapon systems used by the Army are shielded to control the β radiation emitted from

DU. The Army has aggressive programs for managing the radiation exposure potential from DU munitions and tank armor." (Summarized by Daxon, pg. 106). Researchers have conducted investigations to evaluate radiation field strengths. These investigations sought to define the level of exposure for soldiers and other personnel operating or maintaining these weapon systems.

Table 6-1. Comparison of the Relative Radiation Dose per Unit Mass Internalized, for DU and other Substances

ISOTOPE	RELATIVE RADIATION DOSE*
DU	1.0
Naturally Occurring Uranium	1.7
^{226}RA	200,000
^{241}Am	30,000,000

* Doses were calculated based on the committed effective dose equivalent per unit intake factors for inhalation quoted in EPA's Federal Guidance Report No.11 (Eckerman et al, 1988)

Uranium doses were calculated assuming that all were insoluble and, as such, represent worst case (highest) committed effective dose equivalent values (from Daxon).

Continuing from Daxon.....

Danesi (1990) summarized the exposure potential from DU weapon systems. He concluded that intact DU weapons systems, both munitions and armor, presented very little external exposure risk for personnel working with them. Danesi (1990) further suggested that soldiers and support personnel working with or using DU weapon systems are unlikely to exceed the exposure limit for the general population and will not approach the limit for occupational exposure (5,000 mrem/yr.) The Army monitors soldiers and support workers according to NRC occupational exposure standards (10 CFR 20.1201).

Holding a spent DU penetrator (DU metal without shielding) would deliver a skin dose (β and γ) of approximately 200 mrem/hour (Coleman et al., 1983; Cross, 1991: Needham and Coggle, 1991; Piesch et al., 1986; Rohloff and Heinzelmann, 1986) The current occupational exposure radiation dose limit (β and γ) for skin is 50,000 mrem/yr. The only plausible way that a soldier or support person could exceed this skin dose would be if a piece of DU from an expanded penetrator were carried as a souvenir.

The radioactive properties of DU have the greatest potential for health impacts when DU is internalized. DU can be internalized through inhalation or ingestion. Inhalation can occur during DU munitions testing, during a fire involving DU munitions or armor, and when DU particles are re-suspended by testing or fires. The inhalation potential of a particle depends on its dimensions and mass. The effective particle size is determined

from the mass-mean particle-size. Ingestion occurs primarily from hand-to-mouth transfer or from DU-contaminating water or food. Fragment wounds containing DU metal and contamination of any wound with DU occur in combat.

Internalized DU delivers radiation wherever it migrates in the body. Within the body, α radiation is the most important contributor to the radiation hazard posed by DU. The radiation dose to critical body organs depends on the amount of time that DU resides in the organs. When this value is known or estimated, cancer and hereditary risk estimates can be determined. (ICRP, 1977).

The health risks of internal DU exposure are a function of the particle characteristics, route of exposure, duration of exposure, and the species of DU (Eckerman et al., 1988; ICRP, 1981). The rate at which DU is eliminated can be measured in urine or, in the case of ingestion, in the feces. These data can be used to estimate the total amount of DU internalized. From this and other information, researchers can develop health risk models to estimate health risk for various types of internal DU exposure (Boecker et al., 991; Eisenbud, 1987; ICRP, 1981, 1979; Kathren and Weber, 1988; Kocher, 1989; Leggett, 1989; Toohey et al., 1991; Wrenn et al., 1985)."

Health Risks from Chemical Toxicity

Because the radioactivity of DU is very low, the chemical toxicity of DU may be the more significant contributor to human health risk. As previously indicated, DU and natural uranium have essentially the same chemical behavior and toxicity. Therefore, chemical toxicity data developed for any isotope of uranium are applicable to DU. Other heavy metals--such as lead, chromium, tungsten, and uranium--are also chemically toxic. The toxic properties of DU and uranium have been broadly studied (Voegtlin and Hodge, 1949, 1953; Stokinger et al., 1981; Kathren and Weber, 1988; Leggett, 1989; Diamond, 1989; Kocher,1989;Zhao and Zhao, 1990).

As has been the case throughout this report, the absence of exposure assessment data severely limit what can be said about a soldier's potential risk of a cancer outcome from a " DU" exposure. It is believed by a majority of investigators involved in following the DU-exposed soldiers from the several " friendly fire" incidents, that those soldiers with retained metal fragments are and were likely the " most exposed" because their fragment retention constitutes an " on-going" exposure of some seven year's duration. The inhalation exposures that accompanied those events are thought likely to be of greater intensity than other exposure scenarios that have been described including those involving potential exposure during rescue operations, decontamination and equipment overhaul and preparation for transport; and even more remotely exposed, in fact, more aptly environmentally rather than occupationally exposed, those with " bystander" exposure (walking by a burning Bradley, for example.) These examples constitute a model of " concentric rings" of exposure, with those involved in the friendly fire incidents in the center, those involved in the rescue, decontamination (decon) or possibly

rare health surveillance activities in a intermediate circle and the more remotely, possibly one-time, environmentally exposed in the outer-most circle. Various exposure modeling scenarios are being constructed by the Radiation Health groups of the Army, and should provide some improvement regarding exposure opportunities for these potentially exposed groups. Of special import in this work are the respiratory exposure issues surrounding the opportunity to inhale re-suspended DU particles (during decon operations, for example).

Caution is warranted however, because although these modeling scenarios will hopefully fill data gaps too long with us, the models, almost by definition, will be built on multiple assumptions. This does not render the results useless, but also does require acknowledging the uncertainty which accompany their conclusions.

Concerns about uranium exposure as a potential cancer risk are driven by its alpha-emitting radiologic properties. A number of human epidemologic studies have been done in uranium miners exposed to uranium (and other potentially toxic substances in mines) over the past 30 years. Although several of these studies have found lung cancer excesses in miners, attributing these excesses to uranium has been difficult due to the presence of other hazards in the mines including radon gas, silica, other metals and possibly miners' smoking [Samet et al 1984, Gottlieb and Husen 1982; Summarized by ATSDR 1997].

Studies evaluating lung cancer risk in uranium- processing nuclear plant workers have been similarly plagued by worker exposure to other radioactive sources. Several studies found excesses in lung cancer, but could not unequivocally link them to uranium exposure (Cragle et al, 1988; Cookfair et al.,1983). Studies of bone cancer (Sarcomas) associated with uranium exposure also have not shown excesses in humans.(Samet et al 1986; Wrenn and Singh 1983; Summarized in ATSOE 1997]. Several studies of lymphatic and hematopoetic tissue have found small excesses, but again, the questions of exposure to other radioactive sources (e.g. TH ^{230}, a decay product of U ^{234}) is raised. (Archer et al 1973; Waxweiler. 1983). Taken as a group, the human epidemologic evidence that elemental uranium itself has resulted in cancer excesses is not strong. Rather the presence of uranium progeny (radon) or other radiologic or toxic metal exposure sources are compounding and are likely driving the cancer excesses observed.

These data regarding elemental uranium suggest that the radiologic cancer risk of DU exposure is likely even lower than that for elemental uranium due to the relatively lower radioactive activity of DU (0.4 uCI/gm) compared to elemental uranium (0.7 uCi/gm).

As well , the multi-stage theory of cancer development suggests that the more remotely, environmentally DU-exposed, those with by-stander exposure, those with short duration exposure, are likely not to have sustained a statistically significant cancer risk. The small cohort of soldiers with retained metal fragments are likely the group at highest risk for cancer, (due to on-going exposure derived from the retained metal). However, even seven years into the exposure, there is no clear evidence of DU-related

clinical health effects in those soldiers with retained fragments. Latency issues and prudence would suggest, however, that this group continue to be followed.

In summary, while DU is a radiologic hazard, its relatively low radiologic activity, the low likelihood of prolonged duration of exposure (except for the group with retained metal fragments), combined with the mechanistic issues the multi-stage theory of carcinogenesis implies, suggests that a significant cancer risk from DU exposure is small. This is the opinion of both the IOM Committee and the PAC.

Mustard Agent

Mustard agent, an akylating chemical weapon, is capable of causing covalent binding of an alkyl group (small carbon-containing groups) to genetic material (the DNA of a cell). Hence it possesses mutagenic and potentially carcinogenic activity. It is highly reactive and can cause skin and eye burns acutely. There is evidence of an increase in lung cancer from exposure. (IOM, 1993; ATSDR, 1992.)

One confirmed case of mustard agent exposure has been documented in a soldier exploring a captured bunker in Southern Iraq on March 1, 1991. It is unlikely that there was widespread or significant exposure to mustard agent in the absence of other reports of acute effects.

Aflatoxin

Aflatoxin, a naturally occurring toxin elaborated from mold growing on some stored grains, peanuts or other food stuff under certain storage conditions, is raised as a potential environmental carcinogen. There is epidemiologic evidence that aflatoxin ingestion is associated with an excess of liver cancer and that liver cancer incidence is higher in geographic areas where there is aflatoxin excess (e.g. China) Wogan, 1992[Ref.] However, the exposure scenario and evidence which could make this toxicant a plausible candidate for widespread concern is absent.

Increased rates of liver cancer could result decades following low-level exposure, although available evidence reviewed by the committee does not indicate such exposures occurred during the Gulf War." PAC Report p. 112.

Research Regarding Cancer

There is little government sponsored ongoing research activity, specifically regarding cancer risk. Given the summary of biologic plausibility and exposure scenarios recounted thus far, this lack of activity is not particularly inappropriate. If there is a cancer excess to be documented in deployed troops, we know that the latency between first exposure, and onset of disease, is usually many years (normally at least ten), and therefore any excesses are still to be found in the future.

There are a number of applied (rather than human epidemiologic) studies ongoing which do

relate to potential cancer risk. These include the study titled "Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure", part of the U.S. Army Kuwaiti oil fire health risk assessment (project # HHS-3). The depleted uranium (DU) basic studies, including an animal study of imbedded DU metal fragments (project #DOD-7A) being done at the Armed Forces Radiobiology Research Institute (AFRRI) in Bethesda, and an inhalation toxicology study of DU fragment carcinogenicity (project #DOD-7B) performed at the Inhalation Toxicology Laboratory of the Department of Energy in Albuquerque are also ongoing.

Some studies already completed have helped inform this report. For example, the U.S. Army Kuwaiti oil fire health risk assessment results (DOD-16; DOD-18) have been reported in this document in the section discussing polycyclic aromatic hydrocarbons and volatile organic compounds.

Although listed as environmental toxicology studies, several of these projects may have important input regarding exposure assess ment for carcinogens. These include the characterization of emissions from tent heaters (project #DOD-34) ongoing at the U.S. DOE Laboratory at Albuquerque, the Persian Gulf Veterans Health Tracking System (project #DOD-19) at the Center for Health Promotion and Preventive Medicine (CHPPM) at Aberdeen, and the Retrospective Verification of Mustard Gas Exposure Project (VA-47) at the Louisville VAMC, may contribute. Although this study's aim is to correlate mustard gas exposure to reproductive risk, its applicability to cancer risk is also clear.

Another basic research study with a non-cancer focus, but with potential application to the cancer question, is a project titled "DNA Damage From Chemical Agents, and its Repair" (project #VA-6D) at the Portland VAMC. Here the focus is on nervous system insult from mustard exposure. However, some of the measures of DNA- mustard interactions (DNA adducts) may be applicable to cancer (and reproductive hazard) questions.

Epidemiologic studies that are examining the cancer question include an ongoing mortality study of veterans (project VA-1) and a completed study of U.S. military personnel (project #DOD-15).

Also of interest is an ongoing Boston VAMC study of Gulf War and Vietnam veterans cancer incidence (project VA-4C). This study involves linking rosters of Gulf War veterans to state cancer registries in the New England area. These record linkage studies tend not to focus on specific environmental exposures, but would look as Persian Gulf War service as the exposure, and compare results to non-Persian Gulf War deployed veterans. This is a reasonable way to do surveillance for the unlikely, but possible cancer excesses which might arise from Persian Gulf War deployment.

Recommendations

i. The inappropriate use and application of toxic substances (diesel fuel used as a sand suppressant) needs to be identified and stopped. Training in hazardous materials handling and common sense handling of these substances needs to be implemented. The NIEHS model of tiered hazmat training is suggested.

ii. As the PAC report suggested, surveillance for cancer development can be planned for and implemented although care to refine exposure assessment questions for epidemiologic tools needs to be brought to the process.

iii. Future surveillance of the DU-exposed "friendly fire" cohort is required. This group is perhaps the only undisputed carcinogen-exposed cohort identified from the deployment. Although we are heartened by good health outcomes up to now and the relatively lower radioactive intensity of DU compared to natural uranium, the exposure circumstances of retained metal fragments has not been previously encountered and represents an on-going exposure. We are obliged to follow them forward.

PAC Recc pg. 126

"DOD & VA should perform long-term mortality studies of GW veterans appropriate for investigating cancer rates in the Gulf War veteran population in coming decades."

Table 1: Frequency of Self-Reported Environmental Exposures in Gulf War Veterans (GWV)[a] and Active Duty Service Member (ADS) [b]

EXPOSURE	POSITIVE RESPONSE	
	GWV[a] (%)	ADS[b] (%)
Passive Cigarette Smoke	88.5	88
Diesel/Other Fuels/Petrochemical Fumes	90.4	88
Oil Fire Smoke	72.6	71
Tank Heater Fumes	68.6	70
Pyridostigmine Bromide	64.2	74
Personal Pesticide Use	66.7	66
Burning Trash/Feces	73.9	N/A
Skin Exposure to Fuel	73.7	N/A
ATE Non-US Food	71.3	66
Chemical Agent Resistant Paint CARC)	34.5	47
Solvent /Paints	53.6	48
Anthrax Immunization	48.7	49
Ate Contaminated Food	33.2	21
Microwaves	34.2	N/A
Bathed in Contaminated Water	28.6	20
Bathed in Non-Military Water	30.5	N/A
Bathed in/Drank Non-US Water	N/A	32
Botulism Vaccine	26.8	26
Depleted Uranium	14.2	15
Nerve Gas	14.1	61
Took Oral Meds to Prevent Malaria	N/A	22
Mustard Gas/Blistering Agent	N/A	25
Chemical Alarm	N/A	65
Witnessed Casualty	N/A	56
Witnessed SCUD Attack	N/A	54
Witnessed Actual Combat	N/A	37
Wounded in Combat	N/A	2

a = From Office of Public Health & Environmental Hazard
s. DVA. "Review of DVA Revised Gulf War Registry & In-Patient Treatment Files (12/97) N = 10,075
b = Percent based on participants who answered Yes or No (excludes unknown) from DOD CCEP for PGW Veterans (4/96). N = 18,075

TABLE 2: SUMMARY OF MUTAGENICITY AND CARCINOGENICITY OF SELECTED PESTICIDES

AGENT	MUTAGENICITY	CARCINOGENICITY
Carbaryl	• Slight mutagenic risk • May combine with dietary nitrite to form mutagenic constituent	• No tumors in 10 long-term rodent studies • Dietary nitrite constituent was carcinogenic at high doses in one study
Diazinon	• ? Mutagenicity	• Not considered carcinogenic
Dichlorvos	• + in-vitro mutagenicity • - Mutagenicity in live animals	• Classified as "possible human carcinogen" by EPA
Lindane	• Unlikely mutagenic in humans at low dose	• Carcinogenicity in animals is low (IARC) • One isomer is carcinogenic in animals, however.
Pentachlorophenol	• Weakly mutagenic at most • No evidence in humans	• + animal carcinogen (mice) • Limited evidence for carcinogenicity in humans
Pyrethrins	• No information found	• No status established
Warfarin	• No information available	• No information available
Sarin		• Not listed as carcinogenic by IARC or NTP

International Agency for Research on Cancer (IARC); National Toxicology Program (NTP)

See appendix for sources and citations

TABLE 3: SUMMARY OF CARCINOGENCITY OF SELECTED OIL FIRE & SOIL CONTAMINANTS

AGENT	CARCINOGENICITY
Arsenic	• Sufficient evidence of carcinogenicity in humans (IARC)
Cadmium	• Sufficient evidence of carcinogenicity in animals • Limited evidence in humans (IARC)
Hexacholorobenzene	• Sufficient evidence in animals • Inadequate evidence in humans (IARC)
Lead	• Sufficient evidence of carcinogenicity in animals • Inadequate evidence in humans (IARC)
Nickel	• Sufficient evidence of carcinogenicity in animals • Sufficient evidence in humans (IARC)
Polycyclic Aromatic Hydrocarbons (PAHs)	• Sufficient evidence of carcinogenicity in animals for some PAHs (IARC) • Many + epidemiologic studies of increased cancer incidence in humans
Silica	• Sufficient evidence of carcinogenicity in animals • Limited evidence of carcinogenicity in humans (IARC)
Diesel Exhaust	• Sufficient evidence of carcinogenicity in animals • Limited evidence of carcinogenicity in humans (IARC)

International Agency for Research on Cancer (IARC); National Toxicology Program (NTP)

See appendix for sources and citations

TABLE 4: SUMMARY OF CARCINOGENCITY OF SELECTED TOXICANTS

AGENT	CARCINOGENICITY
Mustard Agent	• Limited evidence of carcinogenicity in animals • Sufficient evidence of carcinogenicity in human (IARC)
Turbine Fuel JP-5	• Not listed as a carcinogen by IARC OR NTP
Turbine Fuel Aviation JP-8	• Not listed as a carcinogen by IARC OR NTP
Fuel Naval Distillate M/L-F (NATO F 76)	• Not listed as a carcinogen by IARC OR NTP

International Agency for Research on Cancer (IARC); National Toxicology Program (NTP)

See appendix for sources and citations

References

Agnew J, McDiarmid MA, Fitzgerald S: A survey of reproductive health of women firefighters. (in preparation).

Agnew J, McDiarmid MA, Lees PSJ, Duffy R: Reproductive hazards of fire fighting 1. Non-chemical hazards. Am J Ind Med 19:433-445, 1991.

Alcser KH, Brix KA, Fine LJ, Kallenbach LR, Wolfe RA: Occupational mercury exposure and male reproductive health. Am J Ind Med 15:517-529, 1989.

American Academy of Pediatrics (ARP) Committee on Drugs. The Transfer of Drugs and other Chemicals in Human Breast Milk. Pediatrics 93: 137 - 150, 1994

American Medical Association Council on Scientific Affairs: Effects of physical forces on the reproductive cycle. JAMA 251-247-250, 1984a.

American Medical Association Council on Scientific Affairs (1984b): Effects of pregnancy on work performance. JAMA 251:1995-1997.

Arab SO, Cates W (1983): The increasing concern with infertility: Why now? JAMA 250:2327-2331.

Armstrong DT (1986): Environmental stress and ovarian function. Biol Reprod 34:29-29.

Balarajan R, McDowall M. Congenital malformations and agricultural workers. Lancet 1983;1:1112-1113.

Bamezai R, Kumar N (1992): Sleep deprivation in human males and its effect on SCE rates in chromosomes - a preliminary study. Mutat. Res., 283: 229-232.

Barlow SM, Sullivan FM: "Reproductive Hazards of Industrial Chemicals." New York: Academic Press, 1982, pp 99-100.

Barnard RJ, Weber JS: Carbon monoxide: A hazard to firefighters. Arch Environ Health 34:255-257, 1978.

Bates JT: Coronary artery disease deaths in the Toronto fire department. J Occup Med 29:132-135, 1987.

Beckman L, Nordstrom S: Occupational and environmental risks in and around a smelter in northern Sweden. Hereditas 97:1-7, 1982.

Bell JU, Thomas JA: Effects of lead on mammalian reproduction. In Singhand RL, Thomas JA (eds): "Lead Toxicity." Baltimore: Urban & Schwarzenburg, 1980, pp 169-185.

Brodsky JB, Cohen EN, Whitcher C, Brown BW, Wu ML: Occupational exposure to mercury in dentistry and pregnancy outcome. JADA 11:779-780, 1985.

Brogan WF, Brogan CE, Dadd JT: Herbicides and cleft lip and cleft palate. Lancet 1980:2:597-598.

Clarren SK, Smith DW, Harvey MA, et al: Hyperthermia: A prospective evalution of a possible teratogenic agent in man. J Pediatr 95:81-33, 1979.

References

Agnew J, McDiarmid MA, Fitzgerald S: A survey of reproductive health of women firefighters. (in preparation).

Agnew J, McDiarmid MA, Lees PSJ, Duffy R: Reproductive hazards of fire fighting 1. Non-chemical hazards. Am J Ind Med 19:433-445, 1991.

Alcser KH, Brix KA, Fine LJ, Kallenbach LR, Wolfe RA: Occupational mercury exposure and male reproductive health. Am J Ind Med 15:517-529, 1989.

American Academy of Pediatrics (ARP) Committee on Drugs. The Transfer of Drugs and other Chemicals in Human Breast Milk. Pediatrics 93: 137 - 150, 1994

American Medical Association Council on Scientific Affairs: Effects of physical forces on the reproductive cycle. JAMA 251-247-250, 1984a.

American Medical Association Council on Scientific Affairs (1984b): Effects of pregnancy on work performance. JAMA 251:1995-1997.

Arab SO, Cates W (1983): The increasing concern with infertility: Why now? JAMA 250:2327-2331.

Armstrong DT (1986): Environmental stress and ovarian function. Biol Reprod 34:29-29.

Balarajan R, McDowall M. Congenital malformations and agricultural workers. Lancet 1983;1:1112-1113.

Bamezai R, Kumar N (1992): Sleep deprivation in human males and its effect on SCE rates in chromosomes - a preliminary study. Mutat. Res., 283: 229-232.

Barlow SM, Sullivan FM: "Reproductive Hazards of Industrial Chemicals." New York: Academic Press, 1982, pp 99-100.

Barnard RJ, Weber JS: Carbon monoxide: A hazard to firefighters. Arch Environ Health 34:255-257, 1978.

Bates JT: Coronary artery disease deaths in the Toronto fire department. J Occup Med 29:132-135, 1987.

Beckman L, Nordstrom S: Occupational and environmental risks in and around a smelter in northern Sweden. Hereditas 97:1-7, 1982.

Bell JU, Thomas JA: Effects of lead on mammalian reproduction. In Singhand RL,

Thomas JA (eds): "Lead Toxicity." Baltimore: Urban & Schwarzenburg, 1980, pp 169-185.

Brodsky JB, Cohen EN, Whitcher C, Brown BW, Wu ML: Occupational exposure to mercury in dentistry and pregnancy outcome. JADA 11:779-780, 1985.

Brogan WF, Brogan CE, Dadd JT: Herbicides and cleft lip and cleft palate. Lancet 1980:2:597-598.

Clarren SK, Smith DW, Harvey MA, et al: Hyperthermia: A prospective evalution of a possible teratogenic agent in man. J Pediatr 95:81-33, 1979.

Clarren SK, Smith DW, Harvey MA, Ward RH, Myrianthopoulos NC: Hyperthermia: A prospective evaluation of a possible teratogenic agent in man. J Pediatr 95:81-33, 1979.

Cook RO, Nawrot PS, Hamm CW (1982): Effects of high frequency noise on prenatal development and maternal plasma and urine catecholamine concentrations in the C-1 mouse. Toxicol Appl Pharmacol 66:338-348.

Cordier S, Deplan F, Mandereau L, Hemon D: Paternal exposure to mercury and spontaneous abortions. Br J Ind Med 48:375-381, 1991.

Darcey DJ, Everson RB, Putman KL, Randerath K (1992): DNA adducts and exposure to burning oil. Lancet, i, 339-489.

Davidkova R, Basmadzhieva K: Changes in protein and nucleic acid metabolism as one of the methods for evaluating gonadotoxic action. Probl Khig 4:101-109, 1979.

Daxon EG. Health and Environmental Consequences of Depleted Uranium use in the U.S. army: Technical Report. U.S. Army Environmental Policy Institute, 1995.

DeFerrari M., Artuso M., Bonassi S., Bonatti S., Cavalieri Z.,

Dixon RL, Lee IP: Pharmacokinetic and adaption factors involved in testicular toxicity. Fed Proc 39:66-72, 1980.

Dosaka H, Abe S, Sasaki M, Miyamoto H, Kawakami Y (1987): Sister chromatid exchange induction by benzo(a)pyrene in cultured peripheral blood lymphocytes of lung cancer patients and healthy individuals with or without family history of neoplasms.
Int. J. Cancer 39:329-332.

Doulout FN, Pastori MC, Olivero OA, Gonzalez cid Loria D, Matos E, Sobel N, deBujan EC, Albiano N (1985):

Edmonds L, Layde P, Erickson J (1979): Airport noise and teratogenesis. Arch Environ

Health 34:243-247.

Edward MJ: Hyperthermia as a teratogen: A review of experimental studies and their clinical significance. Teratogen Carcinogen Mutagen 6:563-582, 1986.

Evanoff BA, Rosenstock L: Reproductive hazards in the workplace: A case study of women firefighters. Am J Ind Med 9:503-515, 1986.

Feuer E, Rosenman K: Morality in police and firefighters in New Jersey. Am J Ind Med 9:517-527, 1986.

Figa-Talamanca I, Dell 'Orco V, Pupi A, Dondero F, Gandini L, Lenzi A, Lombardo F, Scavalli P, Mancini G: Fertility and semen quality of workers exposed to high temperatures in the ceramic industry. Reprod Toxicol 6:517-523, 1992.

Field B, Kerr C. Herbicide use and incidence of neural tube defects. Lancet 1979; 1:1341-1342.

Fischman HK, Kelly DD (1987): Sister chromatid exchange induced by behavioral stress. Ann. NY Acad. Sci. 496: 424-435

Fredricsson B, Moller L, Pousette A and Westerholm R: Human sperm motility is affected by plasticizers and diesel particle extracts. Pharm & Toxicol 72:128-133, 1993.

Fries H, Nillus SJ, Pettersson F (1974): Epidemiology of secondary amenorrhea: A retrospective evaluation of etiology with special regard to psychogenic factors and weight loss. Am J Obstet Gynecol 118:473-479.

Fuenekes F, Jongeneelen F, Laan H.v.d and Schoonhof F: Uptake of polycyclic aromatic hydrocarbons among trainers in a firefighting training facility. [Denise couldn't find]

Golding J, Sladden T: Congenital malformations and agricultural workers. Lancet 1983;1:1393.

Gordon JE, Shy CM: Agricultural chemical use and congenital cleft lip and/or palate. Arch Environ Health 1981;36:213-221.

Guidotti T: Human factors in firefighting: ergonomic, cardiopulmonary, and psychogenic stress-related issues. Occup Environ Health 64:1-12, 1992.

Gunnison AF, Sellakumur A, Currie D, Snyder EA: Distribution, metabolism, andtoxicity of inhaled sulfur dioxide and endogenously generated sulfite in the respiratory tract of normal and sulfite oxidase-deficient rates. J Toxicol Environ Health 21:141, 1987.

Hansteen IL (1982): SCE as a monitor of industrial and environmental toxins. In Saunberd,

A.A. (ed.), Sister-Chromatid Exchange, Progress and Topics in Cytogenetics, 2nd ed. Alan R. Liss, New York, pp. 675-698.

Haring OM: Cardiac malformation in rats induced by exposure of the mother to carbon dioxide during pregnancy. Cir Res 8:1218-1227, 1960.

Harrington JM, Stein GF, Rivera RO, de Morales AV: The occupational hazards of formulating oral contraceptives: A survey of plant employees. Arch Environ Health 33:12-15, 1978.

Heinricks WL, Juchan MR: Extraleynatic drug metabolism: The gonads In: Extrahepatic metabolism of drugs and other foreign compounds, TE Gram (ed) SP Medical and Scientific Books, New York, 1984, pp 319-332.

Hemminki K, Saloniemi L, Luoma K, et al: Transplacental carcinogens and mutagens: childhood cancer, malformations and abortions as risk indicators. J Toxicol Environ Health 1980; 6:1115-1126

Henderson J, Baker HWG, Hanna PH: Occupation-related male infertility: A review. Clin Reprod Fertil 4:87-106, 1986.

Infante PF, Wagoner JK, McMichael AJ, Waxweiler RJ, Falk H: Genetic risks of vinyl chloride. Lancet 1:734, 1976.

International Agency for Research on Cancer (IARC): Chemicals, industrial processes, and industries associated with cancer in humans. Volumes 1-29 . IARC Monogr Suppl 4:292, 1982.

International Agency for Research on Cancer (IARC): Overall evaluation of carcinogenicity: An updating of IARC monographs volumes 1 to 42. IARC Monogr 7[Suppl], 1987.

IOM, Veterans at Risk: The Health Effects of Mustard Gas and Lewiste. Wash DC: National Academy Press, 1993.

Jones FN, Tauscher J (1978): Residence under an airport landing pattern as a factor in teratism. Arch Environ Health 33:10-12.

Kalter H, Warkany J (1983): Congenital malformations -- Etiologic factors and their role in prevention. N Engl J Med 308-491.

Kelsey KT, Xia Fen, Bodell WJ, Spengler JD, Christiani DC, Dockery DW, Liber HL (1994): Genotoxicity to human cells induced by air particulates isolated during the Kuwait oil fires. Environ. Res., 64, 18-25

Kimmel CA, Cook RO, Staples RE (1976): Teratogenic potential of noise in mice and rats. Toxicol Appl Pharmacol 36:239-245.

Kline J, Stein Z (1985): Very early pregnancy. In Dixon RL. (ed): "Reproductive Toxicology." New York: Raven Press pp. 251-265.

Knipschild P, Meijer H, Salle H (1981): Aircraft noise and birthweight. Int Arch Occ Environ Health 48:131-136.

Knuutila S, Maki-Paakkanen J, Kahkonen M, Hohkanen E (1978): An increased frequency of chromosomal changes and SCE in cultured blood lymphocytes of 12 subjects vaccinated against smallpox. Hum. Genet., 41, 89-96.

Kucerova M, Gregor V, Horacek J, Dolanska M and Matejckova S: Influence of different occupations with possible mutagenic effects on reproduction and level of induced chromosomal aberrations in peripheral blood. Mutation Res 278:19-22, 1992.

Kucerova M., Polevkova T, Matousek V (1980): Chromosomal aberrations and SCE in lymphocytes of children revaccinated against smallpox. Mutat. Res., 71, 263-267.

Lambert B, Ehrnst A, Hansson K, Lindblad K, Morad M, Werelius B (1979): Sister chromatid exchange in peripheral lymphocytes of subjects vaccinated against measles. Hum. Genet.,50, 291-296.

Lancranjan I, Popescu H, Gavanescu O: Reproductive ability of workmen occupationally exposed to lead. Arch Environ Health 30:396-401, 1975.

Lemon PWR, Hermiston RT: Physiological profile of professional fire fighters. J Occup Med 19:337-340.

Lemon PWR, Hermiston RT: The human energy cost of firefighting. K Occup Med 19:558-562, 1977.

Levine BS, Parker RM. Reproductive Development Toxicity Studies of Pyridostigmine Bromide in rats . Toxicology 69: 291 - 300, 1991

Lindbohm M-L, Hemminki K, Bonhomme MG, Anttila A, Rantala K, Heikkila P, Rosenberg MJ: Effects of paternal occupational exposure on spontaneous abortions. Am J Pub Health 81:1029-1033, 1991a.

Lindbohm M-L, Sallmen M, Anttila A, Taskinen H, Hemminki K: Paternal occupational lead exposure and spontaneous abortions. Scand J Work Environ Health 17:95-103, 1991b.

Longo LD: Carbon monoxide effects on oxygenation of the fetus in utero. Science

194:523-525, 1976.

Longo LD: The biological effects of carbon monoxide on the pregnant women, fetus and newborn infant. Am J Obstet Gynecol 129:69-103, 1977.

Longo LD: Environmental pollution and pregnancy: Risks and uncertainties for the fetus and infant. Am J Obstet Gynecol 137:162-173, 1980.

Lotgering FK, Gilbert RD, Longo LD (1985): Maternal and fetal responses to exercise during pregnancy. Physiol Rev 65:1-36

Lowry WT, Juarez L, Petty CS, Roberts B: Studies of toxic gas production during actual structural fires in the Dallas area. J Forensic Sci 30:59-72, 1985.

Margulies SL: Acute carbon monoxide poisoning during pregnancy. Am J Emerg Med 4:516-519, 1986.

Martin CN, McDermid AC, Garner RC: Testing of known carcinogens and noncarcinogens for their ability to induce unscheduled DNA synthesis in HeLa cells. Cancer Res 38:2621-2627, 1978.

Mattison DR: The mechanisms of action of reproductive toxins. Am J Ind Med 4:65-79, 1983.

Mattison DR (1981): Drugs, xenobiotics and the adolescent: Implications for reproduction. In Soyka LF. Redmond GP (ed): "Drug Metabolism in the Immature Human." New York: Raven Press pp, 129-143.

Mattison DR, Thomford PJ: The mechanism of action of reproductive toxicants 17:364-376, 1989.

Mattison DR, Nightengale MS (1982): Environmental factors in human growth and development, Hunt VR, Smith MK, Worth D (eds): "Prepubertal Ovarian Toxicity," Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, Banbury Report 11 p 409.

Mattison DR, Thomford PJ (1989): The mechanism of action of reproductive toxicants 17:364-376.

McDiarmid MA: Occupational exposure to pharmaceuticals. In Paul MA (ed): Occupational and Environmental Reproductive Hazards: A guide for Clinicians. Baltimore, Williams & Wilkins 1994, pp 280-295.

McDiarmid MA, Jacobson-Kram, Kolodner D, Dester K, Lachiver DP, Scott RM, Petrucelli BG, Gustavson BP, Putma D (1995): Increased frequencies of sister chromatid exchange in soldiers deployed to Kuwait. Mutagenesis vol. 10, no.3, pp. 263-265, 1995.

McDiarmid MA, Lees P, Agnew J, Midzenski M, Duffy R: Reproductive hazards of firefighting II. Chemical hazards. Am J Ind Med 19:447-472, 1991.

McDiarmid MA, Weaver V: Fouling one's own nest revisited. Am J Ind Med 24:1-9, 1993.

McDonald AD, McDonald JC, Armstrong B, Cherry NM, Nolin AD, Robert D: Father's occupation and pregnancy outcome. Br J Ind 46:329-333, 1989.

McGrady AV (1984): Effects of psychological stress on male reproduction: a review. Arch Androl 13:1-7.

Mieusset R, Bujan L, Mansar A, Pontonnier F, Grandjean H: Effects of artificial cryptorchidism on sperm morphology. Fertil Steril 47:150-155, 1987a.

Milham S Jr: "Occupationally Mortility in Washington State 1950-71." Cincinnati NIOSH Division of Surveillance, Hazard Evaluation and Field Studies (NIOSH 76-175-C), 1976.

Miller P, Smith DW, Shepard NH: Small head size after in-utero exposure to atomic radiation. Lancet 2:784-787, 1972.

Miretskaya LM, Shvartsma PY: Studies of chromosome aberrations in human lymphocytes under the influence of formadehyde. I. Formaldehyde treatment of lymphocytes in vitro. Tsitologiia 24:1056-1060, 1982.

Morpurgo G, Bellincampi D, Gualandi G, Baldinelli L, Criscenzi OS: Analysis of mitotic non-disjunction with Aspergillus nidulans. Environ Health Perspect 31:81-95, 1979.

Mosher WD (1988): Fecundity and infertility in the United States. Am J Public Health 78:181-182.

Mukherjee DP, Singh SP: Effect of increased carbon dioxide in inspired air on the morphology of spermatozoa and fertility of mice. J Reprod Fertil 13:165-167, 1967.

Musk AW, Monson RR, Peters RK: Mortality among Boston firefighters, 1915-1975. Br J Ind Med 35:104-198, 1978.

National Fire Protection Association (NFPA) 472. Standard on Professional Competence of Responders to Hazardous Materials Incidents. Quincy, Mass., 1997.

National Institute for Occupational Safety and Health, Centers for Disease Control, U.S. Public Health Service: Newburgh Fire Department, Newburgh, New York. Health Hazard Evaluation Report HETA 81-059-1045, 1982.

National Institute for Occupational Safety and Health, Centers for Disease Control, U.S. Public Health Service: The City of New York Fire Department, New York, New York. Health Hazard Evaluation Report HETA 81-459-1603, 1985.

National Institute for Occupational Safety and Health, Centers for Disease Control, U.S. Public Health Service: International Association of Fire Fighters, Cincinnati, Ohio.Health Hazard Evaluation Report HETA 86-454-1890, 1988.

National Institute for Occupational Safety and Health, Centers for Disease Control, U.S. Public Health Service: Memphis Fire Department, Memphis, Tennessee. Health Hazard Evaluation Report HETA 86-138-2017, 1990.

Nawrot PS, Cook RO, Staples RE (1980): Embryotoxicity of various noise stimuli in the mouse. Teratology 22:279-289.

Office of Technology Assessment, United States Congress (1985): "Reproductive Health Hazards in the Workplace." Washington, DV: United States Government Printing Office, p 199.

Olshan AF, Teschke K, Baird PA: Birth defects among offspring of firemen. Am J Epidemiol 131:312-321, 1990.

Pacynski A, Budzynska A, Przylecki S: Hiperestrogenizm v pracownikow zakladow farmaceutyczaych i ich dzieci jako choroba zawodowa. Endokrynol Pol (Warsaw) 22:149-154, 1971.

Pairon JC, Janrand MC, Kheuang L, Janson X, Brochard P, Bignon J (1990): Sister chromatid exchanges in human lympho-cytes treated with silica. Br. J. Ind. Med. 47: 110-115.

Paul M, Himmelstein J: Reproductive hazards in the workplace: What the practitioner needs to know about chemical exposure. Obstet Gynecol 71:921-938, 1988.

Paul M, Occupational and environmental reproductive hazards: a guide for clinicians / edited by (Eilliams & Wilkins, 1993

Perdersen RA, Manigia F: Ultraviolet light induced unscheduled DNA synthesis by resting and growing mouse oocytes. Mutat Res 49:425-429, 1978.

Peters JM, Theriault GP, Fine LJ, Wegman DH: Chronic effect of fire fighting on pulmonary function. N Engl J Med 291:1320-1322, 1974.

Pleet HG, Graham JM, Smith DW: Central nervous system and facial defects associated with maternal hyperthermia in four to 14 weeks gestation. Pediatrics 67:785-789, 1981.

Pleuche WC. Myasthenia gravis in pregnancy: An update. Am J Obste Gynecol 135:91 - 697, 1979

Poirier MC, Weston A, Schoket B, Shamkhani H, Pans CF, Scott BG, Decker DP, Jacobson-Kram D, McDiarmid MA, Rothman N: Polycyclic aromatic hydrocarbon biomarkers of internal exposure and metabolic polymorphisms in U.S. Army soldiers serving in Kuwait in 1991.

Paul M, Himmelstein J (1988): Reproductive hazards in the workplace: What the practitioner needs to know about chemical exposure. Obstet Gynecol 71:921-938.

Paul M, Kurtz S (1900): Reproductive hazards in the workplace. University of Massachusetts and March of Dimes Birth Defects Foundation Publication.

Paul M, (ed) Occupational and environmental reproductive hazards: a guide for clinicians. Williams & Wilkins, 1993.

Pedersen RA, Manigia F (1978): Ultraviolet light induced unscheduled DNA synthesis by resting and growing mouse oocytes. Mutat Res, 49:425-429.

Pescatore D, Marchini E, Pisano V, Abbondandolo A.(1991): Cytogenetic biomonitoring of an Italian population exposed to pesticides; chromosomal aberration and sister chromatid exchange analysis in peripheral blood lymphocytes. Mutat. Res., 260: 105-113.

Pleet HG, Graham JM, Smith DW: Central nervous system and facial defects associated with maternal hyperthermia in 4 to 14 weeks gestation. Pediatrics 67:785-789, 1981.

Pleuche WC. Myasthenia gravis in pregnancy: An update. Am J Obstet Gynecol 135:91 - 697, 1979

Pratt WF, Mosher WD, Bachrach CA, Horn MC (1984): Understanding U.S. fertility findings from the National Survey of Family Growth, Cycle III. Popul Bull 39:3-42.

Procope BJ: Effect of repeated increase of body temperature on human sperm cells. Int J Fertil 10:333-339, 1965.

Rachootin P, Olsen J: The risk of infertility and delayed conception associated with exposure in the Danish workplace. J Occup Med 25:394-402, 1983.

Rita P, Reddy PP, Venkatram Reddy S. Monitoring of workers occupationally exposed to pesticides in grape gardens of Andhra Pradesh. Environ Res 1987, 44:1-5.

Roan CC, Matanoski GE, McIlnay CQ, et al. Spontaneous abortions, stillbirths, and birth defects in families of agricultural pilots. Arch Environ Health 1984;39:56-60.

Rom WN: Effects of lead on the female reproduction: A review. MT. Sinai Med 43:542-552, 1976.

Romet TT, Frim J: Physiological responses to fire fighting activities. Eur J Appl Physiol 56:633-638, 1987.

Rudiger HW, Kohl F, Mangels W, Von Wichert P, Bartram CR, Wohler W, Passarge E, (1976): Benzpyrene induces sister chromatid exchange in cultured human lymphocytes. Nature 262, 290-292.

Rupa DS, Reddy PP, Sreemannarayana K, Reddi OS (1991): Frequency of sister chromatid exchange in peripheral lymphocytes of male pesticide applicators. Environ. Molec. Mutagen., 18: 136-138.

Saurel-Cubizolles MD, Kaminski M (1987): Pregnant women's working conditions and their changes during pregnancy: A national study in France. Br J Ind Med 44:236-243.

Saurel-Cubizolles MJ, Kamminski M, Llado-Arkhipoff J, Du Mazaubrun C, Estryn-Behar M, Berthier C, Mouchet M, Kelfa C (1985): Pregnancy and its outcome among hospital personnel according to occupation and working conditions. J Epidemiol Community Health 39:129-134.

Savitz D, Sonnenfeld N, Olshan A: Review of epidemiologic studies of paternal occupational exposure and spontaneous abortion. Am J Ind Med 25:361-383, 1994.

Schell L (1981): Environmental noise and human prenatal growth. Am J Phys Anthropol 56:63-70.

Schwartz DA, Logerfo JP. Congenital limb reduction defects in the agricultural setting. Am J Public Health 1988;78:654-657.

Schwartz DA, Newsum L, Heifetz RM. Parental occupation and birth outcome in an agricultural community. Scand J Work Environ Health 1986;12:51-54.

Shapiro R: Genetic effects of bisulfite (sulfur dioxide). Mutat Res 39:149-176, 1977.

Sister chromatid exchanges and chromosomal aberrations in a population exposed to pesticides. Mutat. Res., 143, 237-244.

Smolander J, Louhevara V, Kohonen O: Physiological strain in work with gas protective clothing at low ambient temperature. Am Ind Hyg Assoc J 46:720-723.

Sorsa M, Yager JW (1987): Cytogenetic surveillance of occupational exposures. In Obe, G. and Basler, A. (eds), Cytogenetics, Springer, New York pp. 345-360.

Soules MR (1985): The in vitro fertilization pregnancy rate: Let's be honest with one

another. Fertil 43:511-513.

Sparrow D, Bosse T, Rosner B, Weiss S: The effect of occupational exposure on pulmonary function. A longitudal evaluation of fire fighter and non-fire fighters. Am Rev Respir Dis 125:319-322, 1982.

Stachel B, Dougherty TC, Lahl U, Schlosser M, Zeschmar B: Toxic environmental chemicals in human semen: Analytical method and case studies. Andrologia 21:282-291, 1989.

Steeno OP, Pangkahila A (1984): Occupational influences on male fertility and sexuality. Andrologia 16:5-22.

Taskinen H, Lindbohm ML, Hemminki K (1986): Spontaneous abortions among women working in the pharmaceutical industry. Br. J Ind Med 43:199-205.

Terrill JB, Montogomery RR, Reinhart CF: Toxic gases from fires. Science 200: 1343-1347, 1978.

Vaughan TL, Daling JR, Starzyk PM: Fetal death and maternal occupation: an analysis of birth records in the state of Washington. J Occup Med 1984;26:676-678.

Veghte JH: "Physiologic Response of Fire Fighters Wearing Bunker Clothing (Phase 2)." Biotherm, Inc., Beaver Creek, Ohio, 1987.

Vena JE, Fielder RC: Mortality of a municipal worker cohort: IV: Fire fighters. Am J Ind Med 11:671-684, 1987.

Warren ME, Mays CW (1983): Ionizing Radiation. In Rom WN (ed): "Environmental and Occupational Medicine." Boston: Little Brown and Company, pp 676-679.

Weaver TE, Scott WJ Jr: Acetazolamide teratogenesis: Association of maternal respiratory acidosis and ectrodactyly in C57BL/6J mice. Teratology 30:187-193, 1984.

Wharton MD: Adverse reproductive outcomes: the occupational health issues of the 1980s. Am J Public Health 73:15-16, 1983.

White FM, Cohen FG, Sherman G, McCurdy R. Chemicals, birth defects and stillbirths in New Brunswick: Associations with agricultural activity. Can Med Assoc J 1988;138:117-124.

White MK, Hodus TK: Reduced work tolerance associated with wearing protective clothing and respirators. Am Ind Hyg J 48:304-310, 1987.

Wilmer JL, Erexson GL, Kligerman AD: Attenuation of cytogenic damage bu 2-mercaptoerhane-sulfonate in cultured human lymphocytes exposed to cyclophosphamide

and its reaction metabolites. Cancer Res 46;203-210, 1986.

Wyrobek A: Methods and concepts in detecting abnormal reproductive outcomes of paternal origin. Reprod Toxicol 77:3-16, 1993.

Yazigi RA, Odem RR, Polakoski KL: Demonstration of specific binding of cocaine to human spermatozoa. JAMA 266:1956-1959, 1991.

CARCINOGENS

APPENDIX MATERIALS

PESTICIDES

Carbaryl
Diazinon
Dichlorvos
Lindane
Pentachlorophenol
Pyrethrins
Warfarin
Isopropyl Methylisopropoxfluorophosphine (Sarin)

OIL FIRES AND SOIL SAMPLES

Arsenic
Cadmium
Hexacholorobenzene
Lead
Nickel
Poycyclic Aromatic Hydrocarbons (PAHs)
Silica
Diesel Exhaust

OTHER AGENTS

Mustard Agent
Fuels

- Turbine Fuel JP-5
- Turbine Fuel JP-8
- Fuel Naval Distillate M/L-f-1688414 (NATO F 76)

PESTICIDES

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 9/93.

EXTOXNET primary files maintained and archived at Oregon State University.

Carbaryl

TRADE OR OTHER NAMES

Product names include Carbamine, Denapon, Dicarbam, Hexavin, Karbaspray, Nac, Ravyon, Septene, Sevin, Tercyl, Tricarnam, and Union Carbide 7744.

INTRODUCTION

Carbaryl is a wide-spectrum carbamate insecticide which controls over 100 species of insects on citrus, fruit, cotton, forests, lawns, nuts, ornamentals, shade trees, and other crops, as well as on poultry, livestock and pets. It is also used as a molluscicide and an acaricide. Carbaryl works whether it is ingested into the stomach of the pest or absorbed through direct contact. The chemical name for carbaryl is 1-naphthol N-methylcarbamate.

Carbaryl is formulated as a solid which varies from colorless to white to gray, depending on the purity of the compound. The crystals are odorless. This chemical is stable to heat, light and acids under storage conditions. It is non-corrosive to metals, packaging materials, or application equipment. It is found in all types of formulations including baits, dusts, wettable powder, granules, oil, molassas, aqueous dispersions and suspensions (13).

Carbaryl is a general use pesticide.

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Carbaryl is moderately to very toxic, and is labeled with a WARNING signal word. It can produce adverse effects in humans by skin contact, inhalation or ingestion. The symptoms of acute toxicity are typical of the other carbamates. Direct contact of the skin or eyes with moderate levels of this pesticide can cause burns. Inhalation or ingestion of very large amounts can be toxic to the nervous and respiratory systems resulting in nausea, stomach cramps, diarrhea and excessive salivation. Other symptoms at high doses include sweating, blurring of vision, incoordination, and convulsions. About fifty cases of occupational or accidental illnesses due to exposure to carbaryl have been reported, but no fatalities have been documented. The only documented fatality from carbaryl was through intentional ingestion.

The oral LD50 of carbaryl ranges from 250 mg/kg to 850 mg/kg for rats, and from 100 mg/kg to 650 mg/kg for mice (12, 13). The inhalation LC50 for rats is 0,005 to 0.023 mg/kg (13). Low doses can cause minor skin and eye irritation in rabbits, whose dermal LD50 has been measured at greater than 2,000 mg/kg (12). Technical carbaryl has little potential for skin or eye

Technical carbaryl has little potential for skin or eye irritation.

Occupational workers have the greatest potential for exposure through inhalation or through the skin. The general public's highest risk of exposure is through ingestion of contaminated food (14)

CHRONIC TOXICITY

Athough it may cause minor skin and eye irritation, carbary does not appear to be a significant chronic health risk at or below occupational levels. Male volunteers who consumed low doses of carbaryl for six weeks did not show symptoms, but tests indicated slight changes in their body chemistry (12).

Reproductive and Teratogenic Effects

No reproductive or fetal effects were observed during a long-term study of rats which were fed high doses of carbaryl (12). The evidence for teratogenic effects due to chronic exposure are minimal in test amimals. Birth defects in rabbit and guinea pig offspring occurred only at dosage levels which were highly toxic to the mother. A 1980 New Jersey epidemiological study found no evidence of excess birth defects in a town sprayed with carbaryl for gypsy moth control. There is only limited evidence that carbaryl causes birth defects in humans. The EPA has concluded that carbaryl does not pose a teratogenic risk to humans if used properly (16).

Mutagenic Effects

Numerous studies indicate that carbaryl poses only a slight mutagenic risk (8, 12). However, carbaryl can react with nitrite under certain conditions to give rise to N-nitrosocarbaryl. Nitrosocarbaryl has been shown to be highly mutagenic at low levels in laboratory test systems. This may be a concern to humans because there is a possibility that carbaryl, a pesticide, and nitrite, a substance found in food additives and in human saliva, may react in the human stomach to form nitrosocarbaryl (2, 8). Carbaryl has been shown to affect cell mitosis (cell division) and chromosomes in rats (13).

Carcinogenic Effects

Carbaryl has not caused tumors in ten longterm and lifetime studies of mice and rats. Rats were administered high daily doses of the pesticide for two years, and mice for eighteen months, with no signs of carcinogenicity (3). However, N-nitrosocarbaryl, formed by the reaction of carbaryl and nitrite, has been shown to be carcinogenic in rats at high doses (7). Also, mice exposed to carbaryl in the product, tricaprylin, for four weeks each, developed lung tumors (12).

Organ Toxicity

Ingestion of carbaryl affects the lungs, kidneys and liver. Inhalation will also affect the lungs (14, 17). Nerve damage can occur after administration of high doses for 50 days in rats and pigs (12). Several studies indicate that carbaryl can affect the immune system in animals and insects. These effects however have not been documented in humans.

Fate in Humans and Animals

Most animals, including humans, readily break down carbaryl and rapidly excrete it in the urine and feces. Workers occupationally exposed by inhalation to carbaryl dust excreted 74% of the inhaled dose in the urine in the form of a breakdown product (13). This is consistent with information on other

product (13). This is consistent with information on other species which excreted nearly three quarters of a dose in their urine within 24 hours of administration (14). The metabolism of up to 85% of carbaryl occurs within 24 hours after administration (13).

ECOLOGICAL EFFECTS

Carbaryl is lethal to many nontarget insects. The pesticide is more active in insects than in mammals. The destruction of honeybee populations in sprayed areas is sometimes a problem. Carbaryl is moderately toxic to aquatic organisms, such as rainbow and lake trout, bluegill, and cutthroat. It is also moderately toxic to wild bird species, with low toxicity to Canada geese (12).

Accumulation of carbaryl can occur in catfish, crawfish, and snails, as well as in algae and duckweed. Residue levels in fish were 140 fold greater than the concentration of carbaryl in water. In general, due to its rapid metabolism and rapid degradation, carbaryl should not pose a significant bioaccumulation risk in alkaline waters. However, under conditions below neutrality it may be significant (14).

ENVIRONMENTAL FATE

Carbaryl has a short residual life on treated crops. The insecticide remains at the application site, where it is slowly taken into the plant and metabolized. Insecticidal properties are retained for 3-10 days. Loss of carbaryl is due to evaporation and uptake into plants. Breakdown by sunlight does not appear to be significant.

Degradation of carbaryl in the soil is mostly due to sunlight and bacterial action. It is bound by organic matter and can be transported in soil runoff. Carbaryl has a half-life of 7 days in aerobic soil and 28 days in anaerobic soil (9). Degradation of carbaryl in crops occurs by hydrolysis inside the plants. It has a short residual life of less than two weeks. The metabolites of carbaryl have lower toxicity to humans than carbaryl itself. The breakdown of this substance is strongly dependant on acidity and temperature.

In pond water, carbaryl is broken down by bacteria through chemical processes. Evaporation does not occur. Carbaryl has a half-life of from 1 to 32 days in pond water. In a stream, carbaryl that had washed in from forest spraying, decayed to 50% within a 24 hour period. It has been shown to degrade more slowly in the presence of mud in aquatic habitats. Carbaryl has been detected in groundwater in three separate cases in California.

Carbaryl has a half-life in the air of one to four months. Crops, shade trees, shrubs and other vegetation in bloom should not be sprayed with carbaryl as bee kills are possible.

PHYSICAL PROPERTIES AND GUIDELINES

Carbaryl is a solid which varies from colorless to white or gray, depending on the purity of the compound. The crystals are odorless. Carbaryl is stable to heat, light and acids. It is not stable under alkaline conditions. It is non-corrosive to metals, packaging materials or application equipment.

Exposure Guidelines:

NOEL: 0.06 mg/kg/day

ADI: 0.1 mg/kg/day

STEL: 10 mg/m3

TLV: air TWA 5 mg/m3

CL: 625 mg/m3

Drinking Water Health Advisory: Drinking Water Equivalent Level: (DWEL): 3.5 mg/L (13)

Physical Properties

CAS #: 63-25-2

Chemical Name: 1-naphthyl N-methylcarbamine

Solubility in water: 0.005 g/100 g (20 degrees C), 0.004 g/100 g (30 degrees C)

Solubility in solvents: Carbaryl is soluble in ethanol, petroleum ether, diethyl ether,and chloroform; moderately soluble in polar solvents such as acetone, dimethyl sulfoxide, mixed cresols, and cyclohexanone.

Melting point: 145 degrees C

Vapor pressure: <0.0001 torr (20-25 degrees C)

Log P: <-3.00

Kow: 64.6-229.1 (1, 5, 6, 10)

Koc: 205.0-457.1 (1, 4, 5)

K(d): nonionic

BCF: 28.2-28.8 (1, 5)

H: <9.9 x 10 to the minus 5 power torr/M

BASIC MANUFACTURER

Rhone-Poulenc Ag. Co.
P.O. Box 12014
TW Alexander Dr.
Research Triangle Park, NC 27709
Telephone: 919-549-2000
Emergency: 800-334-7577

Review by Basic Manufacturer:

Comments solicited: October, 1992
Comments received:

REFERENCES

(1) Bracha, P. and O'Brian, R. 1966. J. Econ. Entomol. 59:1255.

(2) Elespuru, R., Lijinski, W., and Setlow, J.K. 1974. Nature (London). 247:386-387.

(3) "Evaluation of Carcinogenic, Teratogenic, and Mutagenic Activities of Selected Pesticides and Industrial Chemicals," Volume 1: "Carcinogenic Study." 1968. National Technical Information Service, Washington, D.C.

(4) Farmer, W.J. 1976. "Leaching, Diffusion, and Sorption." From A Literature Survey of Benchmark Pesticides. Science

Communication Division of George Washington University Medical Center, pp. 185-245.

(5) Fujita, T., et al. 1974. Agric. Biol. Chem. 38:1521.

(6) Mount, M.E. and Oehme, F.W. 1981. Residue Rev. 80:1-64.

(7) Regan, J.D., Setlow, R.B., Francis, A.A., and Lijinsky, W. 1976. Mutat. Res. 38:293

(8) Siebert, D. and Eisenbrand, G. 1974. Mutat. Res. 22:121.

(9) Wauchope, R.D. 1978. J. Environ. Qual. 7:459-472.

(10) Windholz, M., et al., eds. 1976. The Merck Index, 9th ed. Merck and Co., Inc.: Rathway, NJ.

(11) Vettorazzi, Gaston. 1979. International Regulatory Aspects

(12) National Library of Medicine. Hazardous Substances Databank. Carbaryl. February 4, 1992.

(13) U.S. Environmental Protection Agency, Office of Drinking Water. Carbaryl Health Advisory. Draft Report. August 1987.

(14) Baron, Ronald L. (1991). Carbamate Insecticides. in Handbook of Pesticide Toxocology, Volume 3, Classes of Pesticides. Wayland J. Hayyes, Jr. and Edward R. Lawes, Jr. editors. Academic Press, Inc. NY.

(15) Howard, Philip H. (1991). Handbook of Environmental Fate and Exposure data for Organic Chenicals, Volume III. Lewis Publishers, Chelsea, MI.

(16) ACGIH. 1991. Documentation of rgw Threshold Limit Values and Biological Indices. American Conference of Governmental and Industrial Hygienists, Inc., Cincinnati, OH.

(17) Carpenter, C.P., et.al. 1961. Mammalian toxicity of 1-Napthyl-N-Methylcarbamte (Sevin Insecticide). Agricultural and Food Chemistry 9 (1): 30-39.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall, Ithaca, N.Y. 14853-0901.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 9/93.

EXTOXNET primary files maintained and archived at Oregon State University.

Diazinon

TRADE OR OTHER NAMES

Trade names of this product include Knox Out, Spectracide and Basudin. Diazinon may be found in formulations with a variety of other pesticides such as pyrethrins, lindane and disulfoton.

INTRODUCTION

Diazinon is a non-systemic organo-phosphate insecticide used on home gardens and farms to control a wide variety of sucking and leaf eating insects. It is used on rice, fruit trees, sugarcane, corn, tobacco, potatoes and on horticultural plants. It is also an ingredient in pest strips. Diazinon has veterinary uses against fleas and ticks. Nearly 2.6 million pounds of diazinon were used each year prior to 1983 (6).

Some of the older formulations of diazinon were unstable and contained a number of potent impurities such as sulfotepp and monothiono-TEEP (6). Newer products do not contain impurities which increase the risk associated with diazinon use. In 1988 EPA cancelled the registration of diazinon for use on golf courses and sod farms. They cited die-offs of birds which often congregate in these areas.

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Diazinon is classified as slightly toxic to moderately toxic, depending on the formulation. It carries the signal words CAUTION or WARNING. Toxic effects of diazinon are due to the inhibition of acetylcholinesterase. The range of doses that results in toxic effects varies widely with formulation and with the individual species being exposed. The toxicity of encapsulated formulations is relatively low because diazinon is not released readily while in the digestive tract. Some formulations of the compound can be degraded to more toxic forms. This transformation may occur in air, particularly in the presence of moisture, and by ultraviolet radiation. Most modern diazinon formulations in the United States are now stable.

Several independently documented cases of diazinon poisoning have occurred among agricultural applicators and among household residents. In the latter case, poisoning followed indoor spraying of a relatively concentrated (25%) solution of diazinon.

The symptoms associated with diazinon poisoning in humans include weakness, headaches, tightness in the chest, blurred vision, non-reactive pinpoint pupils, salivation, sweating, nausea, vomiting, diarrhea, abdominal cramps, and slurred speech. Death has occurred in some instances from both dermal and oral

exposures at very high levels.

Repeated single dose LD50s range from 2.75 mg/kg/day to nearly 450 mg/kg/day for rats (8). Still others have reported LD50s as high as 720 mg/kg/day (4).

CHRONIC TOXICITY

Chronic effects have been observed at doses ranging from 10 mg/kg/day for swine to 1,000 mg/kg/day for rats. These effects included only visibly recognizable symptoms of toxicity (gross toxicities). Certain effects such as the inhibition of red blood cell cholinesterase, and enzyme response occurred at much lower doses in the rats. No-effect doses have ranged from 0.02 mg/kg/day in humans to 0.1 mg/kg/day in rats. These values are based on inhibition of the enzyme acetylcholinesterase. Enzyme inhibition has been documented in red blood cells, in blood plasma, and in brain cells at varying doses and with different species.

Reproductive and Teratogenic Effects

The data on reproductive and developmental effects due to chronic exposure is limited. One study has shown that injection of diazinon into chicken eggs resulted in skeletal and spinal deformities in the chicks. Bobwhite quail born from eggs treated in a similar manner showed skeletal deformities but no spinal abnormalities. Acetylcholine was significantly affected in this latter study (3). Tests with hamsters and rabbits at low doses (0.125-0.25 mg kg) showed no developmental effects while tests with dogs and pigs at higher levels (1.0-10.0 mg/kg) revealed gross abnormalities (2).

Mutagenic Effects

Tests have revealed the potential for diazinon to be mutagenic, but no fully conclusive evidence exists to support this notion (7). The mutagenicity in humans remains unevaluated.

Carcinogenic Effects

Diazinon is not considered carcinogenic. Test on rats over a two year period at moderate doses (about 45 mg/kg) did not cause tumor development in the test animals.

Organ Toxicity

Diazinon itself is not a potent cholinesterase inhibitor. However, in animals it is converted to diazoxon (a substitution of oxygen for the sulfur molecule), a compound that is a strong enzyme inhibitor.

Fate in Humans and Animals

Metabolism and excretion rates for diazinon are rapid. The half life of the pesticide in animals is about 12 hours. The product is passed out of the body through urine and in the feces. The metabolites account for around 70% of the total amount excreted. Cattle exposed to diazinon may store the compound in their fat over the short term. One study showed that the compound cleared the cows within two weeks after spraying stopped. Application of diazinon to the skin of cows resulted in trace amounts in milk 24 hours after the application.

ECOLOGICAL EFFECTS

Birds are quite susceptible to diazinon poisoning and therefore regulations are in place to protect them from hazards posed by turf and golf course treatments. The EPA in 1988

concluded that the use of diazinon in these areas poses a "widespread and continuous hazard" to birds. Bird kills associated with diazinon use have been reported in every area of the country and at all times of the year. The EPA further concluded that Canadian geese and mallard ducks would be exposed to LC50 concentrations in very short periods of time after application (from 15 to 80 minutes depending on the application rate of the pesticide). Birds are significantly more susceptible to diazinon than other wildlife. LD50s for birds range from 2.75 mg/kg to 40.8 mg/kg/day (5).

Most fish are very sensitive to diazinon. Rainbow trout have a LC50 of 90-140 ppb. In hard water, lake trout and cutthroat trout are somewhat more resistant. Warm water fish such as fathead minnows and goldfish are even more resistant (LC50s ranging from 0.5 ppm to 15 ppm). There is some evidence that saltwater fish are more susceptible than are freshwater fish. Bioconcentration ratios range from 200 in minnows to 17.5 for guppies. Howard (8) states that based on these experimental figures, "diazinon will not be expected to significantly bioconcentrate in aquatic systems." Other studies show that diazinon has been found to concentrate in fish 300-600 times the ambient water concentration. This is a relatively low bioaccumulation level as compared to a very persistent compound like DDT which may accumulate to about 60,000 times background levels.

ENVIRONMENTAL FATE

Diazinon seldom migrates below the top 1.3 centimeters (1/2 inch) in soil but can stay biologically available for six months under conditions of low temperature and low moisture. The average time for 50% degradation in soil is two to four weeks. Bacterial enzymes can speed the breakdown of diazinon and have been used in treating emergency situations such as spills (3). The breakdown rate is also highly dependent on the acidity of water. At highly acidic levels, one half of the compound disappeared within 12 hours while in a neutral solution, the pesticide took six months to degrade to one half of the original concentration. Diazoxon is unstable in soil. Howard (8) notes that the pesticide was detected in 54 wells in California and in tap water in Ottawa, Canada and in Japan. Diazinon has also been detected (but not quantified) in Lake Erie and Lake Ontario.

In plants, a lower temperature and a high oil content tend to increase the persistence of diazinon (5). Generally the half-life is rapid in leafy vegetables, forage crops and grass. The range is from two days to 14 days. In treated rice plants only 10% of the residue was present after nine days. Diazinon is absorbed by plant roots when applied to the soil and translocated to other parts of the plant.

Exposure Guidelines:

NOEL: 0.01mg/kg/day rat

-- 0.02mg/kg/day monkey

-- 0.02mg/kg/day humans

Drinking Water: 0.014 mg/l (ppm)

DWEL: 0.003 mg/l

ADI: 0.002 mg/kg/day

TLV-TWA: 0.1 mg/m3

RfD: 0.00009 mg/kg/day (OPP)

HA: 0.0006 mg/l lifetime

Physical Properties:

CAS #: 333-41-5

Solubility in water: 60 mg/l

Solubility in solvent: Petroleum ether, alcohol, benzene

Melting Point: decomposes >120 degrees C

Vapor Pressure: 6 x 10 to the minus 5 power mm Hg

Partition Coefficient: 1.9-4.2 (log)

Adsorption Coefficient: 1,000 ml/g

BASIC MANUFACTURER

Ciba-Geigy Corp
PO BOX 18300
Greensboro, NC 27419
Telephone:919-632-6000

Review by Basic Manufacturer:

Comments solicited: January, 1992
Comments received: April, 1992

REFERENCES

(1) The Agrochemicals Handbook. 1991. The Royal Society of Chemistry. Cambridge, England

(2) National Research Council (1977). Drinking Water and Health, Advisory Center on Toxicology, Assembly of Life Sciences, Safe Drinking Water Committee, National Academy of Sciences, Washington, DC.

(3) Eisler, Ronald (1986). Diazinon Hazards to Fish, Wildlife and Invertebrates: A Synoptic Review. U.S. Department of the Interior, Fish and Wildlife Service, Contaminant Hazards Reviews, Report number 9, Biological Report 85(1.9).

(4) National Library of Medicine. (1992). Hazardous Substance Databank. TOXNET, Medlars management Section, Bethesda, MD.

(5) Bartsch, Elisabeth (1974). Diazinon II. Residue in Plants, Soil and Water, Residue Reviews, 51:37-68.

(6) Vettorazzi, G. (1976). II Carbamate and Organophosphorous Pesticides Used in Agriculture and Public Health, Residue Reviews 63:1-44.

(7) Gallo, Michael A. and Nicholas J. Lawryk. (1991). Organic Phosphorus Pesticides. in Handbook of Pesticide Toxicology, Volume 2, Classes of Pesticides. Wayland J. Hayes and Edward R. Laws editors.Academic Press, Inc., NY.

(8) Howard, Philip H. (1991). Fate and Exposure Data for Organic Chenicals, Volume III, Pesticides. Lewis Publishers, Chelsea, MI.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall,

Ithaca, N.Y. 14853-0901.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 9/93.

EXTOXNET primary files maintained and archived at Oregon State University.

Dichlorvos

TRADE OR OTHER NAMES

Apavap, Benfos, Cekusan, Cypona, Derriban, DerribanteDevikol, Didivane, Duo-Kill, Duravos, Elastrel, Fly-Die, Fly-Fighter, Herkol, Marvex, No-Pest, Prentox, Vaponite, Vapona, Verdican, Verdipor, Verdisol. Trade names used outside of the U.S. include Doom, Nogos, and Nuvan (2).

REGULATORY STATUS

A Special Review of dichlorvos was initiated in February 1988 because EPA determined that the registered uses of dichlorvos may pose a risk of cancer as well as inadequate margins of safety for cholinesterase inhibition and liver effects to exposed persons (12). The Special Review was not complete as of March 1992 (10). Products containing dichlorvos must bear the signal words "Danger-Poison" (2).

INTRODUCTION

Dichlorvos is used to control household, public health, and stored product insects. It is effective against mushroom flies, aphids, spider mites, caterpillars, thrips, and white flies in greenhouse, outdoor fruit, and vegetable crops (2). Therapeutically, dichlorvos is used to treat a variety of parasitic worm infections in dogs, livestock and humans. Dichlorvos can be fed to livestock to control botfly larvae in the manure. It acts against insects as both a contact and a stomach poison (2). Dichlorvos is available in aerosol and soluble concentrate formulations (2). It is used as a fumigant (2) and has been used to make pet collars and pest strips (3).

Dichlorvos is one of a class of insecticides referred to as organophosphates. These chemicals act by interfering with the activities of cholinesterase, an enzyme that is essential for the proper working of the nervous systems of both humans and insects. Please refer to the Toxicology Information Brief on cholinesterase-inhibition for a more detailed description of this topic.

In 1955, it was discovered that crystalline trichlorfon, another organophosphate pesticide, gave off a vapor which was capable of killing insects. That vapor was dichlorvos, which has since been developed for insect control in enclosed spaces (3).

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Dichlorvos is highly toxic by inhalation, dermal absorption and ingestion (9). Because dichlorvos is volatile, inhalation is the most common route of exposure. As with all organophosphates,

dichlorvos is readily absorbed through the skin. Skin which has come in contact with this material should be washed immediately with soap and water and all contaminated clothing should be removed.

Acute illness from dichlorvos is limited to the effects of cholinesterase inhibition. Compared to poisoning by other organophosphates, dichlorvos causes a more rapid onset of symptoms, which is often followed by a similarly rapid recovery (3). This occurs because dichlorvos is rapidly metabolized and eliminated from the body. Persons with reduced pulmonary (lung) function, convulsive disorders, liver disorders, or recent exposure to cholinesterase inhibitors will be at increased risk from exposure to dichlorvos. Alcoholic beverages may enhance the toxic effects of dichlorvos. High environmental temperatures or exposure of dichlorvos to visible or UV light may enhance its toxicity (9).

Dichlorvos is mildly irritating to skin (9). Concentrates of dichlorvos may cause burning sensations, or actual burns (6). Dichlorvos can be very toxic if it is not immediately washed off, but instead left on the skin long enough for it to become absorbed through the skin and into the bloodstream. One man nearly died after spilling 4 ounces of a 3% oil solution of dichlorvos on his lap. He did not wash it off. Another man only became nauseous and dizzy after spilling a similar amount on his arm. He washed off the dichlorvos with soap and water (6). Do not use organic solvents to remove dichlorvos from the skin (DLA/DOD Hazardous Mat'ls Info. System #0014-29- 438-0000. 1982).

The organophosphate insecticides are cholinesterase inhibitors. They are highly toxic by all routes of exposure. When inhaled, the first effects are usually respiratory and may include bloody or runny nose, coughing, chest discomfort, difficult or short breath, and wheezing due to constriction or excess fluid in the bronchial tubes. Skin contact with organophosphates may cause localized sweating and involuntary muscle contractions. Eye contact will cause pain, bleeding, tears, pupil constriction, and blurred vision. Following exposure by any route, other systemic effects may begin within a few minutes or be delayed for up to 12 hours. These may include pallor, nausea, vomiting, diarrhea, abdominal cramps, headache, dizziness, eye pain, blurred vision, constriction or dilation of the eye pupils, tears, salivation, sweating, and confusion. Severe poisoning will affect the central nervous system, producing incoordination, slurred speech, loss of reflexes, weakness, fatigue, involuntary muscle contractions, twitching, tremors of the tongue or eyelids, and eventually paralysis of the body extremities and the respiratory muscles. In severe cases there may also be involuntary defecation or urination, psychosis, irregular heart beats, unconsciousness, convulsions and coma. Death may be caused by respiratory failure or cardiac arrest (9).

Some organophosphates may cause delayed symptoms beginning 1 to 4 weeks after an acute exposure which may or may not have produced immediate symptoms. In such cases, numbness, tingling, weakness and cramping may appear in the lower limbs and progress to incoordination and paralysis. Improvement may occur over months or years, but some residual impairment will remain (9).

The administration of slow-release formulations of dichlorvos to domestic animals to treat for internal parasites has caused some inhibition of cholinesterase and mild symptoms such as nausea or diarrhea, but no serious signs of illness. Repeated, small doses generally have no effect on treated animals. Doses of up to 4 mg/kg of a slow release formulation, given to cows to reduce flies in their feces, had no visibly adverse effects on the cows. Blood tests of these cows indicated

cholinesterase inhibition (3).

Dichlorvos is very volatile, meaning that it readily forms vapors which may be inhaled. Inhalation is the most common way to be exposed to dichlorvos. Low, repeated doses may be non-toxic. High doses of dichlorvos may be very toxic, especially if inhalation exposure is continuous (6). Dichlorvos produces irritating gases, such as phosphorous and chlorine oxides, when heated (NIH/EPA 1984).

Eye protection should be worn when handling dichlorvos. Application of 1.67 mg/kg in rabbits' eyes produced mild redness and swelling, but no injury to the cornea (9). Dichlorvos may cause eye burns. Organophosphates cause the pupils to constrict (pin point pupils).

The amount of a chemical that is lethal to one-half (50%) of experimental animals fed the material is referred to as its acute oral lethal dose fifty, or LD50. The oral LD50 for dichlorvos in mice is 61 to 175 mg/kg, 100 to 1090 mg/kg in dogs, 15 mg/kg in chickens, 25 to 80 mg/kg in rats, 157 mg/kg in pigs, and 11 to 12.5 mg/kg in rabbits (2, 6, 9). The dermal LD50 for dichlorvos in rats is 70.4 to 250 mg/kg, 206 mg/kg in mice, and 107 mg/kg in rabbits (2, 3, 6, 9).

The lethal concentration fifty, or LC50, is that concentration of a chemical in air or water that kills half of the experimental animals exposed to it for a set time period. The 4-hour LC50 for dichlorvos in rats is 15 mg/m3, and 13 mg/m3 in mice (9).

CHRONIC TOXICITY

Feeding studies indicate that a dosage of dichlorvos very much larger than doses which inhibit cholinesterase are needed to produce illness. Rats tolerated dietary doses as high as 62.5 mg/kg/day for 90 days with no visible signs of illness, while a dietary level of 0.25 mg/kg/day for only 4 days produced a reduction in cholinesterase levels (3).

Rats were exposed to air concentrations of 0, 0.05, 0.5 and 5 mg/m3 of dichlorvos over a 5 week period. Rats in the 0.5 and 5 mg/kg groups exhibited significantly decreased cholinesterase activity in the plasma, red blood cells, and brain. The NOEL for this study was 0.05 mg/m3. In dogs fed dietary doses of 0.0095, 0.016, 0.16, 1.6 or 12.5 mg/kg/day for 2 years, decreased red blood cell cholinesterase activity, increased liver weights and increased liver cell size occurred in the two highest doses tested. The NOEL was 0.08 mg/kg/day (12). Chronic exposure to dichlorvos will cause fluid to build up in the lungs (pulmonary edema) (NIH/EPA; OHM/TADS 1984).

Repeated or prolonged exposure to organophosphates may result in the same effects as acute exposure including the delayed symptoms. Other effects reported in workers repeatedly exposed include impaired memory and concentration, disorientation, severe depressions, irritability, confusion, headache, speech difficulties, delayed reaction times, nightmares, sleepwalking and drowsiness or insomnia. An influenza-like condition with headache, nausea, weakness, loss of appetite, and malaise has also been reported (9).

Reproductive Effects

When male and female rats were given a diet containing 100 ppm (5 mg/kg/day) dichlorvos just before mating, and with this dosage continued through pregnancy and lactation for females, there were no effects on reproduction or on the survival or growth of the offspring, even though severe cholinesterase

inhibition occurred in the mothers and significant inhibition occurred in the offspring. The same results were observed in a 3-generation study with rats fed dietary levels up to (25 mg/kg/day) (3). Once in the bloodstream, dichlorvos may cross the placenta (9).

Teratogenic Effects

A dose of 12 mg/kg was not teratogenic in rabbits and did not interfere with reproduction in any way. There was no evidence of teratogenicity when rats and rabbits were exposed to air concentrations of up to 6.25 mg/m3 throughout pregnancy. Dichlorvos was not teratogenic when given orally to rats (3).

Mutagenic Effects

Dichlorvos can bind to molecules such as DNA. For this reason, there has been extensive testing of dichlorvos for mutagenicity. Several studies reviewed by EPA have shown dichlorvos to be a mutagen (12). Dichlorvos is reported positive in the Ames mutagenicity assay (Mut. Res. 87:211 (1981); 76:169 (1980); 40 (1):19 (1976) and in other tests involving bacterial or animal cell cultures. However no evidence of mutagenicity has been found in tests performed on live animals. Its lack of mutagenicity in live animals may be due to rapid metabolism and excretion of dichlorvos (3).

Carcinogenic Effects

Dichlorvos has been classified as a possible human carcinogen by EPA because of the results of tests on rats and mice (11). When dichlorvos was administered by gavage to mice for 5 days per week for 103 weeks at doses of 10 or 20 mg/kg to males and 20 or 40 mg/kg to females, there was an increased incidence of benign tumors in the lining of the stomach at the high dose for both sexes. When rats given daily doses of 0, 4 or 8 mg/kg for five days per week for 103 weeks, there was an increased incidence of benign tumors of the pancreas and of leukemia in male rats at both doses. At the highest dose, there was also an increased incidence of benign lung tumors in males. In female rats, there was an increase in the incidence of benign tumors of the mammary gland (12). No tumors caused by dichlorvos were found in rats fed up to 25 mg/kg/day for 2 years or in dogs fed up to 11 mg/kg/day for 2 years. No evidence of carcinogenicity was found when rats were exposed to air containing up to 5 mg/m3 for 23 hours/day for 2 years (3). A few tumors were found in the esophagus of mice given dichlorvos orally, even though tumors of this kind are normally rare (9).

Organ Toxicity

Dichlorvos primarily affects the nervous system through cholinesterase inhibition, by which there is a deactivation of cholinesterase, an enzyme required for proper nerve functioning.

Dichlorvos causes fluid to accumulate in the lungs (6). Liver enlargement has occurred in pigs maintained for long periods of time on high doses (500 ppm) (3, 6). Dichlorvos caused adverse liver effects in dogs (12). Lung hemorrhages may occur (14). Cholinesterase inhibition may affect the nervous system. In mice, a single oral dose of 40 micrograms (ug)/kg caused changes in the testes. In male rats, repeated doses caused abnormalities in the tissues of the lungs, heart, thyroid, liver and kidneys (9).

Fate in Humans and Animals

Amongst the organophosphates, dichlorvos is remarkable for

its rapid metabolism and excretion by mammals. Dichlorvos was not detected in the blood of rats, mice or people after exposure to atmospheric concentrations of up to 17 times that normally reached for insect control in homes. Exposure of rats to 11 mg/m3 (250 times the normal exposure) for 4 hours was required before dichlorvos was detectable in the rats. Even then, it was detected only in the kidneys. At 90 mg/m3 (2000 times normal exposure), dichlorvos was detected in most tissues of the rat. Following exposure to 50 mg/m3, the half-life for dichlorvos in the rat kidney was 13.5 minutes. The reason for this rapid disappearance of dichlorvos is the presence of degrading enzymes in both tissues and blood plasma. From the gastrointestinal tract, dichlorvos is absorbed into the portal blood, rather than into the general bloodstream. From the portal blood, it is moved to the liver where it is rapidly detoxified. Thus poisoning by nonlethal doses of dichlorvos is usually followed by rapid detoxification in the liver and recovery. Rats given oral or dermal doses at the LD50 level either died within one hour of dosing or recovered completely (3, 6).

Dichlorvos does not accumulate in body tissues and has not been detected in the milk of cows or rats, even when the animals were given doses high enough to produce symptoms of severe poisoning (3).

ECOLOGICAL EFFECTS

Effects on Birds

Dichlorvos is highly toxic to birds including ducks and pheasants (4, 8). The LD50 for wild birds fed dichlorvos is 12 mg/kg (NIOSH RTECS Online File #82/8110).

Effects on Aquatic Organisms

UV light makes dichlorvos more toxic to aquatic life by 5-150 times (15). NIH/EPA found the grass shrimp to be more sensitive to dichlorvos than the sand shrimp, hermit crab and mummichog (in that order) (1984). For ocean- dwelling species they found: scud > Atlantic silverside > striped killfish > striped mullet > bluehead > American eel > northern puffer; where ">" indicates a greater sensitivity to dichlorvos. The 96-hour LC50 for dichlorvos in fathead minnow is 11.6 mg/l, 0.9 mg/l in bluegill, 5.3 mg/l in mosquito fish, 0.004 ppm in sand shrimp, 3.7 ppm in mummichogs, and 1.8 ppm/96 hours in American eels (NIH/EPA 1984). The 24-hour LC50 for dichlorvos in bluegill sunfish is 1.0 mg/l (2).

Dichlorvos does not significantly bioaccumulate in fish (4).

Effects on Other Animals (Nontarget species)

Dichlorvos is toxic to bees (2).

ENVIRONMENTAL FATE

Breakdown of Chemical in Soil and Groundwater

Dichlorvos does not adsorb to soil particles and it is likely to contaminate groundwater. When spilled on soil, dichlorvos leached into the ground with 18 to 20% penetrating to a depth of 30 cm within 5 days. In soil, dichlorvos is subject to hydrolysis and biodegradation. Volatilization from moist soils is expected to be slow. Half-lives of 7 days were measured on clay, sandy-clay, and loose sandy soil (4).

Dichlorvos is rapidly broken down in the air and in damp media such as soil. The pH of the media determines the rate of breakdown. Alkaline soils, water, etc., show rapid breakdown,

whereas acidic media shows slow degradation. For instance, at a pH of 9.1 the half-life of dichlorvos is about 4.5 hours. At a pH of 1 (very acidic), the half-life is 50 hours (8). Dichlorvos is non-persistent.

Breakdown of Chemical in Water

In water dichlorvos remains in solution and does not adsorb to sediments. It degrades primarily by hydrolysis, with a half-life of approximately 4 days in lakes and rivers. This half-life will vary from 20 to 80 hours between pH 4 and pH 9. Hydrolysis is slow at pH 4 and rapid at pH 9 (4, 5). Biodegradation may occur, especially under acidic conditions which slow hydrolysis, or where populations of acclimated micro-organisms exist, as in polluted waters. Volatilization from water is expected to be slow. The volatilization half-life from river and pond waters have been estimated at 57 and over 400 days respectively (4).

Breakdown of Chemical in Vegetation

Except for cucumbers, roses, and some chrysanthemums, plants tolerate dichlorvos very well (5).

PHYSICAL PROPERTIES AND GUIDELINES

Dichlorvos is a colorless to amber liquid with a mild chemical odor. Dilute dichlorvos breaks down rapidly in the presence of moisture. Concentrated forms are readily decomposed by strong acids and bases (3). Dichlorvos is stable under normal temperatures and pressures, but it may pose a moderate fire hazard if exposed to heat or flame. It may hydrolyze on contact with moisture, and may decompose in the presence of strong acids or bases (3, 9). Thermal decomposition of dichlorvos will release toxic oxides of phosphorus and carbon, toxic and corrosive chlorides and toxic phosgene gas. Dichlorvos is corrosive to iron and steel. It may attack materials such as plastics, rubber and coatings (9). Other metals (stainless steel, aluminum, nickel) are resistant if no water is present.

Dichlorvos increases the effects of malathion (5). Alcoholic beverages promote the absorption of dichlorvos into the bloodstream (8).

Persons who work with organophosphate materials for long periods of time should have frequent blood tests of their cholinesterase levels. If the cholinesterase level falls below a critical point, no further exposure should be allowed until it returns to normal (13).

Protective clothing must be worn when handling dichlorvos. Before removing gloves, wash them with soap and water. Always wash hands, face and arms with soap and water before smoking, eating or drinking.

After work, remove all work clothes and shoes. Shower with soap and water. Wear only clean clothes when leaving the job. Wash contaminated clothing and equipment with soap and water after each use. Keep contaminated work clothes separate from regular laundry.

Exposure Guidelines:

1 mg/m3 OSHA TWA (skin) (9)

0.1 ppm (0.9 mg/m3) ACGIH TWA (skin) (9)

1 mg/m3 NIOSH Recommended TWA (skin) (9)

(9) Occupational Health Services, Inc. 1991 (May 15). MSDS for Dichlorvos. OHS Inc., Secaucus, NJ.

(10) US Environmental Protection Agency. 1992 (March). Status of Pesticides in Reregistration and Special Review (H-7508W). Prevention, Pesticides and Toxic Substances, US EPA, Washington, DC.

(11) _____. 1991 (Feb. 13). Dichlorvos; Revocation of tolerance and food additive regulation. Federal Register 56 (30): 5788-9.

(12) _____. 1988 (Feb. 24). Dichlorvos; Initiation of Special Review. Federal Register 53 (36): 5542-9.

(13) Cheminova Agro A/S. 1991 (June 11). Material Safety Data Sheet : Dimethoate. Cheminova, Lemvig, Denmark.

(14) Pesticides and Human Health. Hallenbeck & Cunningham-Burns. Springer-Verlag.

(15) TOXNET. 1985. National library of medicine's toxicology data network. Hazardous Substances Databank. Public health Service. National Institute of Health. U.S. Department of Health and Human Services. Bethesda, MD: NLM.

(16) National Fire Protection Association (NFPA). Fire Protection Guide. Hazardous Materials. 1978.

(17) Merck Index 9th Ed. 1976.

(18) Handbook of Analytical Toxicology. Sunshine. 1969.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall, Ithaca, N.Y. 14853-0901.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

Air concentrations of 200 mg/m3 are immediately dangerous to life or health (9).

PADI: 8 x 10 to the minus 4 power mg/kg/day, based on a 2-year dog feeding study (12)

Physical Properties

CAS #: 62-73-7

Specific gravity: 1.44 (60 degrees /60 degrees F) (2)

Solubility in water: 1 g/100g at 25 degrees C (17)

Solubility: Miscible in non-polar solvents such as dichloromethane, 2-propanol and toluene (2, 17). Soluble in ethanol, chloroform, acetone, and kerosene (1, 5). Miscible in alcohol and in aromatic and chlorinated hydrocarbon solvents. Solubility in kerosene and mineral oils is about 3% (3).

Boiling point: 140 degrees C at 20 mm Hg (17); 117 degrees C at 11 mm Hg (2); 35 degrees C at 0.05 mm Hg (3); 183 degrees F (84 degrees C) (9)

Flash point: >175 degrees F (>80 degrees C) (2, 16), practically non-flammable (17).

Vapor pressure: 0.01 mm Hg at 30 degrees C (18)

Chemical class/use: Organophosphate insecticide

BASIC MANUFACTURER

Amvac Chemical Corp.
4100 E. Washington Blvd.
Los Angeles CA 90023

Review by Basic Manufacturer

Comments solicited: January, 1992.
Comments received: April, 1992.

REFERENCES

(1) Farm Chemicals Handbook. Ed by R.T. Meister. Meister Publishing Co., Willoughby, OH. 1987.

(2) Meister, R.T. (ed.). 1992. Farm Chemicals Handbook '92. Meister Publishing Company, Willoughby, OH.

(3) Hayes, W.J. and E.R. Laws (ed.). 1990. Handbook of Pesticide Toxicology, Vol. 3, Classes of Pesticides. Academic Press, Inc., NY.

(4) Howard, P.H. (ed.). 1989. Handbook of Environmental Fate and Exposure Data for Organic Chemicals, Vol. III: Pesticides. Lewis Publishers, Chelsea, MI.

(5) The Pesticide Manual. 8th Ed. Ed. by C.R. Worthing. British Crop Protection Council. 1987.

(6) Pesticides Studied in Man. Wayland Hayes, Jr. Williams and Wilkins, Baltimore, MD. 1982.

(7) Herbicides. 2nd Ed. Vols. 1, 2. Kearney. 1975.

(8) The Agrochemicals Handbook. The Royal Society of Chem. 1983.

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 9/93.

EXTOXNET primary files maintained and archived at Oregon State University.

Dichlorvos

TRADE OR OTHER NAMES

Apavap, Benfos, Cekusan, Cypona, Derriban, DerribanteDevikol, Didivane, Duo-Kill, Duravos, Elastrel, Fly-Die, Fly-Fighter, Herkol, Marvex, No-Pest, Prentox, Vaponite, Vapona, Verdican, Verdipor, Verdisol. Trade names used outside of the U.S. include Doom, Nogos, and Nuvan (2).

REGULATORY STATUS

A Special Review of dichlorvos was initiated in February 1988 because EPA determined that the registered uses of dichlorvos may pose a risk of cancer as well as inadequate margins of safety for cholinesterase inhibition and liver effects to exposed persons (12). The Special Review was not complete as of March 1992 (10). Products containing dichlorvos must bear the signal words "Danger-Poison" (2).

INTRODUCTION

Dichlorvos is used to control household, public health, and stored product insects. It is effective against mushroom flies, aphids, spider mites, caterpillars, thrips, and white flies in greenhouse, outdoor fruit, and vegetable crops (2). Therapeutically, dichlorvos is used to treat a variety of parasitic worm infections in dogs, livestock and humans. Dichlorvos can be fed to livestock to control botfly larvae in the manure. It acts against insects as both a contact and a stomach poison (2). Dichlorvos is available in aerosol and soluble concentrate formulations (2). It is used as a fumigant (2) and has been used to make pet collars and pest strips (3).

Dichlorvos is one of a class of insecticides referred to as organophosphates. These chemicals act by interfering with the activities of cholinesterase, an enzyme that is essential for the proper working of the nervous systems of both humans and insects. Please refer to the Toxicology Information Brief on cholinesterase-inhibition for a more detailed description of this topic.

In 1955, it was discovered that crystalline trichlorfon, another organophosphate pesticide, gave off a vapor which was capable of killing insects. That vapor was dichlorvos, which has since been developed for insect control in enclosed spaces (3).

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Dichlorvos is highly toxic by inhalation, dermal absorption and ingestion (9). Because dichlorvos is volatile, inhalation is the most common route of exposure. As with all organophosphates,

dichlorvos is readily absorbed through the skin. Skin which has come in contact with this material should be washed immediately with soap and water and all contaminated clothing should be removed.

Acute illness from dichlorvos is limited to the effects of cholinesterase inhibition. Compared to poisoning by other organophosphates, dichlorvos causes a more rapid onset of symptoms, which is often followed by a similarly rapid recovery (3). This occurs because dichlorvos is rapidly metabolized and eliminated from the body. Persons with reduced pulmonary (lung) function, convulsive disorders, liver disorders, or recent exposure to cholinesterase inhibitors will be at increased risk from exposure to dichlorvos. Alcoholic beverages may enhance the toxic effects of dichlorvos. High environmental temperatures or exposure of dichlorvos to visible or UV light may enhance its toxicity (9).

Dichlorvos is mildly irritating to skin (9). Concentrates of dichlorvos may cause burning sensations, or actual burns (6). Dichlorvos can be very toxic if it is not immediately washed off, but instead left on the skin long enough for it to become absorbed through the skin and into the bloodstream. One man nearly died after spilling 4 ounces of a 3% oil solution of dichlorvos on his lap. He did not wash it off. Another man only became nauseous and dizzy after spilling a similar amount on his arm. He washed off the dichlorvos with soap and water (6). Do not use organic solvents to remove dichlorvos from the skin (DLA/DOD Hazardous Mat'ls Info. System #0014-29- 438-0000. 1982).

The organophosphate insecticides are cholinesterase inhibitors. They are highly toxic by all routes of exposure. When inhaled, the first effects are usually respiratory and may include bloody or runny nose, coughing, chest discomfort, difficult or short breath, and wheezing due to constriction or excess fluid in the bronchial tubes. Skin contact with organophosphates may cause localized sweating and involuntary muscle contractions. Eye contact will cause pain, bleeding, tears, pupil constriction, and blurred vision. Following exposure by any route, other systemic effects may begin within a few minutes or be delayed for up to 12 hours. These may include pallor, nausea, vomiting, diarrhea, abdominal cramps, headache, dizziness, eye pain, blurred vision, constriction or dilation of the eye pupils, tears, salivation, sweating, and confusion. Severe poisoning will affect the central nervous system, producing incoordination, slurred speech, loss of reflexes, weakness, fatigue, involuntary muscle contractions, twitching, tremors of the tongue or eyelids, and eventually paralysis of the body extremities and the respiratory muscles. In severe cases there may also be involuntary defecation or urination, psychosis, irregular heart beats, unconsciousness, convulsions and coma. Death may be caused by respiratory failure or cardiac arrest (9).

Some organophosphates may cause delayed symptoms beginning 1 to 4 weeks after an acute exposure which may or may not have produced immediate symptoms. In such cases, numbness, tingling, weakness and cramping may appear in the lower limbs and progress to incoordination and paralysis. Improvement may occur over months or years, but some residual impairment will remain (9).

The administration of slow-release formulations of dichlorvos to domestic animals to treat for internal parasites has caused some inhibition of cholinesterase and mild symptoms such as nausea or diarrhea, but no serious signs of illness. Repeated, small doses generally have no effect on treated animals. Doses of up to 4 mg/kg of a slow release formulation, given to cows to reduce flies in their feces, had no visibly adverse effects on the cows. Blood tests of these cows indicated

cholinesterase inhibition (3).

Dichlorvos is very volatile, meaning that it readily forms vapors which may be inhaled. Inhalation is the most common way to be exposed to dichlorvos. Low, repeated doses may be non-toxic. High doses of dichlorvos may be very toxic, especially if inhalation exposure is continuous (6). Dichlorvos produces irritating gases, such as phosphorous and chlorine oxides, when heated (NIH/EPA 1984).

Eye protection should be worn when handling dichlorvos. Application of 1.67 mg/kg in rabbits' eyes produced mild redness and swelling, but no injury to the cornea (9). Dichlorvos may cause eye burns. Organophosphates cause the pupils to constrict (pin point pupils).

The amount of a chemical that is lethal to one-half (50%) of experimental animals fed the material is referred to as its acute oral lethal dose fifty, or LD50. The oral LD50 for dichlorvos in mice is 61 to 175 mg/kg, 100 to 1090 mg/kg in dogs, 15 mg/kg in chickens, 25 to 80 mg/kg in rats, 157 mg/kg in pigs, and 11 to 12.5 mg/kg in rabbits (2, 6, 9). The dermal LD50 for dichlorvos in rats is 70.4 to 250 mg/kg, 206 mg/kg in mice, and 107 mg/kg in rabbits (2, 3, 6, 9).

The lethal concentration fifty, or LC50, is that concentration of a chemical in air or water that kills half of the experimental animals exposed to it for a set time period. The 4-hour LC50 for dichlorvos in rats is 15 mg/m3, and 13 mg/m3 in mice (9).

CHRONIC TOXICITY

Feeding studies indicate that a dosage of dichlorvos very much larger than doses which inhibit cholinesterase are needed to produce illness. Rats tolerated dietary doses as high as 62.5 mg/kg/day for 90 days with no visible signs of illness, while a dietary level of 0.25 mg/kg/day for only 4 days produced a reduction in cholinesterase levels (3).

Rats were exposed to air concentrations of 0, 0.05, 0.5 and 5 mg/m3 of dichlorvos over a 5 week period. Rats in the 0.5 and 5 mg/kg groups exhibited significantly decreased cholinesterase activity in the plasma, red blood cells, and brain. The NOEL for this study was 0.05 mg/m3. In dogs fed dietary doses of 0.0095, 0.016, 0.16, 1.6 or 12.5 mg/kg/day for 2 years, decreased red blood cell cholinesterase activity, increased liver weights and increased liver cell size occurred in the two highest doses tested. The NOEL was 0.08 mg/kg/day (12). Chronic exposure to dichlorvos will cause fluid to build up in the lungs (pulmonary edema) (NIH/EPA; OHM/TADS 1984).

Repeated or prolonged exposure to organophosphates may result in the same effects as acute exposure including the delayed symptoms. Other effects reported in workers repeatedly exposed include impaired memory and concentration, disorientation, severe depressions, irritability, confusion, headache, speech difficulties, delayed reaction times, nightmares, sleepwalking and drowsiness or insomnia. An influenza-like condition with headache, nausea, weakness, loss of appetite, and malaise has also been reported (9).

Reproductive Effects

When male and female rats were given a diet containing 100 ppm (5 mg/kg/day) dichlorvos just before mating, and with this dosage continued through pregnancy and lactation for females, there were no effects on reproduction or on the survival or growth of the offspring, even though severe cholinesterase

inhibition occurred in the mothers and significant inhibition occurred in the offspring. The same results were observed in a 3-generation study with rats fed dietary levels up to (25 mg/kg/day) (3). Once in the bloodstream, dichlorvos may cross the placenta (9).

Teratogenic Effects

A dose of 12 mg/kg was not teratogenic in rabbits and did not interfere with reproduction in any way. There was no evidence of teratogenicity when rats and rabbits were exposed to air concentrations of up to 6.25 mg/m3 throughout pregnancy. Dichlorvos was not teratogenic when given orally to rats (3).

Mutagenic Effects

Dichlorvos can bind to molecules such as DNA. For this reason, there has been extensive testing of dichlorvos for mutagenicity. Several studies reviewed by EPA have shown dichlorvos to be a mutagen (12). Dichlorvos is reported positive in the Ames mutagenicity assay (Mut. Res. 87:211 (1981); 76:169 (1980); 40 (1):19 (1976) and in other tests involving bacterial or animal cell cultures. However no evidence of mutagenicity has been found in tests performed on live animals. Its lack of mutagenicity in live animals may be due to rapid metabolism and excretion of dichlorvos (3).

Carcinogenic Effects

Dichlorvos has been classified as a possible human carcinogen by EPA because of the results of tests on rats and mice (11). When dichlorvos was administered by gavage to mice for 5 days per week for 103 weeks at doses of 10 or 20 mg/kg to males and 20 or 40 mg/kg to females, there was an increased incidence of benign tumors in the lining of the stomach at the high dose for both sexes. When rats given daily doses of 0, 4 or 8 mg/kg for five days per week for 103 weeks, there was an increased incidence of benign tumors of the pancreas and of leukemia in male rats at both doses. At the highest dose, there was also an increased incidence of benign lung tumors in males. In female rats, there was an increase in the incidence of benign tumors of the mammary gland (12). No tumors caused by dichlorvos were found in rats fed up to 25 mg/kg/day for 2 years or in dogs fed up to 11 mg/kg/day for 2 years. No evidence of carcinogenicity was found when rats were exposed to air containing up to 5 mg/m3 for 23 hours/day for 2 years (3). A few tumors were found in the esophagus of mice given dichlorvos orally, even though tumors of this kind are normally rare (9).

Organ Toxicity

Dichlorvos primarily affects the nervous system through cholinesterase inhibition, by which there is a deactivation of cholinesterase, an enzyme required for proper nerve functioning.

Dichlorvos causes fluid to accumulate in the lungs (6). Liver enlargement has occurred in pigs maintained for long periods of time on high doses (500 ppm) (3, 6). Dichlorvos caused adverse liver effects in dogs (12). Lung hemorrhages may occur (14). Cholinesterase inhibition may affect the nervous system. In mice, a single oral dose of 40 micrograms (ug)/kg caused changes in the testes. In male rats, repeated doses caused abnormalities in the tissues of the lungs, heart, thyroid, liver and kidneys (9).

Fate in Humans and Animals

Amongst the organophosphates, dichlorvos is remarkable for

its rapid metabolism and excretion by mammals. Dichlorvos was not detected in the blood of rats, mice or people after exposure to atmospheric concentrations of up to 17 times that normally reached for insect control in homes. Exposure of rats to 11 mg/m3 (250 times the normal exposure) for 4 hours was required before dichlorvos was detectable in the rats. Even then, it was detected only in the kidneys. At 90 mg/m3 (2000 times normal exposure), dichlorvos was detected in most tissues of the rat. Following exposure to 50 mg/m3, the half-life for dichlorvos in the rat kidney was 13.5 minutes. The reason for this rapid disappearance of dichlorvos is the presence of degrading enzymes in both tissues and blood plasma. From the gastrointestinal tract, dichlorvos is absorbed into the portal blood, rather than into the general bloodstream. From the portal blood, it is moved to the liver where it is rapidly detoxified. Thus poisoning by nonlethal doses of dichlorvos is usually followed by rapid detoxification in the liver and recovery. Rats given oral or dermal doses at the LD50 level either died within one hour of dosing or recovered completely (3, 6).

Dichlorvos does not accumulate in body tissues and has not been detected in the milk of cows or rats, even when the animals were given doses high enough to produce symptoms of severe poisoning (3).

ECOLOGICAL EFFECTS

Effects on Birds

Dichlorvos is highly toxic to birds including ducks and pheasants (4, 8). The LD50 for wild birds fed dichlorvos is 12 mg/kg (NIOSH RTECS Online File #82/8110).

Effects on Aquatic Organisms

UV light makes dichlorvos more toxic to aquatic life by 5-150 times (15). NIH/EPA found the grass shrimp to be more sensitive to dichlorvos than the sand shrimp, hermit crab and mummichog (in that order) (1984). For ocean- dwelling species they found: scud > Atlantic silverside > striped killfish > striped mullet > bluehead > American eel > northern puffer; where ">" indicates a greater sensitivity to dichlorvos. The 96-hour LC50 for dichlorvos in fathead minnow is 11.6 mg/l, 0.9 mg/l in bluegill, 5.3 mg/l in mosquito fish, 0.004 ppm in sand shrimp, 3.7 ppm in mummichogs, and 1.8 ppm/96 hours in American eels (NIH/EPA 1984). The 24-hour LC50 for dichlorvos in bluegill sunfish is 1.0 mg/l (2).

Dichlorvos does not significantly bioaccumulate in fish (4).

Effects on Other Animals (Nontarget species)

Dichlorvos is toxic to bees (2).

ENVIRONMENTAL FATE

Breakdown of Chemical in Soil and Groundwater

Dichlorvos does not adsorb to soil particles and it is likely to contaminate groundwater. When spilled on soil, dichlorvos leached into the ground with 18 to 20% penetrating to a depth of 30 cm within 5 days. In soil, dichlorvos is subject to hydrolysis and biodegradation. Volatilization from moist soils is expected to be slow. Half-lives of 7 days were measured on clay, sandy-clay, and loose sandy soil (4).

Dichlorvos is rapidly broken down in the air and in damp media such as soil. The pH of the media determines the rate of breakdown. Alkaline soils, water, etc., show rapid breakdown,

whereas acidic media shows slow degradation. For instance, at a pH of 9.1 the half-life of dichlorvos is about 4.5 hours. At a pH of 1 (very acidic), the half-life is 50 hours (8). Dichlorvos is non-persistent.

Breakdown of Chemical in Water

In water dichlorvos remains in solution and does not adsorb to sediments. It degrades primarily by hydrolysis, with a half-life of approximately 4 days in lakes and rivers. This half-life will vary from 20 to 80 hours between pH 4 and pH 9. Hydrolysis is slow at pH 4 and rapid at pH 9 (4, 5). Biodegradation may occur, especially under acidic conditions which slow hydrolysis, or where populations of acclimated micro-organisms exist, as in polluted waters. Volatilization from water is expected to be slow. The volatilization half-life from river and pond waters have been estimated at 57 and over 400 days respectively (4).

Breakdown of Chemical in Vegetation

Except for cucumbers, roses, and some chrysanthemums, plants tolerate dichlorvos very well (5).

PHYSICAL PROPERTIES AND GUIDELINES

Dichlorvos is a colorless to amber liquid with a mild chemical odor. Dilute dichlorvos breaks down rapidly in the presence of moisture. Concentrated forms are readily decomposed by strong acids and bases (3). Dichlorvos is stable under normal temperatures and pressures, but it may pose a moderate fire hazard if exposed to heat or flame. It may hydrolyze on contact with moisture, and may decompose in the presence of strong acids or bases (3, 9). Thermal decomposition of dichlorvos will release toxic oxides of phosphorus and carbon, toxic and corrosive chlorides and toxic phosgene gas. Dichlorvos is corrosive to iron and steel. It may attack materials such as plastics, rubber and coatings (9). Other metals (stainless steel, aluminum, nickel) are resistant if no water is present.

Dichlorvos increases the effects of malathion (5). Alcoholic beverages promote the absorption of dichlorvos into the bloodstream (8).

Persons who work with organophosphate materials for long periods of time should have frequent blood tests of their cholinesterase levels. If the cholinesterase level falls below a critical point, no further exposure should be allowed until it returns to normal (13).

Protective clothing must be worn when handling dichlorvos. Before removing gloves, wash them with soap and water. Always wash hands, face and arms with soap and water before smoking, eating or drinking.

After work, remove all work clothes and shoes. Shower with soap and water. Wear only clean clothes when leaving the job. Wash contaminated clothing and equipment with soap and water after each use. Keep contaminated work clothes separate from regular laundry.

Exposure Guidelines:

1 mg/m3 OSHA TWA (skin) (9)

0.1 ppm (0.9 mg/m3) ACGIH TWA (skin) (9)

1 mg/m3 NIOSH Recommended TWA (skin) (9)

Air concentrations of 200 mg/m3 are immediately dangerous to life or health (9).

PADI: 8 x 10 to the minus 4 power mg/kg/day, based on a 2-year dog feeding study (12)

Physical Properties

CAS #: 62-73-7

Specific gravity: 1.44 (60 degrees /60 degrees F) (2)

Solubility in water: 1 g/100g at 25 degrees C (17)

Solubility: Miscible in non-polar solvents such as dichloromethane, 2-propanol and toluene (2, 17). Soluble in ethanol, chloroform, acetone, and kerosene (1, 5). Miscible in alcohol and in aromatic and chlorinated hydrocarbon solvents. Solubility in kerosene and mineral oils is about 3% (3).

Boiling point: 140 degrees C at 20 mm Hg (17); 117 degrees C at 11 mm Hg (2); 35 degrees C at 0.05 mm Hg (3); 183 degrees F (84 degrees C) (9)

Flash point: >175 degrees F (>80 degrees C) (2, 16), practically non-flammable (17).

Vapor pressure: 0.01 mm Hg at 30 degrees C (18)

Chemical class/use: Organophosphate insecticide

BASIC MANUFACTURER

Amvac Chemical Corp.
4100 E. Washington Blvd.
Los Angeles CA 90023

Review by Basic Manufacturer

Comments solicited: January, 1992.
Comments received: April, 1992.

REFERENCES

(1) Farm Chemicals Handbook. Ed by R.T. Meister. Meister Publishing Co., Willoughby, OH. 1987.

(2) Meister, R.T. (ed.). 1992. Farm Chemicals Handbook '92. Meister Publishing Company, Willoughby, OH.

(3) Hayes, W.J. and E.R. Laws (ed.). 1990. Handbook of Pesticide Toxicology, Vol. 3, Classes of Pesticides. Academic Press, Inc., NY.

(4) Howard, P.H. (ed.). 1989. Handbook of Environmental Fate and Exposure Data for Organic Chemicals, Vol. III: Pesticides. Lewis Publishers, Chelsea, MI.

(5) The Pesticide Manual. 8th Ed. Ed. by C.R. Worthing. British Crop Protection Council. 1987.

(6) Pesticides Studied in Man. Wayland Hayes, Jr. Williams and Wilkins, Baltimore, MD. 1982.

(7) Herbicides. 2nd Ed. Vols. 1, 2. Kearney. 1975.

(8) The Agrochemicals Handbook. The Royal Society of Chem. 1983.

(9) Occupational Health Services, Inc. 1991 (May 15). MSDS for Dichlorvos. OHS Inc., Secaucus, NJ.

(10) US Environmental Protection Agency. 1992 (March). Status of Pesticides in Reregistration and Special Review (H-7508W). Prevention, Pesticides and Toxic Substances, US EPA, Washington, DC.

(11) _____. 1991 (Feb. 13). Dichlorvos; Revocation of tolerance and food additive regulation. Federal Register 56 (30): 5788-9.

(12) _____. 1988 (Feb. 24). Dichlorvos; Initiation of Special Review. Federal Register 53 (36): 5542-9.

(13) Cheminova Agro A/S. 1991 (June 11). Material Safety Data Sheet : Dimethoate. Cheminova, Lemvig, Denmark.

(14) Pesticides and Human Health. Hallenbeck & Cunningham-Burns. Springer-Verlag.

(15) TOXNET. 1985. National library of medicine's toxicology data network. Hazardous Substances Databank. Public health Service. National Institute of Health. U.S. Department of Health and Human Services. Bethesda, MD: NLM.

(16) National Fire Protection Association (NFPA). Fire Protection Guide. Hazardous Materials. 1978.

(17) Merck Index 9th Ed. 1976.

(18) Handbook of Analytical Toxicology. Sunshine. 1969.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall, Ithaca, N.Y. 14853-0901.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 9/93.

EXTOXNET primary files maintained and archived at Oregon State University.

LINDANE

TRADE OR OTHER NAMES

Proprietary names for products containing BHC are Agrocide, Ambrocide, Benesan, Benexane, Borer-Tox, and Gamasan. Lindane may also be found in formulations with a host of fungicides and insecticides.

INTRODUCTION

Lindane is an organochlorine insecticide and fumigant which has been used on a wide range of soil-dwelling and plant-eating insects. Lindane is presently used primarily for seed treatment and in lotions, creams, and shampoos for the control of lice, and mites (scabies) in humans.

Benzene Hexachloride (BHC) is the 100% pure form of the product while lindane is slightly less pure (>99% pure). There are eight separate three dimensional forms (isomers) of BHC; the gamma configuration being one of those forms. As used in this profile lindane and BHC refer only to the gamma isomer of BHC.

Some formulations of lindane are classified as Restricted Use Pesticides (RUP). Restricted Use Pesticides may be purchased and used only by certified applicators. Most uses of lindane in agriculture and in the dairy industry have been cancelled by the EPA. Lindane is no longer manufactured in the United States.

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Lindane is highly toxic and carries the signal word WARNING. It is a central nervous system stimulant with symptoms usually developing within one hour. Symptoms of acute exposure in humans can include mental and motor retardation, central nervous system excitation, clonic (intermittent) and tonic (continuous) convulsions, respiratory failure, pulmonary edema and dermatitis. Other symptoms in humans are more behavioral in nature such as loss of balance and somersaulting (7), grinding of the teeth, and hyperirritability. Lindane can be absorbed through the skin, through inhalation or through direct ingestion.

Most acute effects have been due to accidental or intentional ingestion, although inhalation occurred (especially among children) when it was used in vaporizers. Workers may be exposed to the product through absorption through the skin and through inhalation if handled incorrectly.

The oral LD50 for rats is 88-270 mg/kg, for mice 59-246 mg/kg, and for rabbits 60 mg/kg. The lowest oral dose which may be lethal for a child is estimated to be 180 mg/kg. Lotions (10%) applied for scabies have resulted in severe intoxication in

some children and infants.

CHRONIC TOXICITY

Sixty male workers in a lindane producing factory had no signs of neurological impairment or perturbation after one to thirty years exposure. However another study of chronically exposed workers showed some mild differences in heart beat.

Small amounts of lindane fed to rabbits (1.5-12.0 mg/kg) for five to six weeks, and to rats (6.25-25 mg/kg) for 35 weeks suppressed their immune systems. This adversely affected the organisms' ability to fight off disease. In a two-year rat study, significant liver changes were attributed to the intake of moderately small amounts of lindane in the diets of the test animals (approximately 5 mg/kg/day).

Reproductive Effects

Female rats experienced a disturbance of their reproductive cycle and inhibited fertility with doses of 0.5 mg/kg for four months. Treatments of 0.05 mg/kg did not produce these effects. Lindane was found to be slightly estrogenic to female rats and also caused the seminiferous tubules in male rats to become atrophied at doses of 8 mg/kg/day over a ten day period (7). These tests suggest that the compound may have reproductive effects in human populations.

Teratogenic Effects

Beagles given 7.5 or 15 mg/kg from day five throughout gestation did not produce pups with any noticeable birth defects. Pregnant rats given small amounts of lindane in their food had offspring unaffected by the pesticide (3). Lindane, however, can be passed from the mother to the developing fetus (3). It appears that lindane will not cause developmental effects at low levels of exposure and causes reproductive effects at levels approaching the acute toxicity doses. These effects have not been observed in human populations.

Mutagenic Effects

A variety of tests on mice and on microbes have shown no mutagenicity in the cells tested (7). It has been shown to induce some changes in the chromosomes of cultured human lymphocytes during cell division at fairly low doses. It is unlikely that lindane would pose a mutagenic risk in humans at very low exposure levels.

Carcinogenic Effects

The carcinogenicity of lindane in experimental animals is low (or limited) as judged by the International Agency for Research on Cancer (1). Mice fed 100-500 mg/kg diets for 24 weeks showed no signs of tumors. Rats fed for a lifespan at 5-1,600 mg/kg diet with a mean age at death of 58 weeks, had no increase in tumor incidence.

One of the confounding factors in establishing a link between the insecticide and carcinogenicity is the presence of three different dimensional forms (isomers) of the compound BHC. Each form has a slightly different toxicity.

The International Agency for Research on Cancer has concluded that there is sufficient evidence to show that one of the lindane isomers is carcinogenic and limited evidence to establish the carcinogenicity of the beta and gamma isomers (10).

Fate in Humans and Animals

Of a single dose of 40 mg/kg to rats, 80% was excreted in urine and 20% in feces. Half of the administered lindane is excreted in three or four days. When administered for 18 days at 8 mg/kg, metabolites were found in blood, liver, kidneys, spleen, heart, and the brain. In humans, the mono, di, tri, and tetra-chlorophenolic metabolites are detected in urine with the trichlorophenols predominating. Residues disappear within three weeks after dosing ceases. Cows fed low doses in their daily ration for 35 days produced milk with residues from 0.002 to 0.015 ppm.

ECOLOGICAL EFFECTS

Lindane can be stored in the fat of mammals and birds. Birds of prey in the Netherlands contained up to 89 ppm in this tissue. Residues can also find their way into egg yolks at measurable concentrations for 32 days after dosing (5). Harbor seals from the German North Sea and racoons from North America were found to have lindane in their fat at concentrations ranging from 0.3 ppm to 1.0 ppm (8).

Lindane is very highly toxic to fish. The 96 hr LC50 ranges from 1.7 to 32 ppb for trout and salmon to 44 to 131 ppb for catfish, perch and goldfish. Water hardness did not seem to alter the toxicity to fish but temperature did. An increase in temperature from 2 degrees to 18 degrees C caused a 2.3-fold decrease in rainbow trout toxicity, but a 7 degree to 29 degrees C increase caused a 2.6-fold increase in bluegill toxicity. Chronic, sublethal exposures to lindane produced liver and kidney problems in fish. Most of the lindane in the fish was unmetabolized. In the snail (Physa) most of the lindane was found as the metabolite pentachloro-cyclohexene.

Birds are more tolerant of high doses of lindane than are mammals. Mallards have an LD50 of more than 5000 mg/kg. Pheasants, Japanese quail, and bobwhite quail have LC50 values of 561 ppm, 425 ppm and 882 ppm respectively. Thus lindane is only slightly toxic to these organisms. Egg shell thinning and reduced egg production has occurred in birds exposed to lindane.

Lindane is highly toxic to bees and to aquatic invertebrates. The compound is believed to cause birth defects in amphibians.

ENVIRONMENTAL FATE

On eight types of soil, it was found that lindane residues decreased by 40 to 80% per year. When sprayed on the surface, the half-life was 4-6 weeks with 90% gone in 30-40 weeks. When worked into the soil, the half-life was 15-20 weeks with 90% gone in two to three years. At the end of 15 years, 0.2% remained. The typical half-life for lindane was 400 days. Lindane can be washed off and into the soil, especially when humus content is low (5).

The pesticide has been found in a significant number of groundwater samples in New Jersey, California, Mississippi, South Carolina, and in Italy at very low concentrations (maximum concentration of 0.9 ppb in New Jersey) (8). Lindane is a contaminant in water in the Great Lakes at very low concentrations as well.

Lindane is very stable in both fresh and salt water environments. It will disappear from the water by secondary mechanisms such as adsorption on sediment, biological breakdown by microflora and fauna, and adsorption by fish through gills, skin and food (5). Storage in body fat is directly proportional to concentration in feed.

Plants pick up residues from not only direct application, but through water and vapor phases. While crops such as cauliflower and spinach had less than 0.1 ppm when grown in soil with residues of 0.1 to 0.5 ppm, carrots may accumulate high, persistent concentrations (5). Persistence is seen when plants are rich in lipid content. The half-life in lettuce was three to four days. The metabolism in plants is not well understood, but carrots were estimated to metabolize lindane at a rate of 43 to 47% after eight to ten weeks, based on the uptake by the plant.

Exposure Guidelines:

NOEL (rat): 0.33 mg/kg/day, based on multiple effects

Drinking Water: 4 ug/l (ppb) (EPA); 3 ug/l (ppb) (WHO)

HA: 0.0002 mg/l lifetime

TLV-TWA: 0.5 mg/m3

TLV STEL: 1.5 mg/m3

ADI: 0.008 mg/kg/day (WHO)

RfD: 0.0003 mg/kg/day (EPA)

LEL: 1.55 mg/kg/day

Physical Properties:

CAS #: 58-89-9

Chemical name: gamma-1,2,3,4,5,6-hexachlorocyclohexane

Chemical class/use: organochlorine insecticide

Solubility in water: 7 mg/l

Solubility in other solvents: >5 g/100g in acetone, benzene, ethanol and ethyl acetate

Melting Point: 112.5 degrees C

Vapor Pressure: 3.3 x 10 to the minus 5 power mm Hg

Partition Coefficient: 3.61-3.72 (log octanol/water)

BASIC MANUFACTURER

Drexel Chemical Company
PO Box 9306
2487 Pennsylvania St.
Memphis, Tn 38109
Telephone: 901/774-4370

Review by Basic Manufacturer:

Comments solicited: October, 1992
Comments received:

REFERENCES

(1) U.S. Department of Health and Human Services (1985). Fourth Annual report on Carcinogens, Summary 1985, Public Health Service, NTP 85-002

(2) Johnson, W.W. and M.T. Finley (1980). Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. U.S.

Department of Interior, Fish and Wildlife Service, Resource Publication 137.

(3) National Library of Medicine (1992). Hazardous Substances Databank. TOXNET, Medlars Management Section, Bethesda, MD.

(4) U. S. Environmental Protection Agency (1987). Health Advisory, Office of Drinking Water.

(5) Ulman, E. (1972). Lindane, Monograph of an Insecticide, Verlag K. Schillinger, Federal Republic of Germany.

(6) Menzie, Calvin M. (1980). Metabolism of Pesticides, Update III. U. S. Dept of the Interior, Fish and Wildlife Service, Special Scientific Report, Wildlife No. 232.

(7) Smith, Andrew G. (1991). Chlorinated Hydrocarbon Insecticides. in Handbook of Pesticide Toxicology, Volume 3, Classes of Pesticides. Wayland J. Hayes Jr. and Edward R. Laws, Jr. editors. Academic Press, Inc., NY.

(8) Howard, Philip H. (1991). Handbook of Environmental Fate and Exposure Data for Organic Chemicals. Volume III, Pesticides. Lewis Publishers, Chelsea, MI.

(9) Briggs, Shirley A. 1992. Basic Guide to Pesticides: Their characteristics and hazards. Hemisphere publishing Corp., Washington, DC.

(10) ACGIH. 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices. American Conference of Governmental and Industrial Hygienists. Cincinnati, OH.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall, Ithaca, N.Y. 14853-0901.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices at Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 9/93.

EXTOXNET primary files maintained and archived at Oregon State University.

PENTACHLOROPHENOL

TRADE OR OTHER NAMES

Pentachlorophenol is abbreviated as PCP. Product names include Dowicide EC-7, Penchlorol, Penta, Pentacon, Penwar, Priltox, Sinituho and Weedone.

INTRODUCTION

Pentachlorophenol (PCP) is a chlorinated hydrocarbon insecticide and fungicide. It is used primarily to protect timber from fungal rot and wood-boring insects. PCP products are very toxic to plants and are used as preharvest defoliants and general herbicides. Their use as herbicides is currently restricted to nonagricultural uses along drainage ditches, driveways, and fencerows.

The results described in this profile are mostly from studies that were conducted using technical-grade PCP, because it is technical-grade PCP that people are exposed to when they use commercial PCP products.

Commercial (technical) grades of PCP commonly contain manufacturing by-products, such as dioxin (HxCDD), which can be more toxic than the PCP itself. Another contaminant in PCP is HCB (Hexachlorobenzene). The use of PCP is being phased out because of the discovery of these highly toxic contaminants (9). PCP is a Restricted Use Pesticide (RUP). Restricted Use Pesticides may be purchased and used only by certified applicators.

In 1988 the EPA announced further restrictions on the use of PCP as in the pulp and paper industry where it is used in paper coatings, sizing, adhesives and in inks. Registration for use in cooling towers and for certain oil well operations was also cancelled. The 1988 regulations also required compliance with dioxin (HxCDD) concentration limits in the final product.

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

PCP is a very toxic compound, and is labeled with a DANGER signal word. The exact dose required to produce illness in humans is not known. Skin penetration is the most dangerous route of exposure, but inhalation or ingestion of PCP may also cause toxicity. There are about 50 known cases of poisoning from PCP containing herbicides, molluscicides or wood preservatives, 30 of which have resulted in death. Immersion of a man's hand in a 0.4 percent PCP solution for 10 minutes caused pain and inflammation.

Acute exposure to PCP can cause elevated temperature,

profuse sweating, dehydration, loss of appetite, decreased body weight, nausea, uncoordinated movement and coma. Some of the symptoms may be due to the impurities in the formulation rather than the pentachlorophenol itself (9).

The oral LD50 of PCP for rats is 25-200 mg/kg, depending on the product quality. The oral LD50 for mice and rabbits is 130 mg/kg (6).

The dermal LD50 is 105 mg/kg for rabbits, 96-320 mg/kg for rats, and 261 mg/kg for mice (6). Acute dermal exposure of dogs, rabbits, rat, and guinea pigs to high doses of PCP causes dry wrinkled skin and loss of hair from topically treated areas, high blood pressure and fevor, motor weakness, rapid digestion, and extensive damage to the cardiovascular system.

The inhalation LD50 for rats is between about 10 and 225 mg/kg, and the mouse inhalation LD50 is 355 mg/kg (6).

CHRONIC TOXICITY

Animal experiments suggest that chronic exposure to pure pentachlorophenol may affect reproduction, induce birth defects, and cause acne and other skin diseases.

In humans, the most common exposure to PCP is inhalation in the workplace. Abdominal pain, nausea, fever, and respiratory irritation result from PCP exposure (6). Inhalation of PCP at occupational levels causes eye, skin, and throat irritation, while high levels may affect the circulatory system and cause heart failure. Survivors of toxic exposures may suffer visual and central nervous system damage. Persons regularly exposed to PCP tend to tolerate higher levels of PCP vapors than persons having little contact with these vapors.

Reproductive and Teratogenic Effects

PCP has adverse effects on reproduction in rats when administered orally during pregnancy at very high doses, near lethal levels. Embryo death increased in rats fed high levels of PCP during the sensitive period of pregnancy (6). In hamsters, oral administration of low doses of PCP during the sensitive period of pregnancy caused fetal deaths, and PCP was found in the blood and fat of the fetuses (6). No developmental effects were observed in rats fed high doses of PCP. While PCP is clearly toxic to the developing fetus it does not appear to cause any birth defects.

Prolonged exposure to PCP by humans may result in adverse reproductive effects that are associated with changes in the endocrine gland function and other changes in the body (immunological dysfunction). A number of women with histories of spontaneous abortion, unexplained infertility and menstrual disorders had elevated levels of pentachlorophenol and/or lindane in their blood (11). While this evidence suggests some relationship between reproductive problems and PCP and/or lindane, it does not prove that PCP or lindane were the direct cause of the problems (11).

Mutagenic Effects

Mutagenic effects have not been clearly demonstrated for PCP in laboratory test systems (6). At the most, PCP should be classified as weakly mutagenic. There is no evidence from epidemiological studies of occupationally exposed workers that PCP causes mutations.

Carcinogenic Effects

Clear evidence links PCP exposure with carcinogenic activity in test mice. Limited evidence links PCP with carcinogenicity in humans. One study links PCP with Hodgkin's disease on the basis of a single family's case history and with the occurrence of the disease in carpentry and lumber workers in the United Kingdom (7). The World Health Organization publication cautions against the any conclusions based on such limited data.

Organ Toxicity

The major targets of toxicity of PCP are the liver, kidneys and central nervous system, with toxic effects occurring at low doses. In both rats and monkeys, the liver and kidneys concentrated PCP the most. Immunotoxicity occurred in animals exposed to PCP, but not to those exposed to pure PCP, suggesting the effects were due to impurities. Pure PCP has little effect on the livers of rats. Doses of PCP produced greater liver effects than doses of pure PCP which were 25 times greater (2).

In two-year studies of rats fed high doses of PCP, life spans were not changed, but liver and kidney changes were observed (6).

PCP causes lung, liver, kidney damage and contact dermatitis in humans. Extended periods of exposure to PCP results in persistent chloracne and damage to the nervous system. About two dozen fatalities due to accidental exposure to PCP in industry have been reported. Autopsies revealed changes in the brain, heart, kidneys, lungs, and liver.

Fate in Humans and Animals

PCP is rapidly absorbed through the gastrointestinal tract following ingestion. If deposition in the tissues occurs, the major sites are the liver, kidneys, plasma protein, brain, spleen and fat; but accumulation is not common. Unless kidney and liver functions are impaired, PCP is rapidly eliminated from blood and tissues, and is excreted unchanged via the urine. Single doses of PCP have half-lives in blood of 15 hours in rats, 78 hours in monkeys, and 30-50 hours in humans (2).

ECOLOGICAL EFFECTS

PCP is acutely and chronically highly toxic to cold and warm water fish and moderately toxic to other freshwater and marine organisms. PCP concentrations detected in rivers, streams, or surface water systems, up to now, are below lethal levels. Lethal levels have been exceeded only during accidental spills.

Most wood treated with PCP solutions will "bleed." Bleeding refers to the movement of PCP solution from the interior to the surface of the wood. Whereas pure PCP can evaporate from the surface of the wood into the air, the impurities in the solutions may not. Because of its popular use as a wood preservative, the public could be exposed to low levels of PCP in outdoor wood structures of many kinds.

Cattle and other farm animals have ingested PCP by chewing and licking outdoor wood structures, or from being housed in wooden pens that were treated with PCP solutions. This has caused sickness and death in some of these animals. In late 1976, about 100 Michigan dairy farms had herd health problems due to contact with PCP-treated wood. However, pure PCP or contaminants were detected in the milk of only two herds.

Pure PCP is absorbed by aquatic organisms. Once absorbed by fish, pure PCP is rapidly excreted as is its metabolite, with a biological half-life of only 10 hours. Bioaccumulation may be significant. Several species of fish, invertebrates and algae

have had levels of PCP that were significantly higher (up to 10,000 times) than the concentration in the surrounding waters (11). Biomagnification, that is the concentration of a compound as it passes up the food chain, has not been observed and is not expected to be an important source of exposure because PCP breaks down rapidly in living organisms (11).

ENVIRONMENTAL FATE

PCP is strongly toxic to plants. Its uses as a pre-harvest defoliant and desiccant on such crops as alfalfa and clover illustrate its toxicity to green plants. Lettuce grown on soil containing PCP contained low levels of PCP residues.

After reaching soil, PCP is broken down by sunlight and bacteria (11), and can leave the upper soil layer by evaporation and leaching into groundwater. PCP degrades most rapidly in flooded or anaerobic (airless) soils. The degradation rate increases at higher temperatures and in the presence of organic matter in the soil. The half-life for bacterial degradation ranges from 15 to 48 days, in anaerobic and aerobic laboratory conditions respectively.

PCP is used in wood products that come in contact with water. PCP has been detected at very low levels in rivers and streams (0.01-16 ppb), surface water systems (1.3-12 ppb), and seawater (0.02-11 ppt) (3). The compound has also been found in ground water in California, Oregon and Minnesota at very low concentrations ranging from 0.06 ppt to 0.64 ppb (10). It has been detected in well water in Japan and in Canada also.

Once released into water, PCP may be degraded by sunlight or microorganisms or bind to sediments and suspended particles in water (3). It does not evaporate to a significant degree. In water, biodegradation occurs with a half-life ranging from hours to days. Most biodegradation occurs at the surface. PCP levels measured in the air of two towns were up to 0.93 and 7.8 ppt (7).

PHYSICAL PROPERTIES AND GUIDELINES

Pentachlorophenol is a chlorinated organic compound, a solid which varies in color from white to dark grayish brown, depending on the purity of the compound. The solid beads or flakes have a distinctive odor. This chemical is non-corrosive in the pure state, but degrades rubber when in oil solution.

Exposure Guidelines:

NOEL: 1 mg/kg/day (rat)

ADI: 0.003 mg/l

TOL: 857 mg/l (30 degrees C)

TLV: air

TWA: 0.5 mg/m3 (skin)

STEL: 1.5 mg/m3 (skin)

Drinking water health advisory:
Drinking Water Equivalent Level: 1/05 mg/L (8)

RfD: 0.003 mg/l (EPA)

Physical Properties:

CAS #: 87-86-5

Solubility in water: 0.0014 g/100g (20 degrees C) 0.0018g/100g (25 degrees C); 20 ppm (30 degrees C)

Solubility in solvents: PCP is soluble in acetone, alcohols, ether, and hot benzene; it is slightly soluble in petroleum ether, carbon tetrachloride, and paraffins.

Melting point: 191 degrees C, anhydrous (2)

Boiling point: 309-310 degrees C

Vapor pressure: 1.7 x 10 to the minus 4 torr (20 degrees C)

log P: -3.77

Kow: 4900-141,300 (1,3)

log Kow: 5.15 (4)

Koc: 3-4000

Kd: 1.82 x 10 to the minus 5

BCF: 273-4760 (calculated) (4)

H: 3.2 torr/M

BASIC MANUFACTURER

Chapman Chemical
PO Box 9158
416 E. Brooks Rd.
Memphis, Tennessee 38109
Telephone 901-396-5151
Emergency 901-396-5151

Review by Basic Manufacturer:
Comments solicited: December, 1991
Comments received:

REFERENCES

(1) Figge, K., J. Klahn and J. Koch. 1986. Ecotoxicol. Environ. Safety 11: 320-338.

(2) Mercier, M. 1981. Organochlorine pesticides. p. 170. Pergamon Press.

(3) Murray, H.E., L.E. Ray and C.S. Giam. 1981. Chemosphere 10: 1327-34.

(4) Saarikoski, J., R. Lindstrom, M. Tyynela and M. Viluskela. 1986. Ecotoxicol. Environ. Safety 11: 158-173.

(5) Spacie, A. and J.L. Hamelink. 1982. Environ. Toxicol. Chem. 1: 309-320.

(6) Wagner, Sheldon L. 1983. Clinical Toxicology of Agricultural Chemicals. Noyes Data Corporation.

(7) IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Human. 1979. Vol 20: 303-325.

(8) U.S. Environmental Protection Agency. Office of Drinking Water. Pentachlorophenol Health Advisory. Draft Report. March 1987.

(9) Ecobichon, Donald J. 1991. Toxic Effects of Pesticides. in Casarett and Doull's Toxicology. The Basic Science of

Poisons. Third Edition. Curtis D. Klaassen, Mary O. Amdur, and John Doull editors. Macmillan Publishing Company, NY.

(10) Howard, Philip H. (1991) Handbook of Environmental Fate and exposure Data for Organic Chemicals. Volume III. Pesticides. Lewis Publishers, Chelsea, MI.

(11) U.S. Dept. of Health and Human Services. 1992. Toxicological Profile for Pentachlorophenol. Agency for Toxic Substance and Disease Registry. Draft.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall, Ithaca, N.Y. 14853-0901.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices at Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 3/94

EXTOXNET primary files maintained and archived at Oregon State University.

PYRETHRINS

TRADE OR OTHER NAMES

Several trade names associated with these compounds are Buhach, Chrysanthemum Cinerariaefolium, Ofirmotox, Insect Powder, Dalmation Insect Flowers, Firmotox, Parexan and NA 9184.

INTRODUCTION

Pyrethrins are natural insecticides produced by certain species of the chrysanthemum plant. The flowers of the plant are harvested shortly after blooming and are either dried and powdered or the oils within the flowers are extracted with solvents. The resulting pyrethrin containing dusts and extracts usually have an active ingredient content of about 30%. These active insecticidal components are collectively known as pyrethrins. Two pyrethrins are most prominent, pyrethrin-I and pyrethrin-II. The pyrethrins have another four different active ingredients, Cinerin I and II and Jasmolin I and II. Pyrethrin compounds have been used primarily to control human lice, mosquitoes, cockroaches, beetles and flies. Some "pyrethrin dusts," used to control insects in horticultural crops, are only 0.3% to 0.5% pyrethrins, and are used at rates of up to 50 lb/A. Other pyrethrin compounds may be used in grain storage and in poultry pens and on dogs and cats to control lice and fleas.

The natural pyrethrins are contact poisons which quickly penetrate the nerve system of the insect. A few minutes after application, the insect cannot move or fly away. But, a "knockdown dose" does not mean a killing dose. The natural pyrethrins are swiftly detoxified by enzymes in the insect. Thus, some pests will recover. To delay the enzyme action so a lethal dose is assured, organophosphates, carbamates, or synergists may be added to the pyrethrins.

Semisynthetic derivatives of the chrysanthemumic acids have been developed as insecticides. These are called pyrethroids and tend to be more effective than natural pyrethrins while they are less toxic to mammals. One common synthetic pyrethroid is allethrin.

In this report, the term "pyrethrins" refers to the natural insecticides derived from chrysanthemum flowers; "pyrethroids" are the synthetic chemicals, and "pyrethrum" is a general name covering both compounds. The EPA classifies pyrethrin-I as a Restricted Use Pesticide (RUP). Restricted Use Pesticides may be purchased and used only by certified applicators.

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Synthetic pyrethroid compounds vary in their toxicity as do

the natural pyrethrins. Pyrethrum carries the signal word CAUTION. Inhaling high levels of pyrethrum may bring about asthmatic breathing, sneezing, nasal stuffiness, headache, nausea, incoordination, tremors, convulsions, facial flushing and swelling, and burning and itching sensations (5). The most severe poisonings have been reported in infants, who are not able to efficiently break down pyrethrum. The lowest lethal oral dose of pyrethrum is 750 mg/kg for children and 1,000 mg/kg for adults (5). Oral LD50 values of pyrethrins in rats range from 200 mg/kg to greater than 2,600 mg/kg (4). Some of this variability is due to the variety of constituents in the formulation. Mice have a pyrethrum oral LD50 of 370 mg/kg (5). Animals exposed to toxic amounts may experience tongue and lip numbness, nausea, and diarrhea. Symptoms may also include incoordination, tremors, convulsions, paralysis, respiratory failure, and death.

Pyrethroids can cause two quite different responses at near lethal doses in rats; aggressive sparring and a sensitivity to external stimuli progressing to tremors is the one response and pawing and burrowing behavior, and salivation leading to chronic seizures is the other (8). Human response to these two different types of pyrethroids has not yet been evaluated. Recovery from serious poisoning in mammals is fairly rapid.

Rats and rabbits are not affected by large dermal applications (4, 5). On broken skin, pyrethrum produces irritation and sensitization, which is further aggravated by sun exposure.

CHRONIC TOXICITY

Absorption of pyrethrum through the stomach and intestines and through the skin is slow. However, humans can absorb pyrethrum more quickly through the lungs during respiration. Response appears to depend on the pyrethrum compound used. Overall, pyrethrins and pyrethroids are of low chronic toxicity to humans and the most common problems in humans have resulted from the allergenic properties of pyrethrum (7). Patch tests for allergic reaction are an important tool in determining an individuals sensitivity to these compounds.

Many of the natural and synthetic compounds can produce skin irritation, itching, pricking sensations and local burning sensations. These symptoms may last for about two days (8).

Reproductive Effects

Rabbits that received pyrethrins orally at high doses during the sensitive period of pregnancy had normal litters. A group of rats fed very high levels of pyrethrins daily for three weeks before first mating had litters with weanling weights much lower than normal (4). Overall, pyrethrins appear to have low reproductive toxicity.

Teratogenic Effects

The one rabbit reproduction study performed showed no effect of pyrethrins on development of the offspring (3). More information is needed.

Mutagenic Effects

No information was found.

Carcinogenic Effects

No carcinogenic status has been established for pyrethrins or pyrethroids.

Organ Toxicity

In mammals, tissue storage has not been recorded. At high doses, pyrethrum can be damaging to the central nervous system and the immune system. When the immune system is attacked by pyrethrum, allergies can be worsened.

Animals fed large doses of pyrethrins may experience liver damage. Rats fed pyrethrin at high levels for two years showed no significant effect on survival, but slight, definite damage to the livers was observed (4). Inhalation of high doses of pyrethrum for 30 minutes each day for 31 days caused slight lung irritation in rats and dogs (5).

Fate in Humans and Animals

Pyrethrins, pyrethroids, and their metabolites are not known to be stored in the body nor excreted in the milk (2). The urine and feces of people given oral doses of pyrethrum contain chrysanthemumic acid and other metabolites (2, 4). These metabolites are less toxic to mammals than are the parent compounds (3). Pyrethrins I and II are excreted unchanged in the feces (2). Other pyrethrum components undergo rapid destruction and detoxification in the liver and gastrointestinal tract (4).

ECOLOGICAL EFFECTS

Pyrethrin is extremely toxic to aquatic life, such as bluegill and lake trout while it is slightly toxic to bird species, such as mallards. Toxicity increases with higher water temperatures and acidity. Natural pyrethrins are highly fat soluble, but are easily degraded and thus do not accumulate in the body. These compounds are toxic to bees also.

Because pyrethrin-I, pyrethrin-II, and allethrin have multiple sites in their structures that can be readily attacked in biological systems, it is unlikely that they will concentrate in the food chain (2).

ENVIRONMENTAL FATE

Two pyrethroid synthetic insecticides, permethrin and cypermethrin, break down in plants to produce a variety of products (6). Pyrethrins have little residual effect. In stored grain, 50% or more of the applied pyrethrins disappear during the first three or four months of storage. At least 80% of what remains is removed by handling, processing, and cooking (3).

Pyrethrins alone provide limited crop protection because they are not stable. As a result, they are often combined with small amounts of antioxidants to prolong their effectiveness. Pyrethrum compounds are broken down in water to nontoxic products.

Pyrethrins are inactivated and decomposed by exposure to light and air. Pyrethrins are also rapidly decomposed by mild acids and alkalis. Stored pyrethrin powders lose about 20% of their potency in one year.

As the pyrethrins are purified, their stability decreases; thus, pure pyrethrin-I and pyrethrin-II are the least stable of the pyrethrins (4). Purified pyrethrins are very expensive and are only available for laboratory uses.

PHYSICAL PROPERTIES AND GUIDELINES

The pyrethrins are viscous brown resins, liquids, or solids which inactivate readily in air. Due to differences in the types and amounts of esters in the pyrethrum mixture, its molecular

weight ranges from 316 to 374.

Exposure Guidelines:

NOEL: 10 mg/kg bw/day (rats) (3)

ADI: 0.04 mg/kg body weight (humans) (3)

PEL: 5 mg/m3

TLV-TWA: 5 mg/m3

STEL: 10 mg/m3

Physical Properties:

CAS #: 8003347

Solubility in water: considered to be insoluble in water.

Solubility in solvents: soluble in organic solvents like: alcohol, kerosene, nitromethane, petroleum ether, carbon tetrachloride, and ethylene dichloride.

Boiling point: for pyrethrin I: 146-150 degrees C (1); for pyrethrin II: 192-193 degrees C (1)

Vapor pressure: about 0 mm/Hg

BASIC MANUFACTURER

There are several manufacturers of products in this category.

REFERENCES

(1) Windholz, M., et al., eds. 1983. The Merck Index. 10th ed. Merck & Co., Inc.

(2) Elliot, M; Janes, N.F. Kimmel, E.C.; and Casida, J.E. 1972. Metabolic Fate of Pyrethrin I, Pyrethrin II, and Allethrin Administered Orally to Rats. J. Agr. Food Chem. 20: 300-312.

(3) Vettorazzi, G. 1979. International Regulatory Aspects for Pesticide Chemicals. pp.89-90. CRC Press.

(4) Hayes, Jr., W.J. 1982. pp. 75-81. Pesticides Studied in Man. Williams & Wilkins.

(5) Occupational Health Services, Inc. "Pyrethrum." Material Safety Data Sheet. 1 April 1987. New York: OHS, Inc.

(6) Roberts, T.R. and A.N. Wright. 1981. The metabolism of a pyrethroid metabolite, in plants. Pest. Sci. 12:161.

(7) Ecobichon, Donald J. 1991. Toxic Effects of Pesticides. In Casarett and Doull's Toxicology, The Basic Science of Poisons, Third Edition. Curtis D. Klaassen, Mary O. Amdur, and John Doull editors. Macmillan Publishing Company, NY.

(8) Aldridge, W.N. 1990. An assessment of the Toxicological Properties of Pyrethroids and their Neurotoxicity. Toxicology, Vol 21, Number 2. pp. 89-104.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall, Ithaca, N.Y. 14853-0901.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

E X T O X N E T
EXTENSION TOXICOLOGY NETWORK

A Pesticide Information Project of Cooperative Extension Offices at Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Revised 9/95.

EXTOXNET primary files maintained and archived at Oregon State University.

WARFARIN

TRADE OR OTHER NAMES

The active ingredient warfarin is found in a variety of commercial rodenticides. Some trade names for products containing warfarin include Cov-R-Tox, Co-Rax, d-Con, Dethmor, Mar-Fin, Rattunal, Rax, Rodex, Rodex Blox, Rosex, Solfarin, Tox-Hid, Warf, and Warfarat (3, 4, 11). Warfarin is called coumafene in France, zoocoumarin in the Netherlands and Russia, and coumarin in Japan (1, 3, 8).

REGULATORY STATUS

Warfarin is a general use pesticide (GUP). Check with specific state regulations for local restrictions which may apply. The Signal Word for technical and high concentrations of warfarin is "Danger". The Signal Word "Caution" is used for low concentrations and ready-to-use baits (3).

INTRODUCTION

Warfarin was the first anticoagulant rodenticide introduced and was first registered for use in the United States in 1952 (4, 13). Warfarin is used for controlling rats and house mice in and around homes, animal and agricultural premises, and commercial and industrial sites. It is odorless and tasteless and effective in very low dosages. Action is not rapid; usually about a week is required before a marked reduction in the rodent population is noticeable. Rodents do not tend to become bait-shy after once tasting warfarin; they continue to consume it until its anti-clotting properties have produced death through internal hemorrhaging. The prothrombin content of the blood is reduced and internal bleeding is induced. Repeated ingestion is needed to produce toxic symptoms. This rodenticide can be used year-after-year wherever a rodent problem exists. Mice are harder to control than rats, and complete control may take a longer period. Recently, resistant strains of rats and mice are developing (3, 4, 11, 13).

Warfarin comes in water soluble, ready-to-use bait, concentrate, powder, liquid concentrate, nylon pouch, coated talc and dust formulations. The compound also comes in mixed formulations with pindone, calciferol, and sulphaquinoxaline. It is considered compatible with other rodenticides (1, 2, 3).

Warfarin is only slightly dangerous to humans and domestic animals when used as directed, but care must be taken with young pigs, which are especially susceptible (1).

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

The amount of Warfarin that is lethal to one-half (50%) of experimental animals fed the material is referred to as its acute oral lethal dose fifty, or LD50. The acute oral toxicity for warfarin in rats is variously reported to be 3 mg/kg (3, 4, 6, 7, 11, 12); 1,600 ug/kg (5); 186 mg/kg (Hartley and Kidd, 1987) (7, 11); 58 mg/kg in female rats (9, 12). The acute oral LD50 for rats over 4-5 days is 1 mg/kg/day (1, 2). There was no development of ingestion tolerance indicated regardless of rodent sex or age (3).

The acute oral LD50 for technical sodium warfarin in rats was 323 mg/kg for males and 58 mg/kg for females (12). A single, large dose of warfarin is about as toxic as a single, small dose. On a multiple-dose basis, the reported LD100 for rats is 0.2 mg/kg/day for 5 days (4, 11).

The dermal LD50 for rats was 1,400 mg/kg; 420 mg/kg intraperitoneal LDlo (Lethal Dose, Low. The lowest dose which causes death in test animals.); and 320 mg/m3 inhalation LC50 (5). The same source indicated the acute oral LD50 for mice was 60 mg/kg; 800 mg/kg subcutaneous LDlo; and 165 mg/kg intravenous LD50 (5).

Toxicity values for warfarin in other animals are: an oral LD50 for cats of 2.5-20 mg/kg (6, 12); an acute oral LD50 of 35 mg/kg for a single dose or 3 mg/day for 5 days (1, 2); and 12 mg/kg oral LDlo (5). The acute oral LD50 for dogs exposed to warfarin was 3 mg/kg/day for 5 days (1). Technical sodium warfarin in dogs had an LD50 of 200-300 mg/kg (12). The acute oral LD50 for warfarin in cattle was 200 mg/kg/day for 5 days (1). The LD50 for technical sodium warfarin in guinea pigs was 182 mg/kg (12). The oral LDlo for warfarin in pigs was reported to be 1,200 ug/kg (5). Death followed 5 daily doses of 1 mg/kg for pigs (2, 11).

Studies done on rabbits indicated the dermal LD50 of warfarin to be greater than 8 g/kg (6, 12). Technical sodium warfarin in rabbits had an LD50 of 800 mg/kg. Rabbits exhibited mild to slight conjunctival irritation in response to technical warfarin (12).

Toxicity values for humans exposed to warfarin indicated an oral-woman TDlo of 15 mg/kg/21 weeks intermittent; 10,200 ug/kg oral-man TDlo; and 6,667 mg/kg oral-human LDlo. Average or large doses of warfarin in humans may cause hemorrhage (9). Warfarin is not known to be an eye irritant. It has produced hemorrhages in the retina, however, through its systemic toxicity (11). The compound is considered highly toxic by inhalation and ingestion and moderately toxic by dermal absorption. A dose of warfarin at 200 mg/m3 is considered highly toxic and immediately dangerous to life or health (5).

CHRONIC TOXICITY

A farmer whose hands were intermittently wetted with a 0.5% solution of warfarin over a period of 24 days developed gross hematuria two days after the last contact with the solution; the following day, spontaneous hematomas appeared on the arms and legs. Within four days, there were also epistaxis, punctate hemorrhages of the palate and mouth, and bleeding from the lower lip. The bleeding time was over 30 minutes; the clotting time was 11 minutes and 30 seconds; the prothrombin index was 17; and the prothrombin percentage (thrombotest) was 5. Four days later, after treatment for two days with phytonadione, the values were in the normal range (11).

Another source indicated that two human fatalities occurred after ingesting 0.25% warfarin on corn meal over 15 days (12).

Reproductive Effects

No information currently available.

Teratogenic Effects

Warfarin has been established as a human teratogen, because it causes birth defects in the offspring of women receiving clinical doses of the compound during any trimester of pregnancy. Therapeutic use by pregnant women has resulted in fatal hemorrhaging of the fetus and malformations and mental retardation in infants. However, the amount of warfarin contained in the rodenticide bait is very low. A single ingestion of warfarin-treated bait by an adult female would not be likely to cause teratogenic effects (5, 13, 12).

Other studies also indicated fetal abnormalities in humans exposed to clinical sodium warfarin (12).

Mutagenic Effects

No information currently available.

Carcinogenic Effects

No information currently available.

Organ Toxicity

Warfarin causes organ damage by inhibiting blood coagulation (1). Absorption by the lungs may result in hemorrhagic effects (5).

Animals killed by warfarin exhibit extreme pallor of the skin, muscles, and all the viscera. In addition, evidence of hemorrhage may be found in any part of the body but usually only in one location in a single autopsy. Such blood as remains in the heart and vessels is grossly thin and forms a poor clot or no clot (8, 10). Rats injected intraperitoneally with 14C-warfarin excreted approximately 90% of the activity in 14 days, about half in the urine and half in the feces (8).

Symptoms of human exposure to warfarin include hematuria, back pain, hematoma in arms and legs, bleeding lips, mucous membrane hemorrhage, abdominal pain, vomiting, and fecal blood.

One source stated that serious illness was induced by the ingestion of 1.7 mg of warfarin/kg/day for 6 consecutive days with suicidal intent. This would correspond to eating almost 1 pound of bait (0.025% warfarin) each day for 6 days. All signs and symptoms were caused by hemorrhage and, following multiple transfusions and massive doses of vitamin K, recovery was complete (10).

Fate in Humans and Animals

When 9 normal men and 5 normal women were given a single oral dose of 1.5 mg/kg warfarin, maximal concentration in plasma was reached in 2 to 12 hours. Maximal depression of prothrombin activity was between 36 and 72 hours. Their individual increases in prothrombin time were proportional to their half-times for disappearance of the warfarin from plasma. In other words, the pharmacological effect was greatest in those with slower excretion. The half-times for disappearance from the plasma varied from 15 to 58 hours with an average of 42 hours. Absorption of warfarin from the gastrointestinal tract was apparently complete; no warfarin was found in the stool even after massive doses, and plasma levels and prothrombin activity

responses were virtually identical following oral and intravenous administration at the same rates (8).

Warfarin is readily absorbed by the gastrointestinal tract; absorption in man requires about 3 hours as indicated by a comparison of the rate of action of oral and intravenous doses (10).

Another study indicated that 96 hours after intraperitoneal injection of warfarin, the concentrations of activity in the kidney, liver, and pancreas were 3, 12, and 15 times, respectively, greater than that in the blood (8).

Metabolites in animals include 4-, 6-, 7- and 8-hydroxycoumarin (1, 8).

ECOLOGICAL EFFECTS

Effects on Birds

The acute avian toxicity of warfarin indicates that it is practically non-toxic to game birds. In subacute studies, warfarin ranged from moderately toxic to practically non-toxic to upland game birds and waterfowl (13). Another source indicated that an acute oral mallard duck study was performed with a 10% formulation of warfarin. This formulation of warfarin was considered moderately toxic to mallard ducks (LC50 greater than 120 mg/kg) when administered as a single dose. However, when exposed to 60 mg/kg for a period of 14 days, 4 out of 5 ducks died (12).

Chickens are relatively resistant to warfarin (4).

Effects on Aquatic Organisms

The toxicity of warfarin to aquatic organisms is felt to be of low potential due to the fact that warfarin is insoluble in water. A long field experience shows no potential hazards to aquatic organisms (13).

A 96-hour rainbow trout study was performed using a 0.54% formulation of warfarin sodium salt. With a 96-hour LC50 of greater than 10,000 ppm, this formulation is considered non-toxic to rainbow trout (12).Effects on Other Animals (Nontarget species)

Warfarin used as a prepared bait (0.13%) is considered non-toxic to bees when used as prescribed (1, 3).

The use of warfarin as a hand-placed bait limits the potential for any secondary exposure of nontarget animals. However, because of its high degree of mammalian toxicity and its use patterns, warfarin could adversely affect endangered or threatened species (13). One study exists on a 50/50 percent formulation of warfarin-sulfaquinoxaline technical. The warfarin-sulfaquinoxaline caused secondary poisoning in mammalian carnivores such as mink and dogs when ingesting prey killed after they were provided with treated bait (carrots containing 0.025% by weight of the test material). The first death occurred after 8 days of continuous exposure to treated nutria (12).

A study by Bucklew et al. investigated the short-term influence of warfarin on the growth of the gram-positive spore-forming soil microorganism, Bacillus megaterium. Impregnation of paper disks and subsequent measurement of the zones of growth inhibition showed that spore germination for this bacterium was not affected by the presence of warfarin for 15-21 hours at 21 degrees C and at concentrations as high as 1 mg/ml (about 1,000 ppm) (12).

ENVIRONMENTAL FATE

Breakdown of Chemical in Soil and Groundwater

No information currently available.

Breakdown of Chemical in Surface Water

No information currently available.

PHYSICAL PROPERTIES AND GUIDELINES

Exposure Guidelines:

TLV-TWA: 0.1 mg/m3 (OSHA) (3, 7, 11)

STEL: 0.3 mg/m3 (11)

Physical Properties:

CAS No.: 81-81-2

Chemical name: 4-hydroxy-3-(3-oxo-1-phenylbutyl)coumarin; 4-hydroxy-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-2-one (1, 2)

Chemical Class/Use: Rodenticide, anticoagulant

Specific gravity: greater than 1 (5)

Solubility in water: Practically insoluble (1.7 mg/100 ml at 20 degrees C) (1, 5, 9)

Solubility in other solvents: Soluble to very slightly soluble in acetone, benzene, ethanol, ether, toluene, xylene, methyl ethyl ketone and cyclohexane. Moderately soluble in methanol, ethanol, and isopropanol. In acetone 6.5, chloroform 5.6, dioxane 10.0 (all in g/100 ml at 20 degrees C). Dissolves in aqueous alkalis with the formation of water-soluble salts (1, 2, 7, 8, 9)

Melting point: 161-162 degrees C (1, 7); 159-165 degrees C (3); 318-322 degrees F (5)

Boiling point: decomposes (7, 11)

Vapor pressure: 9 x 10 to the minus 2 mbar at 21.5 degrees C

Koc: 2.96 (calculated) (7)

Kow: 3.20 (calculated) (7)

BASIC MANUFACTURER:

SHACCO, Inc.
P. O. Box 7190
537 Atlas Avenue (53714)
Madison, WI 53707
Phone: 608-221-6200
Fax: 608-221-6208

Review by Basic Manufacturer:
Comments solicited: November, 1994
Comments received:

Prentiss, Inc.
CB 2000
Floral Park, NY 11001
Phone: 516-326-1919
Fax: 516-326-2312

Review by Basic Manufacturer:
Comments solicited: November, 1994
Comments received:

REFERENCES

(1) The Agrochemicals Handbook. 1983. The Royal Society of Chemistry, The University, Nottingham, England.

(2) Worthing, C. R. (ed.). 1983. The Pesticide Manual: A World Compendium. Seventh edition. Published by The British Crop Protection Council.

(3) Farm Chemicals Handbook. 1994. Meister Publishing Co. Willoughby, OH.

(4) Thomson, W.T. 1991. Agricultural Chemicals. Book III: Rodenticides. Thomson Publications, Fresno, CA.

(5) OHS Database. 1994. Occupational Health Services, Inc. 1994 (June) MSDS for Warfarin. OHS Inc., Secaucus, NJ.

(6) U.S. Environmental Protection Agency. 1989. Office of Pesticides. TOX Oneliners -- warfarin. July, 1989.

(7) Montgomery, J. H. 1993. Agrochemicals Desk Reference: Environmental Data. Lewis Publishers. Chelsea, MI.

(8) Hayes, W. J. Jr. 1982. Pesticides Studied in Man. Williams and Wilkins. Baltimore, MD.

(9) Windholz, M. (ed.) 1983. The Merck Index. Tenth edition. Rahway, NJ. Merck and Company.

(10) Hayes, W. J., Jr. 1963. Clinical Handbook on Economic Poisons: Emergency Information for Treating Poisoning. US Department of Health, Education, and Welfare, Public Health Service, Communicable Disease Center, Toxicology Section. Atlanta, Georgia.

(11) Pesticide Management and Education. An on-line pesticide information database in CENET, Cornell Cooperative Extension Network. Cornell University, Ithaca, NY.

(12) United States Environmental Protection Agency. August, 1981. Warfarin and Its Sodium Salt: Pesticide Registration Standard. USEPA, Office of Pesticides and Toxic Substances. Washington, DC. 193 pp.

(13) U.S. Environmental Protection Agency. June, 1991. R.E.D. Facts: Warfarin. USEPA, Office of Pesticides and Toxic Substances. Washington, DC.

This PIP is part of the EXTOXNET Pesticide Information Notebook. For more information, contact the Pesticide Management Education Program, Cornell University, 5123 Comstock Hall, Ithaca, NY 14853.

DISCLAIMER: The information in this profile does not in any way replace or supersede the information on the pesticide product label/ing or other regulatory requirements. Please refer to the pesticide product label/ing.

MATERIAL SAFETY DATA SHEET

LETHAL NERVE AGENT (GB) SARIN

SECTION I - GENERAL INFORMATION

DATE: 14 September 1988
REVISED: 28 February 1996

MANUFACTURER'S ADDRESS:

U.S. ARMY CHEMICAL BIOLOGICAL DEFENSE COMMAND
EDGEWOOD RESEARCH DEVELOPMENT, AND ENGINEERING CENTER (ERDEC)
ATTN: SCBRD-ODR-S
ABERDEEN PROVING GROUND, MD 20101-5423

Emergency telephone #' s: 0700-1630 EST: 410-671-4411/4414
After: 1630 EST: 410- 278-5201, Ask for Staff Duty Officer

CAS REGISTRY NUMBERS: 107-44-8, 50642-23-4

CHEMICAL NAME:

Isopropyl methylphosphonofluoridate

ALTERNATE CHEMICAL NAMES:

O-Isopropyl Methylphosphonofluoridate

Phosphonofluoridic acid, methyl-, isopropyl ester

Phosphonofluoridic acid, methyl-, 1-methylethyl ester

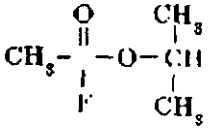
TRADE NAME AND SYNONYMS:

Isopropyl ester of methylphosphonofluoridic acid
Methylisopropoxfluorophosphine oxide
Isopropyl Methylfluorophosphonate
O-Isopropyl Methylisopropoxfluorophosphine oxide
Methylfluorophosphonic acid, isopropyl ester
Isopropoxymethylphosphonyl fluoride
Isopropyl methylfluorophosphate
Isopropoxymethylphosphoryl fluoride
GB
Sarin
Zarin

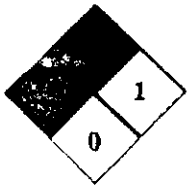
CHEMICAL FAMILY: Fluorinated organophosphorous compound

FORMULA/CHEMICAL STRUCTURE:

C4H10FO2P



NFPA 704 HAZARD SIGNAL:



Health - 4
Flammability - 1
Reactivity - 1
Special - 0

SECTION II - HAZARDOUS INGREDIENTS

INGREDIENTS NAME	FORMULA	PERCENTAGE BY WEIGHT	AIRBORNE EXPOSURE LIMIT (AEL)
GB	C4H10FO2P	100	0.0001 mg/m3

SECTION III - PHYSICAL DATA

BOILING POINT: 158 C (316 F)

VAPOR PRESSURE (mm Hg): 2.9 @ 25 C

VAPOR DENSITY (AIR=1): 4.86

SOLUBILITY: Miscible with water. Soluble in all organic solvents.

SPECIFIC GRAVITY (H2O=1): 1.0887 @ 25 C

FREEZING/MELTING POINT: -56 C

LIQUID DENSITY (g/cc):

1.0887 @ 25 C
1.102 @ 20 C

PERCENTAGE VOLATILE BY VOLUME:

22,000 m/m3 @ 25 C
16,090 m/m3 @ 20 C

APPEARANCE AND ODOR: Colorless liquid. Odorless in pure form.

SECTION IV - FIRE AND EXPLOSION DATA

FLASH POINT (METHOD USED): Did not flash to 280 F

FLAMMABLE LIMIT: Not applicable

LOWER EXPLOSIVE LIMIT: Not available

UPPER EXPLOSIVE LIMIT: Not available

EXTINGUISHING MEDIA: Water mist, fog, foam, CO2.

Avoid using extinguishing methods that will cause splashing or spreading of the GB.

SPECIAL FIRE FIGHTING PROCEDURES: GB will react with steam or water to produce toxic and corrosive vapors. All persons not engaged in extinguishing the fire should be evacuated. Fires involving GB should be contained to prevent contamination to uncontrolled areas. When responding to a fire alarm in buildings or areas containing agents, firefighting personnel should wear full firefighting protective clothing (without TAP clothing) during chemical agent firefighting and fire rescue operations. Respiratory protection is required. Positive pressure, full face piece, NIOSH-approved self-contained breathing apparatus (SCBA) will be worn where there is danger of oxygen deficiency and when directed by the fire chief or chemical accident/incident (CAI) operations officer. In cases where firefighters are responding to a chemical accident/incident for rescue/reconnaissance purposes, they will wear appropriate levels of protective clothing (**See Section VIII**).

Do not breathe fumes. Skin contact with nerve agents must be avoided at all times. Although the fire may destroy most of the agent, care must still be taken to assure the agent or contaminated liquids do not further contaminate other areas or sewers. Contact with the agent liquid or vapor can be fatal.

UNUSUAL FIRE AND EXPLOSION HAZARDS: Hydrogen may be present.

SECTION V - HEALTH HAZARD DATA

AIRBORNE EXPOSURE LIMITS (AEL): The permissible airborne exposure concentration for GB for an 8-hour workday or a 40-hour work week is an 8-hour time weighted average (TWA) of 0.0001 mg/m3. This value is based on the TWA of GB which can be found in "AR 40-8, Occupational Health Guidelines for the Evaluation and Control of Occupational Exposure to Nerve Agents GA, GB, GD, and VX." To date, the Occupational Safety and Health Administration (OSHA) has not promulgated a permissible exposure concentration for GB.

GB is not listed by the International Agency for Research on Cancer (IARC), American Conference of Governmental Industrial Hygienists (ACGIH), Occupational Safety and Health Administration (OSHA), or National Toxicology Program (NTP) as a carcinogen.

EFFECTS OF OVEREXPOSURE: GB is a lethal cholinesterase inhibitor. Doses that are potentially life threatening may be only slightly larger than those producing least effects.

GB

Route Dosage	Form	Effect	Type
ocular	vapor	ECt50	<2 mg-min/m3
inhalation	vapor	ECt50	<2 mg-min/m3
inhalation (15 l/min)	vapor	ICt50	35 mg-min/m3
inhalation	vapor	LCt50	70 mg-min/m3
percutaneous	liquid	LD50	1700 mg/70 kg man

Effective dosages for vapor are estimated for exposure durations of 2-10 minutes.

Symptoms of overexposure may occur within minutes or hours, depending upon dose. They include: miosis (constriction of pupils) and visual effects, headaches and pressure sensation, runny nose and nasal congestion, salivation, tightness in the chest, nausea, vomiting, giddiness, anxiety, difficulty in thinking and sleeping, nightmares, muscle twitches, tremors, weakness, abdominal cramps, diarrhea, involuntary urination and defecation. With severe exposure symptoms progress to convulsions and respiratory failure.

EMERGENCY AND FIRST AID PROCEDURES:

INHALATION: Hold breath until respiratory protective mask is donned. If severe signs of agent exposure appear (chest tightens, pupil constriction, incoordination, etc.), immediately administer, in rapid succession, all three Nerve Agent Antidote Kit(s), Mark I injectors (or atropine if directed by physician). FIRST AID

Injections using the Mark I kit injectors may be repeated at 5 to 20 minute intervals if signs and symptoms are progressing until three series of injections have been administered. No more injections will be given unless directed by medical personnel. In addition, a record will be maintained of all injections given. If breathing has stopped, give artificial respiration. Mouth-to-mouth resuscitation should be used when approved mask-bag or oxygen delivery systems are not available. Do not use mouth-to-mouth resuscitation when facial contamination exists. If breathing is difficult, administer oxygen. Seek medical attention IMMEDIATELY.

EYE CONTACT: Immediately flush eyes with water for at least 15 minutes, then don respiratory protective mask. Although miosis (pinpointing of the pupils) may be an early sign of agent exposure, an injection will not be administered when miosis is the only sign present. Instead, the individual will be taken IMMEDIATELY to a medical treatment facility for observation.

SKIN CONTACT: Don respiratory protective mask and remove contaminated clothing. Immediately wash contaminated skin with copious amounts of soap and water, 10% sodium carbonate solution, or 5% liquid household bleach. Rinse well with water to remove decontaminant. Administer Nerve Agent Antidote Kit(s), MARK I injectors only if local sweating and muscular twitching symptoms are observed. Seek medical attention IMMEDIATELY.

INGESTION: Do not induce vomiting. First symptoms are likely to be gastrointestinal. IMMEDIATELY administer Nerve Agent Antidote Kit(s), MARK I injector(s). Seek medical attention IMMEDIATELY.

SECTION VI - REACTIVITY DATA

STABILITY: Stable when pure.

INCOMPATIBILITY: Attacks tin, magnesium, cadmium plated steel, and some aluminum. Slightly attacks copper, brass, and lead; practically no attack on 1020 steels, Inconel & K-monel.

HAZARDOUS DECOMPOSITION: Hydrolyzes to form HF under acid conditions and isopropyl alcohol & polymers under basic conditions.

HAZARDOUS POLYMERIZATION: Does not occur.

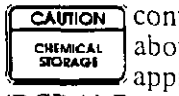
SECTION VII - SPILL, LEAK, AND DISPOSAL PROCEDURES

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED: If leaks or spills occur, only personnel in full protective clothing will remain in area (**See Section VIII**). In case of personnel contamination see **Section V** for emergency and first aid instructions.

RECOMMENDED FIELD PROCEDURES: Spills must be contained by covering with vermiculite, diatomaceous earth, clay, fine sand, sponges, and paper or cloth towels. Decontaminate with copious amounts of aqueous sodium hydroxide solution (a minimum 10 wt. %). Scoop up all material and clothing and place in a DOT approved container. Cover the contents with decontaminating solution as above. After sealing, the exterior of the container will be decontaminated and then labeled according to EPA and DOT regulations. All leaking containers will be over packed with vermiculite placed between the interior and exterior containers. Decontaminate and label according to EPA and DOT regulations. Dispose of the material according to waste disposal methods provided below. Dispose of decontaminate according to Federal, state and local regulations. Conduct general area monitoring with an approved monitor to confirm that the atmospheric concentrations do not exceed the airborne exposure limits (**See Sections II and VIII**).

If 10 wt.% aqueous sodium hydroxide solution is not available then the following decontaminants may be used instead and are listed in the order of preference: Decontaminating Agent, DS (DS2), Sodium Carbonate, and Supertropical Bleach Slurry (STB).

RECOMMENDED LABORATORY PROCEDURES: A minimum of 56 grams of decon solution is required for each gram of GB. Decontaminant and agent solution is allowed to agitate for a minimum of one hour. Agitation is not necessary following the first hour. At the end of the hour, the resulting solution should be adjusted to a pH greater than 11.5. If the pH is below 11.5, NaOH should be added until a pH above 11.5 can be maintained for 60 minutes. An alternate solution for the decontamination of GB is 10 wt.% sodium carbonate in place of the 10% sodium hydroxide solution above. Continue with 56 grams of decon for each gram of agent. Agitate for one hour but allow three hours for the reaction. The final pH should be adjusted to above zero. It is also permitted to substitute 5.25% sodium hypochlorite or 25 wt. % Monoethylamine (MEA) for the 10% sodium hydroxide solution above. MEA must be completely dissolved in water before addition of the agent. Continue with 56 grams of decon for each gram of GB and provide agitation for one hour. Continue with same ratios and time stipulations. Scoop up all material and clothing and place in a DOT approved container. Cover the contents with decontaminating solution as above. After sealing, the exterior of the container will be decontaminated and then labeled according to EPA and DOT regulations. All leaking containers will be over packed with vermiculite placed between the interior and exterior containers. Decontaminate and label according to EPA and DOT regulations. Dispose of according to waste disposal methods provided below. Dispose of decontaminate according to Federal, state and local regulations. Conduct general area monitoring with an approved monitor to confirm that the atmospheric concentrations do not exceed the airborne exposure limits (**See Sections II and VIII**).



WASTE DISPOSAL METHOD: Open pit burning or burying of GB or items containing or contaminated with GB in any quantity is prohibited. The detoxified GB (using procedures above) can be thermally destroyed by incineration in EPA approved incinerators according to appropriate provisions of Federal, state and local Resource Conservation and Recovery Act (RCRA) Regulations.

NOTE: Some states define decontaminated surety material as an RCRA Hazardous waste.

SECTION VIII - SPECIAL PROTECTION INFORMATION

RESPIRATORY PROTECTION:

CONCENTRATION	RESPIRATORY PROTECTIVE EQUIPMENT
< 0.0001 mg/m3	A full face piece, chemical canister, air purifying protective mask will be on hand for escape. (The M9-, M17-, or M40-series masks are acceptable for this purpose. Other masks certified as equivalent may be used)
> 0.0001 or =0.2 mg/m3	A NIOSH/MSHA approved pressure demand full face piece SCBA or supplied air respirators with escape air cylinder may be used. Alternatively, a full face piece, chemical canister air-purifying protective mask is acceptable for this purpose (See DA PAM 385-61 for determination of appropriate level)
>0.2 or unknown mg/m3	NIOSH/MSHA approved pressure demand full f ace piece SCBA suitable for use in high agent concentrations with protective ensemble (See DA PAM 385-61 for examples)

VENTILATION:

Local Exhaust: Mandatory. Must be filtered or scrubbed to limit exit concentration to < 0.0001 mg/m3. Air emissions will meet local, state and federal regulations.

Special: Chemical laboratory hoods will have an average inward face velocity of 100 linear feet per minute (lfpm) +/- 10% with the velocity at any point not deviating from the average face velocity by more than 20%. Existing laboratory hoods will have an inward face velocity of 150 lfpm +/- 20%. Laboratory hoods will be located such that cross drafts do not exceed 20% of the inward face velocity. A visual performance test using smoke producing devices will be performed in the assessment of the hoods ability to contain agent GB.

Other: Recirculation of exhaust air from agent areas is prohibited. No connection is allowed between agent areas and other areas through the ventilation system. Emergency backup power is necessary. Hoods should be tested at least semiannually or after modification or maintenance operations. Operations should be performed 20 centimeters inside hood face.

PROTECTIVE GLOVES:

Butyl Rubber Glove M3 and M4
Norton, Chemical Protective Glove Set

EYE PROTECTION: As a minimum chemical goggles will be worn. For splash hazards use goggles and face shield.

OTHER PROTECTIVE EQUIPMENT: For general lab work, gloves and lab coat will be worn with mask readily accessible. In addition, daily clean smocks, foot covers, and head covers will be required when handling contaminated lab animals.

MONITORING: Available monitoring equipment for agent GB is the M8/M9 Detector paper, detector ticket, blue band tube, M256/M256A1 kits, bubbler, Depot Area Air Monitoring System (DAAMS), Automatic Continuous Air Monitoring System (ACAMS), real time monitoring (RTM), Demilitarization Chemical Agent Concentrator (DCAC), M8/M43, M8A1/M43A2, Hydrogen Flame Photometric Emission Detector (HYFED), CAM-M1, Miniature Chemical Agent Monitor (MINICAM) and the Real Time Analytical Platform (RTAP).

Real-time, low-level monitors (with alarm) are required for GB operations. In their absence, an Immediately Dangerous to Life and Health (IDLH) atmosphere must be presumed. Laboratory operations conducted in appropriately maintained and alarmed engineering controls require only periodic low-level monitoring.

SECTION IX - SPECIAL PRECAUTIONS

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING: When handling agents, the buddy system will be incorporated. No smoking, eating and drinking in areas containing agents are permitted. Containers should be periodically inspected for leaks either visually or by a detector kit). Stringent control over all personnel practices must be exercised

Decontamination equipment will be conveniently located. Exits must be designed to permit rapid evacuation. Chemical showers, eyewash stations, and personal cleanliness facilities must be provided. Wash hands before meals and each worker will shower thoroughly with special attention given to hair, face, neck, and hands, using plenty of soap and water before leaving at the end of the work day.

OTHER PRECAUTIONS: GB must be double contained in liquid and vapor tight containers when in storage or outside a ventilation hood.

For additional information see "AR 385-61, The Army Toxic Chemical Agent Safety Program," "DA PAM 385-61, Toxic Chemical Agent Safety Standards," and "AR 40-8, Occupational Health Guidelines for the Evaluation and Control of Occupational Exposure to Nerve Agents GA, GB, GD, and VX."

SECTION X - TRANSPORTATION DATA

PROPER SHIPPING NAME: Poisonous liquids, n.o.s.

DOT HAZARD CLASSIFICATION: 6.1, Packing Group I,

Hazard Zone A

DOT LABEL: Poison

DOT MARKING: Poisonous liquid, n.o.s. (Isopropyl methylphosphonofluoridate) UN2810, Inhalation Hazard

DOT PLACARD: Poison

EMERGENCY ACCIDENT PRECAUTIONS AND PROCEDURES: **See Sections IV, VII and VIII.**

PRECAUTIONS TO BE TAKEN IN TRANSPORTATION: Motor vehicles will be placarded regardless of quantity. Drivers will be given full information regarding shipment and conditions in case of an emergency. AR 50-6 deals specifically with the shipment of chemical agents. Shipments of agent will be escorted in accordance with AR 740-32.

While the Edgewood Research Development, and Engineering Center, Department of the Army believes that the data contained herein are factual and the opinions expressed are those of the experts regarding the results of the tests conducted, the data are not to be taken as a warranty or representation for which the Department of the Army or Edgewood Research Development, and Engineering Center assume legal responsibility. They are offered solely for your consideration, investigation, and verification. Any use of this data and information must be determined by the user to be in accordance with applicable Federal, State, and local laws and regulations.

OIL FIRES

AND

SOIL SAMPLES

REASONABLY ANTICIPATED TO BE CARCINOGEN: CADMIUM AND CERTAIN CADMIUM COMPOUNDS

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of cadmium (Cd) (CAS No. 7440-43-9) and the following cadmium compounds in experimental animals: cadmium chloride (10108-64-2), cadmium oxide (1306-19-0), cadmium sulfate (10124-36-4), and cadmium sulfide (1306-23-6) (IARC V.2, 1973; IARC V.11, 1976; IARC S.4, 1982; IARC S.7, 1987; ATSDR, 1989f). An IARC Working Group did not evaluate the carcinogenicity of cadmium carbonate (513-78-0), cadmium fluoborate (14486-19-2), or cadmium nitrate (10325-94-7). When administered by intramuscular injection, cadmium powder induced rhabdomyosarcomas and some fibrosarcomas in female rats. When administered by subcutaneous or intramuscular injection, cadmium sulfide induced local sarcomas in rats of both sexes. When administered by subcutaneous injection, cadmium sulfate induced local sarcomas and interstitial cell tumors of the testis in rats. When administered by subcutaneous injection, cadmium chloride induced interstitial cell tumors of the testis in rats, sarcomas and spindle cell sarcomas in male rats, and interstitial cell tumors of the testis in mice. When administered by injection into the ventral prostate, cadmium chloride induced a low incidence of prostatic carcinomas in rats. Male rats exposed continuously to cadmium chloride aerosols developed dose-related increases in adenocarcinomas, epidermoid (squamous cell) carcinomas, combined epidermoid carcinomas and adenocarcinomas, and mucoepidermoid carcinomas of the lung (Takenaka et al., 1983). When administered through intratracheal instillation, cadmium chloride induced invasive prostatic carcinomas in rats (ATSDR, 1989f). When administered by subcutaneous injection, cadmium oxide induced local tumors in female rats (IARC V.11, 1976). When administered by intratracheal instillation, cadmium oxide induced an increased incidence of mammary tumors and an increase in tumors at multiple sites in male rats (ATSDR, 1989f).

An IARC Working Group reported that there is limited evidence for the carcinogenicity of cadmium and certain cadmium compounds in humans (IARC S.4, 1982; IARC S.7, 1987). Studies have suggested that human exposure to cadmium (primarily as the oxide) is associated with increased risks of prostatic, respiratory, and genito-urinary cancers (IARC V.2, 1973; IARC V.11, 1976; IARC S.4, 1982; IARC S.7, 1987; ATSDR, 1989f). In one follow-up study of an investigation of cadmium-nickel battery workers and cadmium-copper alloy factory workers, additional cases of nasopharyngeal, colorectal, prostatic, and lung cancer were reported. In another study, the mortality of cadmium-copper alloy workers who were exposed to cadmium fume was compared with that of workers exposed indirectly to cadmium but also to arsenic. A third group of iron or brass founders was included, and the mortality rates were compared separately with statistics for the general population. Significantly increased mortality from prostatic, genito-urinary and lung cancers was seen for people working in the vicinity but not for the cadmium workers themselves. In follow-up studies of four populations of cadmium-exposed workers, excess lung cancer was noted among male workers employed at 1 of 17 plants in a group that had had "ever medium" exposure for 10 years or more; an excess risk of prostatic cancer was seen in a group that had had "always low" exposures for 10 years or more. In a follow-up study of cadmium smelter workers, a significant trend was noted for cumulative cadmium exposure and lung cancer mortality. Potential confounding factors in these studies, such as smoking and exposure to nickel and arsenic, do not appear to account for the excess of lung cancer deaths. There have been several studies that have not detected a correlation between excess cancer mortality and exposure to cadmium (for a discussion on the carcinogenicity of metals, see the Introduction, p. viii) (ATSDR, 1989f).

PROPERTIES

Cadmium occurs as a soft, blue-white, malleable metal or grayish-white powder. It is soluble in acid, ammonium nitrate, and hot sulfuric acid and insoluble in cold and hot water. Cadmium carbonate occurs as a white amorphous powder that is soluble in acids, potassium cyanate, and ammonium salts and insoluble in ammonia and water, both cold and hot. Cadmium chloride occurs as small, white-to-colorless, hexagonal crystals. It is soluble in water and acetone and insoluble in ethanol. Cadmium fluoborate is extremely hygroscopic and very soluble in water. When heated to

KNOWN CARCINOGEN: ARSENIC AND CERTAIN ARSENIC COMPOUNDS

CARCINOGENICITY

There is limited evidence for the carcinogenicity of arsenic (CAS No. 7440-38-2) and the following arsenic compounds in experimental animals: arsenic pentoxide (1303-28-2), arsenic trioxide (1327-53-3), calcium arsenate (7778-44-1), calcium arsenite (1:1) (52740-16-6), calcium arsenite (2:1) (15194-98-6), calcium arsenite (2:3) (27152-57-4), disodium hydrogen arsenate (10048-95-0), lead arsenate (7784-40-9), potassium arsenate (7784- 41-0), potassium arsenite (13464-35-2), sodium arsenate (7631-89- 2), and sodium arsenite (7784-46-5) (IARC V.2, 1973; IARC V.23, 1980; IARC S.4, 1982; IARC S.7, 1987). When injected subcutaneously during the first 3 days of life into mice whose mothers had been injected subcutaneously once during gestation, arsenic trioxide induced lung adenomas. When administered by intratracheal instillation, arsenic trioxide induced low incidences of carcinomas, adenomas, papillomas and adenomatoid lesions of the respiratory tract in hamsters of both sexes. It induced a low incidence of adenocarcinomas at the site of its implantation into the stomach of rats. A high incidence of lung carcinomas was induced in rats after a single intratracheal instillation of a pesticide mixture containing calcium arsenate. Intratracheal instillations of calcium arsenate into male hamsters resulted in a borderline increase in the incidence of lung adenomas, whereas no such effect was observed with arsenic trisulfide. When administered in the drinking water, sodium arsenite enhanced the incidence of renal tumors induced in male rats by intraperitoneal injection of N-nitrosodiethylamine.

An IARC Working Group reported that there is sufficient evidence for the carcinogenicity of inorganic arsenic compounds in humans (IARC S.7, 1987). (See the Introduction, p. viii, for a discussion on the carcinogenicity of metals.) Many cases of skin cancer have been reported among people exposed to arsenic through medical treatment with inorganic trivalent arsenic compounds. In some instances, skin cancers have occurred in combination with other cancers, such as liver angiosarcoma, intestinal, and urinary bladder cancers and meningioma. Epidemiological studies of cancer after medical treatment with arsenic have shown an excess of skin cancers, but no clear association with other cancers has been obtained. No relation was found between prostatic cancer and treatment of syphilis with arsenicals. An association between environmental exposure to arsenic through drinking water and skin cancer has been observed and confirmed. Epidemiological studies in areas where drinking water contained 0.35-1.14 mg/l arsenic elevated risks for cancers of the bladder, kidney, skin, liver, lung, and colon in both men and women. Occupational exposure to inorganic arsenic, especially in mining and copper smelting, has quite consistently been associated with an increased risk of cancer. An almost tenfold increase in the incidence of lung cancer was found in workers most heavily exposed to arsenic, and relatively clear dose-response relationships have been obtained with regard to cumulative exposure. Other smelter worker populations have been shown to have consistent increases in lung cancer incidence, as well as increases of about 20% in the incidence of gastrointestinal cancer and of 30% for renal cancer and haematolymphatic malignancies. The observation in an earlier study of an increase in lung risk among a population of smelter workers has been confirmed, with a risk of sixfold to eightfold among roasters. With regard to histological type of lung cancer, a significant, relative excess of adenocarcinomas and a slight excess of oat cell cancers were seen among smelter workers.

PROPERTIES

Arsenic and certain arsenic compounds occur in crystalline, powder, amorphous, or vitreous forms. Elemental arsenic is not soluble in water; calcium arsenate, and calcium arsenites (1:1), (2:1), and (2:3) are sparingly soluble in water; the remaining arsenicals are soluble in water. Arsenic pentoxide, potassium arsenite, and the three sodium salts are soluble in ethanol. Arsenic, arsenic pentoxide, arsenic trioxide, the calcium arsenites, lead arsenate, and potassium arsenate are soluble in various acids. When heated to decomposition, arsenic compounds emit toxic arsenic fumes.

Arsenic is available in a technical grade (99% pure) and in a high-purity grade (99.999+% pure) which is intended for semiconductor use. Arsenic pentoxide, sodium arsenite, sodium arsenate, potassium

REASONABLY ANTICIPATED TO BE CARCINOGEN: LEAD ACETATE AND LEAD PHOSPHATE (CAS Nos. 301-04-2 and 7446-27-7)

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of lead acetate and lead phosphate in experimental animals (IARC V.1, 1972; IARC, V.23, 1980; IARC S.4, 1982; IARC S.7, 1987). When administered in the diet, lead acetate induced renal adenomas and carcinomas and cerebral gliomas in rats of both sexes. Subcutaneous injections of lead phosphate induced renal cortical tumors, including adenomas, papillomas, cystadenomas, and carcinomas in rats.

An IARC Working Group reported that there was inadequate evidence for the carcinogenicity of lead and lead compounds in humans (IARC S.7, 1987).

PROPERTIES

Lead acetate and its trihydrate (6080-56-4) occur in the form of white or colorless crystals or flakes; the commercial grades are frequently brown or gray lumps. Lead acetate has a sweetish taste and a slight acetic odor. In the United States, lead acetate is usually marketed as lead acetate trihydrate, and is available in reagent, purified, and technical grades. Typically, trace impurities are iron and chlorides (Cl^-). Lead acetate and its trihydrate are soluble in water, slightly soluble in alcohol, and very soluble in glycerol. Lead phosphate occurs either in the form of hexagonal crystals or as a white powder that is insoluble in water and alcohol. It is soluble in acids and alkali. When heated to decomposition, lead acetate, lead acetate trihydrate, and lead phosphate emit toxic fumes of lead oxide.

USE

Lead acetate is often used for the preparation of other lead salts by the wet method (Kirk-Othmer V.14, 1981). The commercial form of lead acetate, lead acetate trihydrate, is used as a mordant in cotton dyes, as a lead coating for metals, as a drier in paints, varnishes, and pigment inks, and as a colorant in hair dyes (IARC V.23, 1980; Sax, 1987; Sittig, 1985). It is also used in antifouling paints, waterproofing, insecticides, and the gold cyanidation process (Sax, 1987). Lead acetate has been used in explosives and in dilute solutions as poultices and washes for treatment of poison ivy. Formerly, it was used as a pharmaceutical in astringents (IARC V.23, 1980). Lead phosphate is used as a stabilizer in styrene and casein plastics and in small amounts in special glasses (IARC V.23, 1987; Sax, 1987).

PRODUCTION

Current domestic production volumes for lead acetate and lead phosphate are not available. There is no evidence that lead phosphate is produced in commercial quantities in the United States. In 1986, there were seven producers and five suppliers of lead acetate, and one supplier of lead phosphate (Chem Sources, 1986). U.S. imports of lead acetate were 115,411 lb in 1985 and 111,201 lb in 1984 (USDOC Imports, 1985; USDOC Imports, 1986). According to EPA, seven producers in 3 regions reported that domestic production of lead acetate was about 407,000 lb in 1980. In 1978, 250 lb of lead acetate were imported (IARC V.23, 1980). The 1979 TSCA Inventory identified six companies producing 661,000 lb of lead acetate in 1977, and 1 importer with no volume reported, with some site limitations. The CBI Aggregate was between 1 million and 100 million lb. The TSCA Inventory identified one importer of lead phosphate in 1977, but no volume was reported (TSCA, 1979). Lead acetate was first produced commercially in the U.S. in 1944 (IARC V.23, 1980).

EXPOSURE

The primary routes of potential human exposure to lead acetate and lead phosphate are ingestion, inhalation, and dermal contact. Lead acetate is absorbed about 1.5 times as fast as other lead compounds. In 1978, sales of hair dyes containing lead acetate exceeded 1 million bottles (Sittig, 1985). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 132,000 and

18,000 workers were possibly exposed to lead acetate and lead phosphate, respectively, in the workplace (NIOSH. 1976). However, OSHA has estimated that 223,000 workers may be exposed to lead acetate, 28,000 to lead phosphate dibasic, and 27,000 to lead phosphate tribasic. The differences are the result of different methods used to estimate exposure (Sittig, 1985). It has been estimated that airborne emissions of lead in the United States are 46.9 million lb per year (Chem. Engr. News, 1988a). The ACGIH has established a threshold limit value of 0.15 mg/m3, as lead for inorganic compounds (dust and fumes), as an 8- hr time-weighted average (TWA) in air (ACGIH, 1986).

REGULATIONS

CPSC initially banned the use of certain lead-containing paints and similar surface-coating materials in consumer products under the Federal Hazardous Substances Act (FHSA). The ban on lead or lead compounds applied when the lead content exceeded 0.5% of the weight of the product, but excluded artists' paints and related materials. The Consumer Product Safety Act (CPSA) amended the limit of lead content in paints from 0.5% to 0.06% of the weight of the product. CPSC evaluated consumer exposure to lead inks in printed consumer products and found no lead in printed matter intended for children; lead was found in some inks used in printed products, but the levels in the final products did not warrant further action. CPSC found little lead in other printed consumer products. EPA regulates lead and certain lead compounds under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Superfund Amendments and Reauthorization Act (SARA), and Safe Drinking Water Act (SDWA). The dissociated lead ion addressed in these regulations would provide a degree of control over many lead compounds, including lead acetate and lead phosphate. EPA has established a maximum concentration for lead of 0.05 µg/l in wastes for the protection of health under RCRA, and has published a water quality criteria document under CWA for the protection of human health. Under SDWA, EPA published a primary drinking water standard for lead of 0.05 mg/l, which was not based on carcinogenicity. Reportable quantities (RQs) of 5,000 lb (subject to carcinogenicity assessment) has been established for lead acetate and 1 lb (statuatory) for lead phosphate under CERCLA. FDA regulates the use of lead acetate in hair dyes under the Food, Drug, and Cosmetic Act (FD&CA). OSHA established a permissible exposure limit (PEL) of 50 µg/m3 as an 8-hr TWA and 50 µg/100 g as the maximum permissible lead level in blood; the standard requires personal protective equipment, engineering and work practice controls, and medical surveillance with provisions for medical removal. OSHA regulates lead on the basis of acute and chronic toxicity for several organ systems, but not on the basis of carcinogenicity. OSHA regulates lead acetate and lead phosphate under the Hazard Communication Standard and as chemical hazards in laboratories.

REASONABLY ANTICIPATED TO BE CARCINOGEN: HEXACHLOROBENZENE (CAS No. 118-74-1)

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of hexachlorobenzene in experimental animals (IARC S.4, 1982; IARC S.7, 1987). When administered in the diet, hexachlorobenzene induced liver tumors in female rats and mice of both sexes and hepatomas, liver hemangioendotheliomas, and thyroid adenomas in hamsters of both sexes (IARC V.20, 1979; Smith & Cabral, 1980).

There is inadequate evidence for the carcinogenicity of hexachlorobenzene in humans. Hepatocellular carcinoma has been associated with porphyria resulting from consumption of grain treated with hexachlorobenzene (IARC S.7, 1987). An IARC Working Group reported that although there was no case report or epidemiological study available to evaluate the carcinogenicity of hexachlorobenzene in humans, it should be regarded as if it presented a carcinogenic risk to humans (IARC V.20, 1979).

PROPERTIES

Hexachlorobenzene is a white solid which is insoluble in water, and is soluble in benzene, chloroform, and ether. Under most environmental conditions, it has a very low degradation rate. When heated to decomposition, hexachlorobenzene emits highly toxic fumes of hydrochloric acid and other chlorinated compounds. Technical-grade hexachlorobenzene is available as wettable powder, liquid, and dust formulations.

USE

Hexachlorobenzene is used primarily as a pesticide, an industrial chemical, and is a by-product of many chemical and pesticide manufacturing processes. In the United States, hexachlorobenzene is used mainly as a fungicide to control wheat bunt and smut fungi on grains. It is also used as a chemical intermediate in dye manufacture, in the synthesis of other organic chemicals, and as a wood preservative. Hexachlorobenzene forms as an impurity during the synthesis of several herbicides and pesticides, including the herbicide dimethyltetrachloro- terephthalic acid and the pesticide pentachloronitrobenzene (IARC V.20 1979).

PRODUCTION

Since 1982, hexachlorobenzene has not been produced commercially in the United States, but imports in 1982 totalled 38,000 lb (SRI, 1987). NCI reported that hexachlorobenzene is not now imported or produced commercially in the United States. The 1979 TSCA Inventory identified two companies producing 5.5 million lb of hexachlorobenzene and one company importing 5,500 lb in 1977, with some site limitations (TSCA, 1979). Fourteen industries surveyed as sources of hexachlorobenzene wastes reported that about 8.5 million lb of hexachlorobenzene wastes were produced annually. Another report indicates that production of hexachlorobenzene in the United States ended in 1976, although EPA indicated that from 1975 through 1977 three producers and importers in three regions reported domestic production of 3.7 million lb of hexachlorobenzene and imports of 3,800 lb. Commercial production of hexachlorobenzene in the United States was first reported in 1933 (IARC V.20, 1979).

EXPOSURE

The primary routes of potential human exposure to hexachlorobenzene are ingestion, inhalation, and dermal contact. The production and use of hexachlorobenzene as a fungicide over the past several decades and its occurrence as a by-product in the manufacture of other chemicals indicate that potential widespread human exposure may occur in both occupational and nonoccupational settings. It has been estimated that airborne emissions of hexachlorobenzene in the United States are between 46.3 thousand and 63.9 thousand lb per year. These emissions result primarily from pesticide use and the manufacture of chlorinated solvents (Chem. Engr. News, 1988a). The National Occupational Hazard Survey,

REASONABLY ANTICIPATED TO BE CARCINOGEN: NICKEL AND CERTAIN NICKEL COMPOUNDS

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of nickel (7440-02-0) and the following nickel compounds in experimental animals: nickel acetate (373-02-4), nickel carbonate (3333-67-3), nickel carbonyl (13463-39-3), nickel hydroxide (12054-48-7 or 12125-56-3), nickelocene (1271-28-9), nickel oxide (1313-99-1), and nickel subsulfide (12035-72-2) (IARC V.2, 1973; IARC V.11, 1976; IARC S.4, 1982; IARC S.7, 1987). When injected intramuscularly, nickel induced incidences of fibrosarcomas in rats and hamsters of both sexes, local sarcomas in rats of both sexes, and local tumors with some metastases to pre-vertebral lymph nodes in female rats. When injected intrapleurally, nickel powder induced round cell and spindle cell tumors at the injection site in female rats. When administered by inhalation, nickel induced lymphosarcomas in female mice and anaplastic intraalveolar carcinomas, including one with extensive pulmonary adenomatosis, in male and female guinea pigs. Subdermal implantation of nickel pellets induced sarcomas surrounding the pellet in female and male rats. When injected intramedullarly into the femur, rats developed neoplasms at or near the site, including fibrosarcomas (neurogenic in origin), and one reticulum cell sarcoma with metastases. The same route of administration induced one metastasizing endothelial fibrosarcoma in a rabbit (IARC V.11, 1976; IARC V.2, 1973). When administered intraperitoneally, nickel acetate induced an excess of lung adenomas and carcinomas in mice (IARC S.4, 1982). When implanted intramuscularly, nickel carbonate induced sarcomas at the site of the implanted pellet. When administered nickel carbonyl through inhalation, male rats developed one pulmonary adenocarcinoma with metastases, extensive squamous metaplasms of the epithelium, neoplasms of the lung, one mixed adenocarcinoma and squamous cell carcinoma with metastases to the kidney and mediastinum, and papillary bronchiolar adenomas. Injection of nickel carbonyl into the tail vein of rats of both sexes induced malignant tumors including undifferentiated leukemia, pulmonary lymphomas, and individual incidences of liver, kidney, and mammary carcinomas. When millipore diffusion chambers containing nickel hydroxide were implanted in rats, local tumors were induced. When administered by intramuscular injection, nickelocene induced fibrosarcomas in rats and hamsters of both sexes. When administered by intramuscular injection, nickel oxide induced injection site sarcomas in mice and rats; administration by intramuscular implantation induced rhabdomyosarcomas and fibrosarcomas in mice and implantation site sarcomas in rats. When administered by intramuscular implantation, nickel subsulfide induced rhabdomyosarcomas and fibrosarcomas in mice and rats, rhabdomyosarcomas with distant metastases and implantation site sarcomas in rats, and tumors in mice. Palpable local tumors arose at implantation sites after nickel subsulfide pellets were removed from rats at various times. Intratracheal injection of nickel subsulfide induced malignant neoplasms of the lungs, adenocarcinomas, and squamous cell carcinomas, in rats of both sexes. Intramuscular injection of nickel subsulfide induced injection site sarcomas and rhabdomyosarcomas in rats and mice and fibrosarcomas and undifferentiated sarcomas in male rats; in addition, the sarcomas metastasized to distant sites, e.g., lungs, liver, heart, spleen, mediastinum, and mesentery and para-aortic lymph nodes (IARC V.2, 1973; IARC V.11, 1976). Nickel subsulfide induced malignant tumors in rats after insertion into heterotransplanted tracheas and after intrarenal, intratesticular, and intraocular administration (IARC S.4, 1982).

An IARC Working Group determined that there is limited evidence for the carcinogenicity of nickel and certain nickel compounds, and sufficient evidence for the carcinogenicity of nickel refining in humans (IARC S.4, 1982). A subsequent IARC Working Group determined that there is sufficient evidence for the carcinogenicity of the group of nickel compounds in humans. However, the specific carcinogenic substance(s) could not be identified (IARC S.7, 1987). Several epidemiological studies demonstrated excess incidences of cancers of the nasal cavity, lung, and possibly the larynx in workers exposed to nickel or nickel compounds. The cancer hazards seemed to be associated with the early stage of nickel refining, and with exposure primarily to nickel subsulfide and nickel oxide (IARC V.2, 1973; IARC V.11, 1976; IARC S.4, 1982; IARC S.7, 1987). Nickel refining as an occupational exposure is now listed in the Introduction of this Annual Report, p. viii (also see p. viii for a discussion on the carcinogenicity of metals).

REASONABLY ANTICIPATED TO BE CARCINOGEN: POLYCYCLIC AROMATIC HYDROCARBONS, 15 LISTINGS

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of the following polycyclic aromatic hydrocarbons (PAHs) in experimental animals: benz[a]anthracene (56-55-3), benzo[b]fluoranthene (205- 99-2), benzo[j]fluoranthene (205-82-3), benzo[k]fluoranthene (207- 08-9), benzo[a]pyrene (50-32-8), dibenz[a.h]acridine (226-36-8), dibenz[a,j]acridine (224-42-0), dibenz[a,h]anthracene (53-70-3), 7H-dibenzo[c,g]carbazole (194-59-2), dibenzo[a,e]pyrene (192-65- 4), dibenzo[a,h]pyrene (189-64-0), dibenzo[a.i]pyrene (189-55-9), dibenzo[a,l]pyrene (191-30-0), indeno[1,2,3-cd]pyrene (193-39-5), and 5-methylchrysene (3697-24-3) (IARC V.3, 1973; IARC V.32, 1987; IARC S.7, 1987).

When administered by gavage, benz[a]anthracene induced papillomas of the forestomach in mice. In another gavage study, benz[a]anthracene induced lung adenomas and hepatomas in mice. When administered topically, benzo[a]anthracene induced skin papillomas in mice. When administered by a single subcutaneous injection, benz[a]anthracene induced sarcomas in adult mice and pulmonary adenomas and adenocarcinomas in newborn mice. When administered by bladder implantation, benz[a]anthracene induced local carcinomas in mice (IARC V.3, 1973).

When administered topically, benzo[j]fluoranthene induced skin papillomas and carcinomas in female mice. When injected directly into the pulmonary tissues of female rats, benzo[j]fluoroanthene and benzo[k]fluoranthene induced squamous cell carcinomas. When administered topically, benzo[k]fluoranthene was active as an initiator of skin tumors in female mice. When administered by subcutaneous injection, benzo[k]fluoranthene induced local sarcomas in mice of both sexes (IARC V.32, 1983).

When administered by gavage, benzo[a]pyrene induced malignant and benign forestomach tumors in mice and hamsters and mammary tumors in female rats. When administered in the diet, benzo[a]pyrene increased the incidence of forestomach tumors and induced lung adenomas in mice. When administered topically, benzo[a]pyrene induced skin carcinomas and papillomas in mice, rats, guinea pigs, and rabbits. When administered by inhalation, benzo[a]pyrene induced tracheal papillomas and carcinomas in hamsters and squamous cell carcinomas of the lung in rats. When administered by intratracheal instillation, benzo[a]pyrene induced lung tumors in rats, tracheobronchial tumors in hamsters, and squamous carcinomas of the lung in two of six subhuman primates. When administered by subcutaneous injection, benzo[a]pyrene induced local sarcomas in rats, hamsters, guinea pigs, newts, subhuman primates, and adult mice; hepatomas and lung adenomas were produced in newborn mice. When administered by intraperitoneal injection, benzo[a]pyrene induced abdominal fibrosarcomas in mice of both sexes and mammary and uterine carcinomas in rats. When administered by intravenous injection, benzo[a]pyrene induced mammary carcinomas in female rats. When administered by intrabronchial implantation, benzo[a]pyrene induced local tumors in rats. When administered by subcutaneous or intraperitoneal injections to mice at the 11th, 13th, and 15th day of pregnancy, benzo[a]pyrene increased the incidence of lung adenomas and initiated skin carcinogenesis in the offspring (IARC V.3, 1973).

When administered topically, benzo[b]fluoranthene induced skin tumors in mice (IARC V.3, 1973). When administered by subcutaneous injection, benzo[b]fluoranthene induced local sarcomas in mice. When administered topically, dibenz[a,h]acridine induced skin tumors. When administered by intravenous injection, dibenz[a,h]acridine increased the incidence of lung tumors in mice (IARC V.3, 1973).

When administered topically, dibenz[a,j]acridine induced skin tumors in mice. When administered by subcutaneous injection, dibenz[a,j]acridine induced local sarcomas and increased the incidence of lung tumors in mice (IARC V.3, 1973).

When administered in the diet, dibenz[a,h]anthracene induced squamous cell carcinomas and papillomas of the forestomach in mice. When administered as an olive oil emulsion in place of the drinking water,

dibenz[a,h]anthracene induced alveologenic carcinomas of the lung and hemangioendotheliomas in mice of both sexes and mammary carcinomas in female mice. When administered by intratracheal injection, dibenz[a,h]anthracene induced lung squamous cell carcinomas in rats. When administered by subcutaneous injection, dibenz[a,h]anthracene induced local sarcomas in rats, guinea pigs, pigeons, fowl, adult mice, and newborn mice; the incidence of lung adenomas was increased in newborn mice. When injected directly into lung tissues, dibenz[a,h]anthracene induced lung adenomas. When injected into the kidney of frogs, dibenz[a,h]anthracene induced renal adenocarcinomas. (IARC V.3, 1973).

7H-Dibenzo[c,g]carbazole induced subcutaneous injection site tumors in rats. When administered by gavage, 7H- dibenzo[c,g]carbazole induced forestomach papillomas and carcinomas and benign and malignant hepatomas in mice. When administered by intratracheal injection, 7H-dibenzo[c,g]carbazole induced respiratory tract tumors in hamsters (IARC V.3, 1973).

When administered topically, dibenzo[a,e]pyrene, dibenzo[a,h]pyrene, dibenzo[a,i] pyrene, and 5-methylchrysene induced skin tumors in mice. Dibenzo[a,h]pyrene also induced skin tumors in rats. These four compounds and dibenzo[a,l]pyrene induced local sarcomas in mice when administered by subcutaneous injection (IARC V.3, 1973).

An IARC Working Group concluded that there were no adequate data available to evaluate the carcinogenicity of PAHs in humans (IARC V.3, 1973; IARC V.32, 1983). However, there are a number of epidemiologic and mortality studies that show increased incidences of cancer in humans exposed to mixtures of PAHs (ATSDR, 1987b). Mortality studies have demonstrated that exposure to coke oven emissions, which contain a variety of PAHs, caused increased incidences of lung and genitourinary cancer mortality in coke oven workers (see Coke Oven Emissions, p.Ê867) (IARC V.34, 1984; Lloyd, 1971; Redmond et al., 1972). Workers exposed to creosote containing numerous PAHs developed skin tumors (see Soots, Tars, and Minerals Oils, p. 872). Exposures to other chemical mixtures that contain PAHs, such as cigarette smoke, coal tar, coal tar pitch, and bitumens, have been associated with increased incidences of lung cancer in humans. Dermal exposure to coal tar and shale oils containing PAHs have been associated with increased incidences of skin tumors in humans (IARC V. 35, 1985; ATSDR, 1990e).

PROPERTIES

The 15 PAHs listed occur as needles, plates, crystals, leaflets, or prisms ranging from colorless to pale yellow to golden yellow. Four of the 15 PAHs, benz[a]anthracene, dibenzo[a,i]pyrene, indeno[1,2,3-cd]pyrene, and 5-methylchrysene, show fluorescence ranging from greenish yellow to brilliant bluish violet to brown. Solubility characteristics vary for each PAH, but in general they are slightly soluble to insoluble in ethanol, and are soluble to slightly soluble in acetic acid, benzene, and acetone. Several PAHs are soluble in toluene, xylene, 1,4- dioxane, and other organic solvents. Some of the PAHs are soluble in mineral and/or olive oil, and dibenz[a,h]anthracene is soluble in cyclohexane. PAHs are insoluble in diethyl ether and petroleum ether, and most are insoluble in water. When heated to decomposition, benzo[a]pyrene emits acrid smoke, and benzo[j]fluoranthene, benzo[k]fluoranthene, dibenz[a,h]anthracene, and 5-methylchrysene emit acrid smoke and irritating fumes. Dibenz[a,h]acridine, dibenz[a,j]acridine, and 7H- dibenzo[c,g]carbazole emit toxic nitrogen oxide (NOx) fumes when heated to decomposition.

USE

Twelve of the 15 PAHs are used only in biochemical, biomedical, laboratory, and/or cancer research. There are no known uses or applications for the remaining three PAHs, dibenzo[a,h]pyrene, dibenzo[a,i]pyrene, and 5-methylchrysene (IARC V.32, 1983).

At least 8 of the 15 PAHs are present in coal tar which is used as a fuel in the steel industry in open-hearth and blast furnaces. Coal tar is also used in the clinical treatment of skin disorders such as eczema, dermatitis, and psoriasis. Coal tar is distilled to produce a variety of coal tar products including coal tar pitch and creosote. At least 6 of the 15 PAHs are present in coal tar pitch which is used primarily as a binder for aluminum smelting electrodes in the aluminum reduction process. Coal tar pitch is also

REASONABLY ANTICIPATED TO BE CARCINOGEN: SILICA, CRYSTALLINE (RESPIRABLE SIZE)

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of respirable crystalline silica in experimental animals (IARC V.42, 1987; IARC S.7, 1987). When administered by inhalation, quartz (14808-60-7) induced significant increases in the incidence of adenocarcinomas and squamous cell carcinomas of the lung in rats of both sexes in one study and female rats (nose-only inhalation) in another study. In three studies in which quartz was administered by single or repeated intratracheal instillation, there was a significant increase in the incidence of adenocarcinomas and squamous cell carcinomas in rats. Different specimens of quartz, with particles in the respirable range, were tested in the inhalation and intratracheal instillation studies. No pulmonary tumors were observed in hamsters in four experiments using repeated intratracheal instillation of quartz dusts. When administered as a single interpleural or intraperitoneal injection, suspensions of several types of quartz induced thoracic and abdominal malignant lymphomas, primarily of the histiocytic type, in rats of both sexes. When administered as a single intrapleural injection, cristobalite (14464-46-1) or tridymite (15468-32-3), with particles in the respirable range, induced malignant lymphomas, primarily of the histiocytic type, in rats of both sexes. When administered as a single intravenous injection, one sample of quartz failed to induce a significant difference in the presence or multiplicity of pulmonary adenomas in strain A mice of both sexes.

An IARC Working Group reported that there is limited evidence for the carcinogenicity of crystalline silica in humans (IARC S.7, 1987; IARC V.42, 1987). A number of studies have investigated the occurrence of lung cancer in persons diagnosed as having silicosis after occupational exposure to dust containing respirable crystalline silica. Of three case-control studies, two showed an association between silicosis and lung cancer. Seven cohort studies and one proportionate mortality study all demonstrated that lung cancer occurs more frequently in silicotics than in the general population. This increase has been seen among miners, quarry workers, foundry workers, ceramic workers, granite workers, and stone cutters. In some of these studies, the risk of lung cancer increased with duration of employment. Only rarely, however, were data obtained on smoking and on potential confounding exposures and the comparability of the referent population assured (IARC V.42, 1987; IARC S.7, 1987).

PROPERTIES

Silica is noncombustible, colorless or white, tasteless "crystals". It occurs naturally in crystalline and amorphous forms and the specific gravity and melting point depend on the crystalline form. The basic structural units of the silica mineral are silicon tetrahedra, SiO2. These are linked in the four corners with other tetrahedra. Slight variations in the orientation of the silicon tetrahedra result in the different polymorphs of silica. In crystalline silica, silicon and oxygen atoms are arranged in definite regular patterns throughout (Parmeggiani, 1983). Quartz, cristobalite, and tridymite are the three most common crystalline forms of free silica. Quartz, cristobalite, and tridymite are interrelated and may change their form under different temperature and pressure conditions. The quartz structure is more compact than that of tridymite or cristobalite (IARC V.42, 1987). Quartz melts to glass and has the lowest coefficient of expansion by heat of any known substance. Silica is insoluble in water and most acids but dissolves in hydrofluoric acid forming gaseous silicon tetrafluoride. It is slowly attacked by heating with concentrated phosphoric acid. Crystallized forms of silica are rarely attacked by alkalies (Merck, 1989).

USE

Naturally occurring silica materials are classified by end use or industry. Sand and gravel is produced almost exclusively for road building and concrete construction, depending on particle size and shape, surface texture, and porosity (IARC V.42, 1987). High-purity silica sand that may be extracted from sand and gravel operations is also a major industrial commodity. Industrial quartz crystal is another major industrial classification of silica materials (USDOI, 1990). Quartz and quartzite products are high-purity products.

The United States Department of Labor
Occupational Safety and Health Administration

Diesel Exhaust

Diesel exhaust is a pervasive airborne contaminant in workplaces where diesel-powered equipment is used. Due to expanding use of diesel equipment, more and more workers are exposed to diesel exhaust. Over one million workers exposed to diesel exhaust face the risk of adverse health effects ranging from headaches to nausea to cancer and respiratory disease. Currently available control technology could significantly limit many diesel exhaust exposures, although additional information and research are needed on the methods to monitor diesel particulates and determine the level of risk such particulates cause. OSHA is developing an action plan to reduce worker exposures to this hazard but is not initiating rulemaking at this time.

Hazard Description

Over one million workers exposed to diesel exhaust face the risk of adverse health effects ranging from headaches to nausea to cancer and respiratory disease, including mine workers, bridge and tunnel workers, railroad workers, loading dock workers, truck drivers, material handling machine operators, farm workers, auto, truck and bus maintenance garage workers, and longshoring employees. (1)

Studies show exposed workers have an elevated risk of lung cancer. There is some evidence of risk of bladder cancer. Workers also may experience dizziness, drowsiness, headaches, nausea, decrement of visual acuity, and decrement in forced expiratory volume. (2-4)

Diesel exhaust has been implicated as a cause of reactive airway disease. (5)

Laboratory tests have shown diesel exhaust to be toxic, mutagenic and carcinogenic. (1-4, 6)

Numerous studies with rats have consistently demonstrated significant increases in pulmonary tumors with at least 24 months of exposure to concentrations greater than 2 mg/m3. While these studies are of good quality, there are uncertainties about the factors for extrapolating animal data to predict human risk. (1-4, 6)

Numerous epidemiological studies showed a positive carcinogenic risk associated with exposure to diesel exhaust. (1-4, 11) Although no study has been fully successful in estimating historical exposures and using those estimates to establish a dose-response curve, at least two recent major studies have published quantitative assessments of current exposures in groups of workers studied epidemiologically. (7-10) One study found that current exposures to submicrometer elemental carbon (used as a surrogate for diesel exhaust) in the trucking industry, while generally low compared to some occupational exposures (e.g. miners in enclosed spaces), are measurably higher than background levels measured in residential areas (averaging 3.8 ug/m3 in truck drivers to 13.8 ug/m3 in dock workers). (7) A second study found that average exposures to respirable particulates, adjusted for tobacco smoke, in the railroad industry ranged from 17 ug/m3 in clerks to 134 ug/m3 for locomotive shop workers. Differences in climate, facilities, equipment and work practices were found to affect exposures to diesel exhaust within the railroad industry. (10)

In 1989, the International Agency for Research on Cancer (IARC) concluded that there is sufficient evidence for the carcinogenicity of whole diesel exhaust in experimental animals and that there is limited evidence for carcinogenicity of whole diesel exhaust in humans. IARC classified diesel exhaust as a probable human carcinogen (Group 2A). (6)

In 1994, the Air Resources Board of the State of California released a preliminary draft document on the Health Risk Assessment for Diesel Exhaust. The draft report concluded that the evidence that diesel exhaust is carcinogenic in rats is clearly sufficient and, in humans, the carcinogenic evidence appears to be sufficient. (2)

In 1994, the Environmental Protection Agency (EPA) also released a preliminary draft of a Health Assessment Document for Diesel Emissions. In that document, EPA concluded that on the basis of limited evidence for carcinogenicity of diesel engine emissions in humans, supported by adequate evidence in animals and positive mutagenicity data, diesel engine emissions are considered to best fit the weight-of-evidence for category B1 (considered to be a probable human carcinogen). (3)

The Health Effects Institute's Diesel Working Group published a special report on diesel exhaust in April 1995. This document finds that diesel emissions have the potential to cause adverse health effects including cancer and other pulmonary and cardiovascular diseases. However, the document concludes that the lack of definitive exposure data precludes using available epidemiological data to develop quantitative estimates of cancer risk, and raises questions about the validity of using rat bioassay data to characterize the potential human risk associated with ambient exposure to diesel emissions. (11)

OTHER AGENTS

KNOWN CARCINOGEN: MUSTARD GAS (CAS No. 505-60-2)

CARCINOGENICITY

There is limited evidence for the carcinogenicity of mustard gas in experimental animals (IARC V.9, 1975; IARC S.4, 1982). When administered by inhalation or intravenous injection, mustard gas caused increased incidences of lung tumors in mice of both sexes. Subcutaneous administration of mustard gas induced local fibrosarcomas or sarcomas in mice of both sexes.

An IARC Working Group reported that there is sufficient evidence for the carcinogenicity of mustard gas in humans (IARC V.9, 1975; IARC S.4, 1982). Several studies have shown an increased mortality from respiratory tract cancer among individuals exposed to mustard gas. This mortality was greater in those individuals with long-term occupational exposure than in those with sporadic exposure.

PROPERTIES

Mustard gas is a colorless, oily liquid with a weak, sweet, agreeable odor. It is sparingly soluble in water and soluble in fat, fat solvents, and other common organic solvents. Mustard gas volatilizes in steam. It is combustible when exposed to heat or flame. When heated to decomposition, it emits very toxic fumes of sulfur oxides (SOx), hydrochloric acid, and other chlorinated compounds.

USE

Mustard gas is used primarily as a model compound in biological studies of alkylating agents. Researchers have tested mustard gas as an antineoplastic agent, but its clinical use as a tumor inhibitor has been minimal. Use of mustard gas in chemical warfare occurred mainly during World War I (IARC V.9, 1975).

PRODUCTION

There are no domestic producers or importers of mustard gas, and no production volumes are reported. There is no indication that mustard gas is manufactured or used in the United States at the present time. U.S. companies produced and stockpiled the chemical during World War II, and stocks may have existed in the United States as recently as 1974 (IARC V.9, 1975). If production of mustard gas as a chemical warfare agent were to be resumed, it would probably be excluded from regulation under the National Security Clause contained in each regulatory authority.

EXPOSURE

The primary routes of potential human exposure to mustard gas are inhalation and dermal contact. The greatest risk of exposure to date has been for military personnel, but there is also some small risk for persons living near military installations that stockpile mustard gas. The average and maximum atmospheric concentrations likely to have been produced under military conditions have been estimated to be 3 and 5 ppm, respectively (IARC V.9, 1975). No data are available concerning the extent of occupational exposure. REGULATIONS EPA regulates mustard gas under the Superfund Amendments and Reauthorization Act (SARA), subjecting it to reporting rules. Emergency response plans are required

under SARA if the threshold planning quantity of 500 lb is exceeded. EPA has not established a reportable quantity (RQ) for mustard gas under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), but has proposed regulating it as a hazardous constituent of waste under the Resource Conservation and Recovery Act (RCRA). OSHA regulates mustard gas under the Hazard Communication Standard and as a chemical hazard in laboratories.

DOD Hazardous Materials Information System
DoD 6050.5-LR
AS OF April 1996
Proprietary Version - For U.S. Government Use Only

FSC: 9130
NIIN: 002732379
Manufacturer's CAGE: 0AHD1
Part No. Indicator: A
Part Number/Trade Name: **TURBINE FUEL, AVIATION JP-5**

General Information

Item Name: TURBINE FUEL, AVIATION
Company's Name: CHEVRON ENVIRONMENTAL HEALTH CENTER INC.
Company's Street: 15299 SAN PABLO AVE.
Company's P. O. Box: 4054
Company's City: RICHMOND
Company's State: CA
Company's Country: US
Company's Zip Code: 94804-0054
Company's Emerg Ph #: 415-233-3737
Company's Info Ph #: 415-233-3737
Distributor/Vendor # 1:
Distributor/Vendor # 1 Cage:
Distributor/Vendor # 2:
Distributor/Vendor # 2 Cage:
Distributor/Vendor # 3:
Distributor/Vendor # 3 Cage:
Distributor/Vendor # 4:
Distributor/Vendor # 4 Cage:
Safety Data Action Code:
Safety Focal Point: D
Record No. For Safety Entry: 001
[illegible] Entries This Stk#: [illegible]
[illegible] SMC
Date MSDS Prepared: 18NOV89
Safety Data Review Date: 22AUG91
Supply Item Manager: KY
MSDS Preparer's Name:
Preparer's Company:
Preparer's St Or P. O. Box:
Preparer's City:
Preparer's State:
Preparer's Zip Code:
Other MSDS Number:
MSDS Serial Number: BKMDX
Specification Number: MIL-T-5624
Spec Type, Grade, Class: JP-5 GRADE
Hazard Characteristic Code: F4
Unit Of Issue: GL
Unit Of Issue Container Qty:
Type Of Container:
[illegible] Weight:

Report for NIIN: 002732379

NRC/State License Number: N/R
Net Explosive Weight: N/R
Net Propellant Weight-Ammo: N/R
Coast Guard Ammunition Code: N/R

Ingredients/Identity Information

Proprietary: NO
Ingredient: DISTILLATE, WIDE BOILING RANGE; ALIPHATIC AND AROMATIC
Ingredient Sequence Number: 01
Percent: >75
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: 1006818DS
CAS Number:
OSHA PEL: NOT ESTABLISHED
ACGIH TLV: NOT ESTABLISHED
Other Recommended Limit: NONE SPECIFIED

Proprietary: NO
Ingredient: HEXANE (N-HEXANE)
Ingredient Sequence Number: 02
Percent: <25
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: MN9275000
CAS Number: 110-54-3
OSHA PEL: 500 PPM
ACGIH TLV: 50 PPM; 9293
Other Recommended Limit: NONE SPECIFIED

Ingredient: BENZENE (SARA III)
Ingredient Sequence Number: 03
Percent: <.1
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: CY1400000
CAS Number: 71-43-2
OSHA PEL: 1PPM/5STEL;1910.1028
ACGIH TLV: 10 PPM; A2; 9192
Other Recommended Limit: NONE SPECIFIED

Proprietary: NO
Ingredient: ETHYL BENZENE (SARA III)
Ingredient Sequence Number: 04
Percent: 0.1
Ingredient Action Code:
Ingredient Focal Point: D

Report for NIIN: 002732379

Other Recommended Limit: NONE SPECIFIED

Proprietary: NO
Ingredient: XYLENES (O-,M-,P- ISOMERS) (SARA III)
Ingredient Sequence Number: 05
Percent: <.3
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: ZE2100000
CAS Number: 1330-20-7
OSHA PEL: 100 PPM/150 STEL
ACGIH TLV: 100 PPM/150STEL;9192
Other Recommended Limit: NONE SPECIFIED

Proprietary: NO
Ingredient: TOLUENE (SARA III)
Ingredient Sequence Number: 06
Percent: <.1
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: XS5250000
CAS Number: 108-88-3
OSHA PEL: 200 PPM/150 STEL
ACGIH TLV: 50 PPM; 9293
Other Recommended Limit: NONE SPECIFIED

==========

Physical/Chemical Characteristics

==========

Appearance And Odor: PALE YELLOW LIQUID.
Boiling Point: 365F,185C
Melting Point: N/R
Vapor Pressure (MM Hg/70 F): 6.04
Vapor Density (Air=1): N/R
Specific Gravity: 0.82
Decomposition Temperature: UNKNOWN
Evaporation Rate And Ref: N/R
Solubility In Water: INSOLUBLE
Percent Volatiles By Volume: N/R
Viscosity: N/R
pH: N/R
Radioactivity: N/R
Form (Radioactive Matl):
Magnetism (Milligauss): N/P
Corrosion Rate (IPY): UNKNOWN
Autoignition Temperature:

==========

Fire and Explosion Hazard Data

==========

Flash Point: 140F,60C
Flash Point Method: PMCC
Lower Explosive Limit: N/R
Upper Explosive Limit: N/R
Extinguishing Media: USE WATER FOG, CARBON DIOXIDE, FOAM, OR DRY CHE

Report for NIIN: 002732379

Special Fire Fighting Proc: DO NOT ENTER ENCLOSED AREA WITHOUT PROTECTIVE EQUIPMENT AND A SELF CONTAINED BREATHING APPARATUS TO PROTECT AGAINST DECOMPOSITION PRODUCTS OR OXYGEN DEPLETION.
Unusual Fire And Expl Hazrds: LIQUID EVAPORATES & FORM VAPOR/FUMES WHICH CAN IGNITE & BURN WITH EXPLOSIVE VIOLENCE. UNSEEN VAPORS CAN SPREAD & IGNITE IN OTHER AREAS. HAZARD IS > ABOVE 85F.

Reactivity Data

Stability: YES
Cond To Avoid (Stability): HIGH HEAT, OPEN FLAMES AND OTHER SOURCES OF IGNITION.
Materials To Avoid: MAY REACT WITH STRONG OXIDIZING AGENTS, SUCH AS CHLORATES, NITRATES, PEROXIDES, ETC.
Hazardous Decomp Products: NORMAL COMBUSTION FORMS CARBON DIOXIDE AND WATER VAPOR; INCOMPLETE COMBUSTION CAN PRODUCE CARBON MONOXIDE.
Hazardous Poly Occur: NO
Conditions To Avoid (Poly): NOT APPLICABLE

Health Hazard Data

LD50-LC50 Mixture: LD50 (ORAL RAT) IS UNKNOWN
Route Of Entry - Inhalation: YES
Route Of Entry - Skin: YES
Route Of Entry - Ingestion: YES
Health Haz Acute And Chronic: THIS PRODUCT IS NOT EXPECTED TO CAUSE PROLONGED OR SIGNIFICANT EYE OR SKIN IRRITATION. PROLONGED BREATHING OF VAPORS CAN CAUSE CENTRAL NERVOUS SYSTEMS EFFECTS. IF INGESTED, IT IS PRACTICALLY NON-TOXIC, BUT BECAUSE OF ITS LOW VISCOSITY, IT CAN DIRECTLY ENTER THE LUNGS & CAN CAUSE SEVERE INJURY TO THE LUNGS OR DEATH.
Carcinogenicity - NTP: NO
[illegible] - IARC: NO
[illegible] - OSHA: NO
Explanation Carcinogenicity: NONE OF THE CHEMICALS IN THIS PRODUCT IS LISTED BY IARC, NTP OR OSHA AS A CARCINOGEN.
Signs/Symptoms Of Overexp: INHALATION-HEADACHE, DIZZINESS, LOSS OF APPETITE, WEAKNESS AND LOSS OF COORDINATION INGESTION-IF ASPIRATED IT CAN CAUSE DEATH.
Med Cond Aggravated By Exp: NONE SPECIFIED BY MANUFACTURER.
Emergency/First Aid Proc: EYE-FLUSH WITH WATER FOR 15 MINUTES. SKIN-REMOVE CONTAMINATED CLOTHES. WASH WITH SOAP AND WATER. SEE A DOCTOR. INHALATION-REMOVE TO FRESH AIR. SEE A DOCTOR IF SYMPTOMS OCCUR. INGESTION-DO NOT INDUCE VOMITING. GIVE WATER OR MILK TO DRINK. GET MEDICAL ATTENTION

Precautions for Safe Handling and Use

Steps If Matl Released/Spill: ELIMINATE ALL OPEN FLAMES. STOP THE SOURCE OF THE LEAK OR RELEASE. CLEAN UP SPILL AS SOON AS POSSIBLE, OBSERVING PRECAUTIONS IN PROTECTIVE EQUIPMENT. CLEAN UP SMALL SPILL USING APPROPRIATE TECHNIQUES SUCH AS SORBENT MATERIALS OR PUMPING.
Neutralizing Agent: NOT APPLICABLE
Waste Disposal Method: PLACE CONTAMINATED MATERIALS IN DISPOSABLE [illegible] IN A MANNER CONSISTENT WITH APPLICABLE

Report for NIIN: 002732379

REGULATIONS. CONTACT LOCAL ENVIRONMENTAL OR HEALTH AUTHORITIES FOR APPROVE DISPOSAL OF THIS MATERIAL.
Precautions-Handling/Storing: DO NOT USE OR STORE NEAR FLAME, SPARKS OR HOT SURFACES. USE ONLY IN WELL VENTED AREA. KEEP CONTAINER CLOSED. DO NOT WELD, HEAT OR DRILL CONTAINER.
Other Precautions: EMPTIED CONTAINER STILL CONTAINS HAZARDOUS OR EXPLOSIVE VAPOR OR LIQUID. CAUTION! DO NOT USE PRESSURE TO EMPTY DRUM OR EXPLOSION MAY RESULT. WARNING! NOT FOR USE AS PORTABLE HEATER OR APPLIANCE FUEL. TOXIC FUMES MAY ACCUMULATE & CAUSE DEATH

Control Measures

Respiratory Protection: THIS MATERIAL MAY BE AN INHALATION HAZARD &, UNLESS VENTILATION IS ADEQUATE, THE USE OF AN APPROVED RESPIRATOR IS RECOMMENDED. REFER TO THE OSHA BENZENE STANDARD TO DETERMINE WHAT TYPE OF RESPIRATOR IS REQUIRED BASED ON EXPOSURE LEVELS.
Ventilation: USE THIS MATERIAL ONLY IN WELL VENTILATED AREAS.
Protective Gloves: PROTECTIVE GLOVES IS RECOMMENDED.
Eye Protection: NO SPECIAL EYE WEAR IS USUALLY NECESSARY
Other Protective Equipment: SAFETY SHOWER AND EYE BATH. INDUSTRIAL TYPE WORK CLOTHING IS REQUIRED TO AVOID PROLONGED OR REPEATED CONTACT.
Work Hygienic Practices: WASH THOROUGHLY AFTER HANDLING AND BEFORE EATING OR DRINKING. LAUNDER CONTAMINATED CLOTHING BEFORE REUSE.
Suppl. Safety & Health Data:

DOD Hazardous Materials Information System
DoD 6050.5-LR
AS OF April 1996
Proprietary Version - For U.S. Government Use Only

FSC: 9130
NIIN: 010315816
Manufacturer's CAGE: 0AHD1
Part No. Indicator: A
Part Number/Trade Name: **TURBINE FUEL, AVIATION JP-8**

General Information

Item Name: TUBINE FUEL, GROUND
Company's Name: CHEVRON ENVIRONMENTAL HEALTH CENTER INC.
Company's Street: 15299 SAN PABLO AVE.
Company's P. O. Box: 4054
Company's City: RICHMOND
Company's State: CA
Company's Country: US
Company's Zip Code: 94804-0054
Company's Emerg Ph #: 415-233-3737
Company's Info Ph #: 415-233-3737
Distributor/Vendor # 1:
Distributor/Vendor # 1 Cage:
Distributor/Vendor # 2:
Distributor/Vendor # 2 Cage:
Distributor/Vendor # 3:
Distributor/Vendor # 3 Cage:
Distributor/Vendor # 4:
Distributor/Vendor # 4 Cage:
Safety Data Action Code:
Safety Focal Point: D
Record No. For Safety Entry: 001
Total Safety Entries This Stk#: 026
Status: S
New MSDS Prepared: 15JUL92
Safety Data Review Date: 06NOV92
Supply Item Manager: KY
MSDS Preparer's Name:
Preparer's Company:
Preparer's St Or P. O. Box:
Preparer's City:
Preparer's State:
Preparer's Zip Code:
Other MSDS Number:
MSDS Serial Number: BPGDJ
Specification Number: MIL-T-83133
Spec Type, Grade, Class: GRADE JP8
Hazard Characteristic Code: F4
Unit Of Issue: GL
Unit Of Issue Container Qty: BULK
Type Of Container: BULK
Net Unit Weight: UNKNOWN

Report for NIIN: 010315816

NRC/State License Number:
Net Explosive Weight: N/R
Net Propellant Weight-Ammo:
Coast Guard Ammunition Code: N/R

Ingredients/Identity Information

Proprietary: NO
Ingredient: KEROSENE
Ingredient Sequence Number: 01
Percent: UNKNOWN
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: OA5500000
CAS Number: 8008-20-6
OSHA PEL: 100 PPM
ACGIH TLV: 100 PPM 9091
Other Recommended Limit: NONE RECOMMENDED

Proprietary: NO
Ingredient: DISTILLATES, HYDRODESULFURIZED MIDDLE
Ingredient Sequence Number: 02
Percent: UNKNOWN
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: 1005733DH
CAS Number: 64742-80-9
OSHA PEL: NOT ESTABLISHED
ACGIH TLV: NOT ESTABLISHED
Other Recommended Limit: NONE RECOMMENDED

[illegible]
Ingredient: SULFUR
Ingredient Sequence Number: 03
Percent: 3%
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: WS4250000
CAS Number: 7704-34-9
OSHA PEL: NOT ESTABLISHED
ACGIH TLV: NOT ESTABLISHED
Other Recommended Limit: NONE RECOMMENDED

Physical/Chemical Characteristics

Appearance And Odor: COLORLESS TO PALE YELLOW LIQUID
Boiling Point: >401F,>205C
Melting Point: -53F,-47C
Vapor Pressure (MM Hg/70 F): UNKNOWN
Vapor Density (Air=1): UNKNOWN
[illegible] 0.84 @ 15C
Decomposition Temperature: UNKNOWN
[illegible] UNKNOWN

Report for NIIN: 010315816

Solubility In Water: INSOLUBLE
Percent Volatiles By Volume: 100
Viscosity: 8 CST @ -20C
pH: N/R
Radioactivity: N/R
Form (Radioactive Matl):
Magnetism (Milligauss): N/P
Corrosion Rate (IPY): UNKNOWN
Autoignition Temperature:

Fire and Explosion Hazard Data

Flash Point: 100F,38C
Flash Point Method: TCC
Lower Explosive Limit: 0.6%
Upper Explosive Limit: 4.7%
Extinguishing Media: CARBON DIOXIDE, DRY CHEMICAL, FOAM, AND WATER FOG.
Special Fire Fighting Proc: WEAR SELF-CONTAINED BREATHING APPARATUS AND BUNKER GEAR.
Unusual Fire And Expl Hazrds: LIQUID EVAPORATES AND FORMS VAPOR WHICH CAN CATCH FIRE AND BURN WITH EXPLOSIVE VIOLENCE. FIRE HAZARD IS GREATER AS LIQUID TEMPERATURE RISES ABOVE 85F.

Reactivity Data

Stability: YES
Cond To Avoid (Stability): DO NOT STORE OR USE NEAR SOURCES OF IGNITION. AVOID CONTACT WITH INCOMPATIBLE MATERIALS.
Materials To Avoid: STRONG OXIDIZING AGENTS
Hazardous Decomp Products: NORMAL COMBUSTION FORMS CARBON DIOXIDE & WATER VAPOR: INCOMPLETE COMBUSTION FORMS CARBON MONOXIDE.
Hazardous Poly Occur: NO
Conditions To Avoid (Poly): NONE

Health Hazard Data

LD50-LC50 Mixture: ORAL LD50 (RAT) IS > 5 ML/KG
Route Of Entry - Inhalation: YES
Route Of Entry - Skin: NO
Route Of Entry - Ingestion: NO
Health Haz Acute And Chronic: ACUTE: MAY CAUSE CENTRAL NERVOUS SYSTEM EFFECTS IF VAPORS INHALED. MAY CAUSE IRRITATION OF SKIN ON CONTACT. SWALLOWING MAY CAUSE ASPIRATION OF MATERIAL INTO LUNGS WHICH WILL DAMAGE THE LUNGS.
Carcinogenicity - NTP: NO
Carcinogenicity - IARC: NO
Carcinogenicity - OSHA: NO
Explanation Carcinogenicity: NO INGREDIENT OF A CONCENTRATION OF 0.1% OR GREATER IS LISTED AS A CARCINOGEN OR SUSPECTED CARCINOGEN.
Signs Symptoms Of Overexp: INHALED: NAUSEA, HEADACHE, DIZZINESS, DROWSINESS, LOSS OF APPETITE, LOSS OF COORDINATION, WEAKNESS. SKIN: PAIN OR FEELING OF HEAT, SWELLING, AND BLISTERING. INGESTED: NAUSEA, VOMITING.

Report for NIIN: 010315816

Med Cond Aggravated By Exp: NONE SPECIFIED BY MANUFACTURER.
Emergency/First Aid Proc: INHALED: REMOVE PERSON TO FRESH AIR. EYES: FLUSH WITH LOTS OF WATER FOR 15 MINUTES. SEE DOCTOR. SKIN: REMOVE CONTAMINATED CLOTHES. WASH THOROUGHLY WITH SOAP AND WATER. INGESTED: DO NOT INDUCE VOMITING. IF CONSCIOUS, GIVE WATER OR MILK TO DILUTE MATERIAL. GET IMMEDIATE MEDICAL ATTENTION.

Precautions for Safe Handling and Use

Steps If Matl Released/Spill: ELIMINATE ALL SOURCES OF IGNITION. CONTAIN SPILL. PUMP TO SALVAGE CONTAINERS OR ABSORB WITH INERT MATERIALS AND PLACE IN CONTAINERS FOR DISPOSAL. REPORT ALL SPILLS THAT GET INTO WATERWAYS OR SEWERS. KEEP MATERIAL FROM ENTERING SEWERS OR WATERWAYS.
Neutralizing Agent: NONE SPECIFIED BY MANUFACTURER.
Waste Disposal Method: DISPOSE OF IN ACCORDANCE WITH LOCAL, STATE AND FEDERAL REGULATIONS.
Precautions-Handling/Storing: DO NOT USE OR STORE NEAR FLAME, SPARKS, HOT SURFACES, OR WELDING. KEEP CONTAINER CLOSED. USE ONLY IN A WELL-VENTILATED AREA.
Other Precautions: DO NOT WELD, DRILL, CUT OR HEAT EMPTY CONTAINER; IT MAY CONTAIN RESIDUE WHICH CAN CATCH FIRE OR EXPLODE. DO NOT USE AS PORTABLE HEATER OR APPLIANCE FUEL. TOXIC FUMES MAY ACCUMULATE AND CAUSE DEATH.

Control Measures

Respiratory Protection: NONE NORMALLY REQUIRED.
Ventilation: USE ADEQUATE MECHANICAL VENTILATION.
Protective Gloves: NITRILE
Eye Protection: NONE NORMALLY REQUIRED.
Other Protective Equipment: CLOTHING TO PREVENT REPEATED OR PROLONGED CONTACT.
Work Hygienic Practices: WASH HANDS AFTER USE AND BEFORE EATING, DRINKING OR SMOKING. LAUNDER CONTAMINATED CLOTHES BEFORE REUSE.
Suppl. Safety & Health Data: AVIATION FUEL SHOULD BE FILTERED DURING TRANSFER INTO FUEL TANKS.

DOD Hazardous Materials Information System
DoD 6050.5-LR
AS OF April 1996
Proprietary Version - For U.S. Government Use Only

FSC: 9140
NIIN: 002732377
Manufacturer's CAGE: 0AHD1
Part No. Indicator: A
Part Number/Trade Name: FUEL, NAVAL DISTILLATE MIL-F-16884H (NATO F76)

General Information

Item Name: DIESEL FUEL DFM
Company's Name: CHEVRON ENVIRONMENTAL HEALTH CENTER
Company's Street: 15299 SAN PABLO AVE.
Company's P. O. Box: 4054
Company's City: RICHMOND
Company's State: CA
Company's Country: US
Company's Zip Code: 94804-0054
Company's Emerg Ph #: 800-457-2022
Company's Info Ph #: 800-582-3835
Distributor/Vendor # 1: FUEL SERVICE INC
Distributor/Vendor # 1 Cage: 9M887
Distributor/Vendor # 2:
Distributor/Vendor # 2 Cage:
Distributor/Vendor # 3:
Distributor/Vendor # 3 Cage:
Distributor/Vendor # 4:
Distributor/Vendor # 4 Cage:
Safety Data Action Code:
Safety Focal Point: D
Record No. For Safety Entry: 001
Total Records This Stk#: 002
Status:
Date MSDS Prepared: 10JUL89
Safety Data Review Date: 16DEC92
Supply Item Manager: KY
MSDS Preparer's Name: UNKNOWN
Preparer's Company: CHEVRON ENVIRONMENTAL HEALTH CENTER
Preparer's St Or P. O. Box: SAME
Preparer's City:
Preparer's State:
Preparer's Zip Code:
Other MSDS Number:
MSDS Serial Number: BGXGK
Specification Number: MIL-F-16884
Spec Type, Grade, Class: NONE
Hazard Characteristic Code: F4
Unit Of Issue: GL
Unit Of Issue Container Qty: AS SPECIFIED
Type Of Container: BULK
[illegible]: UNKNOWN

Report for NIIN: 002732377

NRC/State License Number: N/R
Net Explosive Weight: N/R
Net Propellant Weight-Ammo: N/R
Coast Guard Ammunition Code: N/R

Ingredients/Identity Information

Proprietary: NO
Ingredient: PETROLEUM MID-DISTILLATE (DIESEL MARINE FUEL)
Ingredient Sequence Number: 01
Percent: 100
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: 1004302PE
CAS Number: 68476-34-6
OSHA PEL: 5 MG/M3 AS OIL MIST
ACGIH TLV: 5 MG/M3 AS OIL MIST
Other Recommended Limit: NONE RECOMMENDED

Proprietary: NO
Ingredient: ADDITIVES (MAY INCLUDE:ANTI-RUST AGENT, METAL DEACTIVATOR, ANTI-OXIDANT)
Ingredient Sequence Number: 02
Percent: <1
Ingredient Action Code:
Ingredient Focal Point: D
NIOSH (RTECS) Number: 1000144AD
CAS Number:
OSHA PEL: N/K
ACGIH TLV: N/K
Other Recommended Limit:

Physical/Chemical Characteristics

Appearance And Odor: PALE YELLOW LIQUID. ODOR OF KEROSENE.
Boiling Point: >315F,>157C
Melting Point: UNKNOWN
Vapor Pressure (MM Hg/70 F): 2
Vapor Density (Air=1): UNKNOWN
Specific Gravity: 0.82
Decomposition Temperature: UNKNOWN
Evaporation Rate And Ref: NO DATA AVAILABLE
Solubility In Water: NEGLIGIBLE
Percent Volatiles By Volume: N/K
Viscosity: 1.7 CST @ 40C
pH: N/R
Radioactivity: N/R
Form (Radioactive Matl):
Magnetism (Milligauss): N/P
Corrosion Rate (IPY): N/R
Flash Point Temperature: N/K

Report for NIIN: 002732377

FRESH AIR. IF SYMPTOMS PERSISTS, GET MEDICAL ATTENTION. INGESTION: DO NOT INDUCE VOMITING. GIVE WATER OR MILK TO DRINK ONLY IF CONSCIOUS. IF VOMITIN OCCURS, KEEP HEAD BELOW HIPS. GET MEDICAL ATTENTION.

Precautions for Safe Handling and Use

Steps If Matl Released/Spill: ELIMINATE IGNITION SOURCES. STOP LEAK OR RELEASE. CLEAN UP RELEASES AS SOON AS POSSIBLE. WEAR PROTECTIVE EQUIPMENT AS REQUIRED. CONTAIN LIQUID TO PREVENT FURTHER CONTAMINATION. ABSORB WITH INERT MATERIALS OR PUMP. REPORT LARGE SPILLS TO AUTHORITIES.
Neutralizing Agent: NONE
Waste Disposal Method: PLACE CONTAMINATED MATERIALS IN DISPOSABLE CONTAINERS AND DISPOSE OF IN A MANNER CONSISTENT WITH APPLICABLE REGULATIONS. CONTACT LOCAL ENVIRONMENTAL OR HEALTH AUTHORITIES FOR APPROVE DISPOSAL OF THIS MATERIAL.
Precautions-Handling/Storing: *DO NOT USE OR STORE NEAR FLAME, SPARKS OR* HOT SURFACES. USE ONLY IN WELL VENTILATED AREA.
Other Precautions: EMPTIED CONTAINERS STILL CONTAIN HAZARDOUS OR EXPLOSIVE VAPOR OR LIQUID. CAUTION! DO NOT USE PRESSURE TO EMPTY DRUM OR EXPLOSION MAY RESULT. WARNING! DO NOT USE AS PORTABLE HEATER OR APPLIANCE FUEL. TOXI FUMES MAY ACCUMULATE & CAUSE DEATH.

Control Measures

Respiratory Protection: WEAR APPROVED RESPIRATORY PROTECTION WHEN WORKING WITH THIS MATERIAL UNLESS VENTILATION IS ADEQUATE TO KEEP AIRBORNE *CONCENTRATIONS BELOW RECOMMENDED EXPOSURE STANDARDS.*
Ventilation: USE ADEQUATE VENTILATION TO KEEP THE AIRBORNE CONCENTRATIONS OF THIS MATERIAL BELOW THE RECOMMENDED EXPOSURE STANDARD.
Protective Gloves: NEOPRENE OR BUTYL RUBBER GLOVES
Eye Protection: SAFETY GLASSES RECOMMENDED
Other Protective Equipment: WEAR IMPERVIOUS CLOTHING AS NEEDED TO PR PROLONGED AND REPEATED SKIN CONTACT.
Work Hygienic Practices: WASH THOROUGHLY AFTER HANDLING AND BEFORE EA DRINKING OR SMOKING. LAUNDER CONTAMINATED CLOTHING BEFORE REUSE.
Suppl. Safety & Health Data: BRIEF OR INTERMITTENT SKIN CONTACT WITH THIS PRODUCT IS NOT EXPECTED TO PRODUCE ANY SERIOUS EFFECTS IF IT IS WASHED FR THE SKIN. WHILE NORMAL HANDLING OF THIS PRODUCT IS NOT LIKELY TO CAUSE CANCER IN HUMANS, SKIN CONTACT AND BREATHING OF MISTS, FUMES OR VAPORS SHOULD BE REDUCED TO A MINIMUM.

Report for NIIN: 002732377

Fire and Explosion Hazard Data

Flash Point: 140F,60C
Flash Point Method: PMCC
Lower Explosive Limit: UNKNOWN
Upper Explosive Limit: UNKNOWN
Extinguishing Media: CARBON DIOXIDE, DRY CHEMICAL, AND WATER FOG.
Special Fire Fighting Proc: DO NOT ENTER ANY ENCLOSED OR CONFINED FIRE SPACE WITHOUT PROPER PROTECTIVE EQUIPMENT. THIS MAY INCLUDE SELF CONTAINED BREATHING APPARATUS.
Unusual Fire And Expl Hazrds: LIQUID EVAPORATES. INVISIBLE VAPOR CAN SPREAD EASILY AND CATCH FIRE AND BURN WITH EXPLOSIVE VIOLENCE. FIRE HAZARD INCREASES AT LIQUID TEMPERATURES ABOVE 85F.

Reactivity Data

Stability: YES
Cond To Avoid (Stability): DO NOT USE OR STORE NEAR FLAME, SPARKS OR HOT SURFACES.
Materials To Avoid: STRONG OXIDIZING AGENTS SUCH AS CHLORATES, NITRATES, PEROXIDES ETC.
Hazardous Decomp Products: NORMAL COMBUSTION FORMS CARBON DIOXIDE AND WATER VAPOR; INCOMPLETE COMBUSTION CAN PRODUCE CARBON MONOXIDE.
Hazardous Poly Occur: NO
Conditions To Avoid (Poly): NOT APPLICABLE

Health Hazard Data

LD50-LC50 Mixture: NONE SPECIFIED BY MANUFACTURER.
Route Of Entry - Inhalation: YES
Route Of Entry - Skin: NO
Route Of Entry - Ingestion: YES
Health Haz Acute And Chronic: MAY BE A MILD SKIN IRRITANT. PROLONGED BREATHING OF VAPOR CAN CAUSE CENTRAL NERVOUS SYSTEM EFFECTS. BECAUSE OF THE LOW VISCOSITY OF THIS SUBSTANCE, IT CAN DIRECTLY ENTER THE LUNGS IF IT IS SWALLOWED. THIS CAN OCCUR DURING THE ACT OF SWALLOWING OR WHEN VOMITING THIS SUBSTANCE. ASPIRATION CAN CAUSE SEVERE INJURY OR DEATH.
Carcinogenicity - NTP: NO
Carcinogenicity - IARC: NO
Carcinogenicity - OSHA: NO
Explanation Carcinogenicity: TOXICOLOGY DATA FOR SIMILAR MID-DISTILLATES SUGGEST PROLONGED OR REPEATED SKIN CONTACT MAY INCREASE RISK OF SKIN CANCER.
Signs/Symptoms Of Overexp: EYE: MILD IRRITATION. SKIN: PAIN OR FEELING OF HEAT, DISCOLORATION, SWELLING AND BLISTERING. INHALED: HEADACHE, DIZZINESS, LOSS OF APPETITE, WEAKNESS AND LOSS OF COORDINATION. INGESTION: SYSTEMIC TOXICITY OF THIS SUBSTANCE SHOULD BE PRACTICALLY NON-TOXIC TO INTERNAL ORGANS. ASPIRATION MAY CAUSE LUNG INJURY & DEATH.
Med Cond Aggravated By Exp: NONE EXPECTED.
Emergency First Aid Proc: EYE: FLUSH IMMEDIATELY WITH PLENTY OF WATER FOR 15 MINUTES WHILE LIFTING EYELIDS. GET MEDICAL ATTENTION. SKIN: REMOVE CONTAMINATED CLOTHING. WASH WITH SOAP AND WATER. INHALATION: [illegible]