PPG

Inter-Office Correspondence

DATE: June 16, 1988

TO: Lynn Royston

FROM: J. A. Barter

SUBJECT: Lake Charles Liver Function Tests

There are no formal reports, in the EA files, on the liver function tests or the meetings in which the medical surveillance protocol was developed through several draft stages. Two copies of the final protocol are attached for your use. I have also enclosed a portion of a Proposed Rule, on Air Contaminants, from the Occupational Safety and Health Administration (Federal Register 53, 20959-21398, June 7, 1988). This proposal is an attempt by OSHA to revise a number of OSHA exposure limits in one action. The rule bases proposed exposure limits on rationales for avoiding certain kinds of health effects, one of which is avoidance of liver and kidney effects. The section dealing with the part of the rule is attached. This section contains the background scientific information for these effects. The section discusses the nature of the effects, the reversibility of most occupationally caused liver effects, and the sensitivity and utility of liver enzymes as a diagnostic tool. I believe that this document should be very helpful in justifying what we are doing since both ethylene dichloride (EDC) and 1,1,2,2-tetrachloroethane are potentially present in our derivatives area as well as several other materials which are potential liver toxins but not specifically on the OSHA list.

I'll be in the office June 20-23, 1988 if you have a need to discuss this further.

J. A. Barter

J. A. Barter

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SL 042799

Federal Register

Tuesday
June 7, 1988

Part II

# Department of Labor

## Occupational Safety and Health Administration

29 CFR Part 1910

Air Contaminants; Proposed Rule

CAS: 1330-20-7; 95-47-6; 108-38-3; 106-42-3; Chemical Formula: $C_6H_4(CH_3)_2$
H.S. No. 1431

The current OSHA limit for xylene is 100 ppm as an 8-hour TWA. The ACGIH also recommends a TLV-TWA of 100 ppm, but adds a 15-minute STEL of 150 ppm. NIOSH recommends an exposure limit of 100 ppm TWA, with a 200-ppm 10-minute ceiling. Xylene and its isomers are clear, flammable liquids with an aromatic hydrocarbon odor.

Rats and rabbits exposed to a mixture of xylene isomers at a concentration of 690 ppm for 8 hours daily, six days per week showed no blood abnormalities, but rabbits exposed on the same regimen at 1150 ppm for 55 days showed a decrease in red and white blood cell counts and an increase in platelet count (Fabre and Truhaut 1954).

Studies of workers exposed to xylene revealed headache, fatigue, lassitude, irritability, and gastrointestinal disturbances as the most common symptoms (Gerarde 1960). At unspecified exposure levels, Browning (1965) also noted gastrointestinal disturbances, in addition to kidney, heart, liver, and neurological damage; blood dyscrasias, some of which result in death, were also reported in these workers. A study by Nelson, Ege, Ross et al. (1943), in which human volunteers were exposed to 200 ppm xylene, found eye, nose, and throat irritation in the subjects at this level of exposure.

NIOSH developed a Criteria Document for xylene in 1975, in which the work of Morley and his colleagues (1970) was discussed. These authors observed liver dysfunction and renal impairment in three workers overexposed to xylene (estimated concentration of 10,000 ppm). One of these workers died, but the others recovered slowly. Furniture polishers were reported by Matthaus (1964) to have suffered corneal damage as a result of exposure to xylene at unknown concentrations.

OSHA preliminarily concludes that both a TWA and STEL are necessary to prevent risk of narcosis, blood effects, and irritant effects at the elevated levels possible at the current exposure limit. To reduce this risk, OSHA is proposing a 150-ppm STEL and a 100-ppm TWA. The health evidence forms a reasonable basis for proposing a revision to this level. At the time of the final rule, OSHA will establish a new limit for xylene if the Agency determines that this limit will substantially reduce significant risk.

ZINC CHLORIDE (FUME)
CAS: 7646-85-7; Chemical Formula: $ZnCl_2$
H.S. No. 1435

OSHA's current PEL for zinc chloride is 1 mg/m³ as an 8-hour TWA. The ACGIH has established a TLV-TWA of 1 mg/m³, with a STEL of 2 mg/m³. Zinc chloride fume is white and has an acrid odor.

Zinc chloride fume is highly caustic and damages the mucous membranes of the nasopharynx and respiratory tract. Exposure to the fumes of zinc chloride may result in a severe pneumonitis that is caused by irritation of the respiratory tract (Gafafer 1964). One instance in which a worker inhaled zinc chloride fumes resulted in advanced pulmonary fibrosis that ended in death (Milliken, Waugh, and Kadish 1963), and 10 deaths and 25 non-fatal cases of pneumonitis occurred in workers caught in a tunnel when 79 smoke generators caught fire and generated zinc chloride fumes (Hunter 1955). Other studies have shown that zinc chloride exposures cause skin ulceration (Sax 1957). It has also been suggested that zinc chloride exposure may have chronic effects (Hamilton and Hardy 1974). In an investigation of the adverse effects of zinc chloride fume exposures, Ferry (personal communication 1966, as cited in the ACGIH 1986, p. 643) reported that no sensory effects occurred when 30 minute exposures were limited to 0.07 and 0.4 mg/m³; however, this researcher noted that these levels did corrode metal.

OSHA preliminarily concludes that the risk of damage to the eyes, skin, and respiratory tract associated with exposure to zinc chloride fume should be substantially reduced by establishing a STEL and TWA to protect against elevated short-term and long-term exposures to this substance. The health evidence forms a reasonable basis for proposing a revision to this level. At the time of the final rule, OSHA will establish a new limit for zinc chloride if the Agency determines that this limit will substantially reduce significant risk.

*Preliminary Conclusions*

OSHA's preliminary finding is that sensory irritation poses an occupational health risk to workers exposed to these substances at the existing hazardous levels. Among the adverse health consequences of exposure to sensory irritants are acute breathing difficulty, eye tearing, conjunctivitis, sensitization, persistent coughing, and upper respiratory tract irritation. In addition to the pain and suffering associated with these signs and symptoms, workers experiencing irritant effects find it difficult if not impossible to concentrate on the job at hand; thus they work less safely and less productively than non-exposed employees. Reducing exposures from levels that have been associated with these effects to levels where such consequences are substantially less likely to occur will reduce the risk posed to workers at current levels.

The health evidence for these substances forms a reasonable basis for proposing revised or new limits. At the time of the final rule, OSHA will establish new or revised limits for these sensory irritants if the Agency determines that these limits will substantially reduce significant risks.

4. Substances for Which Proposed Limits Are Based on Avoidance of Liver or Kidney Effects

*Introduction*

The liver or kidneys are the primary target organs affected by toxic exposures to a number of industrial chemicals. In recognition of this target organ toxicity, OSHA is proposing new or revised limits for 17 hepato- or nephrotoxic compounds (12 hepatotoxins and five nephrotoxins). For these substances, the liver or kidney is probably the organ most sensitive to the effects of exposure. Thus, establishing permissible exposure limits that are low enough to prevent toxicity to these target organs generally also protects other organ systems.

Seventeen compounds for which revised limits are being proposed produce kidney or liver effects in overexposed individuals. For seven of these substances, OSHA is proposing to lower the PEL, and for one other substance, OSHA is also proposing the adoption of a short-term exposure limit. For five liver or kidney toxins, OSHA is proposing a PEL where none formerly existed, and in three cases, OSHA proposes to retain the current PEL but to add a STEL where none formerly existed. For four chemicals in this category, NIOSH recommends limits lower than those established by the ACGIH, and for one of these substances, OSHA proposes adoption of the NIOSH RELs; in three cases, the NIOSH and ACGIH limits are essentially the same. The sections below discuss liver and kidney toxins separately. Table C4-1 shows these hepatotoxic substances, their OSHA, ACGIH, and NIOSH limits, and their CAS and HS numbers; Table C4-2 provides the same information for the nephrotoxins in this group.

**Liver Toxicity**

*Description of the Health Effects*

Although the precise mechanisms by which these compounds cause liver damage are only partly understood, the development and manifestation of liver

toxicity are similar for all of them. In general, liver toxicity is a graded response, i.e., the severity of the lesion is directly proportional to the intensity/duration of exposure. Although many of the effects caused by exposure to these substances are reversible, some are not.

Liver damage is not a single entity; the manner in which it is manifested depends on the dose, duration, and particular chemical agent involved. For example, acute exposures may cause lipid to accumulate in the hepatocytes, cellular death, and/or hepatobiliary dysfunction. In contrast, chronic exposures may lead to cirrhotic changes and the development of neoplasms. Fatty accumulation and necrosis can be either localized or widespread, and chemical-induced lesions resulting from chronic exposures can cause marked changes of the entire liver (Plaa 1986).

Typically, the earliest and most sensitive indicators of liver toxicity are alterations in biochemical liver functions, such as changes in specific enzyme activities. These may be accompanied by changes in the morphology of specific organelles in hepatocytes. For example, relatively low doses of halogenated aliphatic hydrocarbons, such as allyl chloride, carbon tetrabromide, and 1,1-dichloroethane, cause an increase in the activity of microsomal mixed function oxidase enzymes. This increase is ordinarily accompanied by proliferation of the endoplasmic reticulum.

BILLING CODE 4510-26-M

Table C4-1. List of Substances For Which Limits Are Based Primarily on Avoidance of Liver Toxicity

| H.S. Number/ Chemical Name | CAS No. | Current PEL* | ACGIH TLV** | NIOSH REL*** |
|---|---|---|---|---|
| 1011 Allyl chloride | 107-05-1 | 1 ppm TWA | 1 ppm TWA<br>2 ppm STEL | 1 ppm TWA<br>3 ppm Ceiling<br>(15 min) |
| 1072 Carbon tetrabromide | 558-13-4 | - | 0.1 ppm TWA<br>0.3 ppm STEL | - |
| 1089 o-Chlorostyrene | 2039-87-4 | - | 50 ppm TWA<br>75 ppm STEL | - |
| 1108 Cyclohexanone | 108-94-1 | 50 ppm TWA | 25 ppm TWA, Skin | 25 ppm TWA |
| 1145 Dioxane | 123-91-1 | 100 ppm TWA,<br>Skin | 25 ppm TWA, Skin | 1 ppm Ceiling<br>(30 min) |
| 1168 Ethylene dichloride+ | 107-06-2 | 50 ppm TWA<br>100 ppm STEL<br>200 ppm Ceiling | 10 ppm TWA | 1 ppm TWA<br>2 ppm Ceiling<br>(15 min) |
| 1205 Hydrazine | 302-01 1 | 1 ppm TWA, Skin. | 0.1 ppm TWA, Skin | 0.03 ppm Ceiling<br>(120 min) |
| 1269 Methylcyclohexanol | 25639-42-3 | 100 ppm TWA | 50 ppm TWA | |
| 1295 Octachloro-<br>naphthalene | 2234-13 1 | 0.1 mg/m$^3$ TWA,<br>Skin | 0.1 mg/m$^3$ TWA<br>0.3 mg/m$^3$ STEL<br>Skin | |

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Table C4-1. List of Substances For Which Limits Are Based Primarily on Avoidance of Liver Toxicity (continued)

| H.S. Number/ Chemical Name | CAS No. | Current PEL* | ACGIH TLV** | NIOSH REL*** |
|---|---|---|---|---|
| 1341 Propylene dichloride | 78-87-5 | 75 ppm TWA | 75 ppm TWA<br>110 ppm STEL | — |
| 1385 1,1,2,2-Tetrachloroethane | 79-34-5 | 5 ppm TWA, Skin | 1 ppm TWA, Skin | Lowest feasible level |
| 1407 1,2,3-Trichloropropane | 96-18-4 | 50 ppm TWA | 10 ppm TWA, Skin | — |

* OSHA's TWA limits are for 8-hour exposures; its STELs are for the durations specified; and its ceilings are peaks not to be exceeded for any period of time.

** The ACGIH TWA-TLV is for an 8-hour exposure; its STELs are 15-minute limits not to be exceeded more than 4 times per day with a minimum of 60 minutes between successive STEL exposures; and its ceilings are peaks not to be exceeded for any period of time.

*** NIOSH TWA limits are for 10-hour exposures unless otherwise specified, and its ceilings are peaks not to be exceeded for any period of time unless a duration is specified in parentheses.

+ Proposed limit is the NIOSH REL.

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Table C4-2. List of Substances For Which Limits are Based Primarily on Avoidance of Kidney Toxicity

| H.S. Number/ Chemical Name | CAS No. | Current PEL* | ACGIH TLV** | NIOSH REL*** |
|---|---|---|---|---|
| 1129 1,3-Dichloropropene | 542-75-6 | - | 1 ppm TWA, Skin | -- |
| 1132 Dicyclopentadiene | 77-73-6 | - | 5 ppm TWA | - |
| 1166 Ethyl silicate | 78-10-4 | 100 ppm TWA | 10 ppm TWA | - |
| 1195 Hexachlorobutadiene | 87-68-3 | - | 0.02 ppm TWA, Skin | - |
| 1203 Hexone (Methyl isobutyl ketone) | 108-10-1 | 100 ppm TWA | 50 ppm TWA 75 ppm STEL | 50 ppm TWA |

* OSHA's TWA limits are for 8-hour exposures; its STELs are for the durations specified; and its ceilings are peaks not to be exceeded for any period of time.

** The ACGIH TWA-TLV is for an 8-hour exposure; its STELs are 15-minute limits not to be exceeded more than 4 times per day with a minimum of 60 minutes between successive STEL exposures; and its ceilings are peaks not to be exceeded for any period of time.

*** NIOSH TWA limits are for 10-hour exposures unless otherwise specified, and its ceilings are peaks not to be exceeded for any period of time unless a duration is specified in parentheses.

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Many compounds that damage the liver, such as 1,1,2,2-tetrachloroethane, also cause an abnormal accumulation of fat, especially triglycerides, in liver cells. In experimental animals this effect is manifested as an accumulation of microscopic vacuoles in liver cells. In humans, however, the only grossly detectable manifestation of this effect is increased liver size, which is an indication of severe fat accumulation in the liver.

At sufficiently high doses, most substances that damage the liver cause cell death that leads to tissue necrosis or gangrene. This necrosis may initially be localized, but at higher or more sustained exposure levels the entire liver may be involved. Moderate to severe liver necrosis is usually accompanied by increased concentrations of marker enzymes such as glutamate-pyruvate transaminase or glutamate-oxaloacetate transaminase in the serum; the detection of these substances in the serum of exposed individuals can thus be a useful diagnostic tool.

*Dose-Response Characteristics*

The development of liver and other organ damage in humans and animals is progressive; it begins with subcellular changes, progresses to the cellular level, and is finally manifested as whole-organ damage. This progression is related to the intensity/duration of dose; i.e., as dose increases, cellular death becomes widespread and eventually causes liver dysfunction. The extent to which liver damage is reversible follows a similar continuum; since the liver can regenerate, minor cellular damage or transient disease states are usually reversible if exposure ceases. However, if exposure continues, the capacity of the liver to regenerate is exceeded and permanent damage results.

As is the case for some chemically induced toxic effects, there appears to be a NOE level below which hepatotoxic effects do not occur.

The following paragraphs describe OSHA's preliminary results for all of the substances in this group of hepatotoxins and discuss the nature of the risk experienced by exposed workers.

ALLYL CHLORIDE
CAS: 107-05-1; Chemical Formula: $CH_2=CHCH_2Cl$
H.S. No. 1011

The current OSHA PEL for allyl chloride is a 1 ppm (3 mg/m³) 8-hour TWA; the ACGIH-recommended TLV-TWA is also 1 ppm, with a 15-minute STEL of 2 ppm. NIOSH has recommended a 1 ppm 10-hour TWA and a 3 ppm 15-minute STEL for this substance. Allyl chloride is a colorless liquid with an unpleasant, pungent odor.

Studies of animal exposures to allyl chloride indicate that the chemical is among the most toxic of the halogenated aliphatic hydrocarbons, producing mucous membrane irritation, mild narcosis, and, at higher concentrations, histologic lesions of the lungs and kidneys (Adams, Spencer, and Irish 1940). Even single exposures lasting only a few minutes at concentrations between 1 and 100 mg/liter (332 to 32,000) caused mucous membrane irritation in various laboratory animals (Adams, Spencer, and Irish 1940). Further animal studies have confirmed liver and kidney pathology in many species (Torkelson, Wolf, Oyen, et al. 1959) and female rats exhibited kidney pathology after exposure to 3 ppm for 6 months.

Human exposures to concentrations of 1 to 113 ppm caused abnormal liver test results (Hausler and Lenich 1968). OSHA therefore proposes that both a STEL of 2 ppm and a 1 ppm TWA are required. The Agency preliminarily concludes that a combined limit is necessary to protect employees from the risk of mucous membrane irritation potentially associated with the elevated short-term exposures to allyl chloride currently permitted by the 8-hour TWA alone. The health evidence forms a reasonable basis for proposing a revision to this level. At the time of the final rule, OSHA will establish a new limit for allyl chloride if the Agency determines that this limit will substantially reduce significant risk.

CARBON TETRABROMIDE
CAS: 558-13-4; Chemical Formula: $CBr_4$
H.S. No. 1072

OSHA's current Z tables have no limits for exposure to carbon tetrabromide. The ACGIH limit is a 0.1 ppm TWA and a 0.3 ppm STEL. Carbon tetrabromide's hepatotoxic effects include both fatty infiltration and necrosis. The 0.1 ppm and 0.3 ppm levels were selected based on an observed no-effect level at 0.1 ppm; this finding derives from a study in which rats were exposed to carbon tetrabromide by inhalation for 7 hours per day, 5 days per week for 6 months (Torkelson and Rowe 1981). OSHA believes that controlling workplace exposures to these levels will prevent adverse effects in exposed workers. OSHA preliminarily concludes that establishing a limit for this previously unregulated chemical will protect workers against the risk of experiencing its hepatotoxic effects and will achieve a substantial reduction in this risk. The health evidence forms a reasonable basis for proposing a new limit for carbon tetrabromide. At the time of the final rule, OSHA will promulgate a new limit if the Agency determines that this limit will substantially reduce significant risk.

o-CHLOROSTYRENE
CAS: 2039-87-4; Chemical Formula: $C_8H_7Cl$
H.S. No. 1089

OSHA has no current limit for o-chlorostyrene. The ACGIH recommends a TLV-TWA of 50 ppm with a TLV-STEL of 75 ppm. o-Chlorostyrene is a liquid.

In an unpublished report, the Dow Chemical Company (1973) describes the results of an o-chlorostyrene inhalation study in rats, rabbits, guinea pigs, and dogs. Dow exposed the animals to an average concentration of 101 ppm for 7 hours daily, 5 days a week, for a total of 130 exposures in 180 days. No adverse effects were observed in any species in terms of appearance, growth, behavior, mortality, hematology, BUN, alkaline phosphatase, SGPT, BSP, organ weights, or gross pathology (Dow Chemical Company, unpublished report, 1973). Microscopic examination of animal tissue revealed a somewhat higher incidence of pathological liver and kidney changes. There is evidence indicating that the warning properties of o-chlorostyrene do not permit workers to recognize concentrations of o-chlorostyrene of 100 ppm. Based on o-chlorostyrene's structural analogy to styrene, for which short-term exposures of 100 ppm have been demonstrated to produce neuropathic and narcotic effects (Stewart, Dodd, Baretta, and Schaffer 1968), a short-term limit is necessary (ACGIH 1986, p. 136).

OSHA is proposing a PEL of 50 ppm as an 8-hour TWA and a 15-minute STEL of 75 ppm for o-chlorostyrene. The Agency preliminarily concludes that both of these limits will protect against the risk of narcosis and neuropathy to which workers could potentially be exposed in the absence of any OSHA limit. The health evidence forms a reasonable basis for proposing a revision to this level. At the time of the final rule, OSHA will establish a new limit for o-chlorostyrene if the Agency determines that this limit will substantially reduce significant risk.

CYCLOHEXANONE
CAS: 108-94-1; Chemical Formula: $C_6H_{10}O$
H.S. No. 1108

OSHA has a current limit of 50 ppm TWA for cyclohexanone. Both the ACGIH and NIOSH recommend a time-weighted average of 25 ppm, and the ACGIH also recommends a skin notation. Cyclohexanone is a white to pale yellow oily liquid with an odor

similar to that of acetone and peppermint.

Cyclohexanone has a low order of acute toxicity in animals. A concentration of 2000 ppm inhaled for 4 hours was lethal to 1 of 6 rats; at 4000 ppm, all of the exposed animals died. In rabbits, the dermal $LD_{50}$ was 1000 mg/kg (Smyth et al. 1969). Rabbits showed marked irritation and some corneal injury when undiluted cyclohexanone was instilled in the eye (Carpenter and Smyth 1946). Guinea pigs exposed to 4000 ppm for 6 hours showed narcotic symptoms, lacrimation, salivation, depression of body temperature and heart rate, and corneal opacity (Specht et al. 1940). Rabbits exhibited degenerative changes of the liver and kidneys after 50 daily 6-hour inhalation exposures to 190 ppm (Treon, Crutchfield, and Kitzmiller 1943). Exposures to 309 ppm cyclohexanone on the same regimen caused conjunctival congestion, while exposures to 3000 ppm were lethal to some of the exposed animals (Treon, Crutchfield, and Kitzmiller 1943). In humans, Nelson and co-workers (1943) report that irritation caused by exposure to cyclohexanone was intolerable at 50 ppm, however, 25 ppm was not objectionable to most subjects in 3- to 5-minute exposures.

OSHA is proposing a 25-ppm 8-hour TWA and a skin notation for cyclohexanone. The Agency preliminarily concludes that these two limits will prevent the risk of respiratory and skin irritation associated with cyclohexanone exposures at levels below the existing PEL of 50 ppm. The health evidence forms a reasonable basis for proposing a revision to this level. At the time of the final rule, OSHA will establish a new limit for cyclohexanone if the Agency determines that this limit will substantially reduce significant risk.

DIOXANE
CAS: 123-91-1; Chemical Formula: $O(CH_2CH_2)_2O$
H.S. No. 1145

OSHA's current PEL for dioxane is 100 ppm as an 8-hour TWA, with a skin notation. NIOSH recommends a 1-ppm 30-minute ceiling for dioxane, and the ACGIH has established a 25-ppm TLV-TWA, with a skin notation. The proposed 25-ppm PEL reflects new toxicological data for this substance. A 2-year drinking water study conducted by the Dow Chemical Company, in which male and female rats were given water containing 1.0, 0.1, or 0.01 percent dioxane, showed that animals given the highest dose developed liver and nasal tumors, as well as pathological changes in the liver and kidney. Rats in the 0.1-percent group showed renal tubular sloughing and hepatocellular degeneration but no significant increase in neoplasms. Because this study demonstrated hepato- and nephrotoxic effects at doses 10 times lower than the dose causing cancer in animals, the ACGIH established the TLV based on dioxane's liver and kidney effects rather than its carcinogenicity. A study by Torkelson et al. (1974) in four species of animals exposed to multiple daily airborne exposures of dioxane at 50 ppm showed no gross or histopathologic organ changes, leading the ACGIH to recommend 25 ppm as an appropriate level to protect against liver and kidney effects in exposed workers (ACGIH 1986). In this case, the ACGIH is using a safety factor to establish the 8-hour limit, i.e., is applying a safety factor of 2 to the results of an animal study in four species that showed no gross or histopathological changes at 50 ppm.

The 25-ppm TLV is based on hepato- and nephrotoxic effects, since the ACGIH evaluation determined that these effects were more severe than the potential for carcinogenicity. OSHA does not generally accept such a rationale; however, OSHA is unable to perform the necessary risk assessment to evaluate the question of carcinogenicity in time for this rulemaking. The 1-ppm (ceiling) REL is based on cancer potential and appears to represent the "lowest concentration reliably measured," a criterion that would not satisfy OSHA feasibility requirements. OSHA therefore proposes that a PEL of 25 ppm TWA, with a skin notation, be adopted at the present time to reduce the risk that currently exists. As future priorities permit, OSHA will consider the need for a more stringent PEL.

ETHYLENE DICHLORIDE
CAS: 107-06-2; Chemical Formula: $ClCH_2CH_2Cl$
H.S. No. 1168

The current OSHA standard for ethylene dichloride is 50 ppm as an 8-hour TWA, a 100-ppm ceiling (maximum duration of 5 minutes in any 3 hours), and a 200-ppm peak; these limits were derived from limits recommended by the American National Standards Institute in 1969. In 1980, the ACGIH reduced its TLV to 10 ppm as an 8-hour TWA. NIOSH (1978) has concluded that ethylene dichloride should be considered a potential human carcinogen and has recommended 1-ppm 10-hour TWA and 2-ppm 15-minute short-term limits. Several studies indicate that the current OSHA PELs are insufficient to protect workers against hepatotoxic and other adverse effects. A paper by Kozik (1957) reported that workers generally exposed below 16 ppm but occasionally exposed to levels between 30 and 50 ppm experienced adverse liver and nervous system effects. In addition, Brzozowski (1954) reported abnormal changes in the blood of 50 percent of workers (8 of 16) exposed to between 10 and 37 ppm of ethylene dichloride. The ACGIH also cited numerous animal studies that consistently show hepatotoxic effects caused by exposure to ethylene dichloride; the ACGIH concluded that ethylene dichloride "clearly belongs in the group of hepatotoxic halogenated hydrocarbons" (ACGIH 1986). Based on these findings, the ACGIH (1986) recommended a reduction in the 8-hour TLV-TWA to 10 ppm.

In August 1978, NIOSH recommended that exposure to ethylene dichloride be minimized in response to an NCI bioassay (1978) showing that ethylene dichloride induced liver cancer in both sexes of mice and rats. NIOSH (1978) subsequently recommended a 1-ppm 10-hour TWA and a 2-ppm 15-minute short-term limit.

OSHA preliminarily concludes that the studies of Kozik (1957) and Brzozowski (1954) clearly indicate that a risk of hepatotoxicity, nervous system effects, and hematopoietic effects exists at the current 50-ppm 8-hour TWA PEL. The 10-ppm TLV recommended by the ACGIH does not afford protection at the levels (10 to 37 ppm) where abnormal blood changes were measured in 50 percent of the workers studied. Therefore, OSHA believes it necessary to reduce its current limits for ethylene dichloride to reduce this risk (as well as to protect against potential carcinogenic effects) and is proposing to revise these limits to 1 ppm as a TWA and 2 ppm as a STEL. The Agency's preliminary feasibility analysis is based on limited data at these levels; OSHA requests additional feasibility information from the public. The health evidence forms a reasonable basis for proposing a revision to this level. At the time of the final rule, OSHA will establish a new limit for ethylene dichloride if the Agency determines that this limit will substantially reduce significant risk.

HYDRAZINE
CAS: 302-01-2; Chemical Formula: $H_2N-NH_2$
H.S. No. 1205

The current OSHA limit for hydrazine is 1 ppm as an 8-hour TWA, with a skin notation. The ACGIH (1986) has recommended a TLV-TWA of 0.1 ppm, also with a skin notation. Because of its potential carcinogenic hazard, NIOSH (1978a) has recommended that

PROTOCOL FOR MEDICAL SURVEILLANCE OF Current Protocol

THE LAKE CHARLES DERI\ Revised 5/11/89

PURPOSE

PPG Industries' policy is to protect
being of its employees and to be in c
applicable laws, standards, rules and
in the Blueprint. These guidelines a
Charles physicians assessing employee
the Derivative Area of that plant. T
meant to assist the Lake Charles plan
implementing the policy. PPG physici
exercise their clinical judgements an
consult with the PPG Corporate Medica

EMPLOYEES INCLUDED

Employees assigned, or with the potential for assignment (shipping and operations employees and maintenance employees) to the Derivative Area, will participate in the Lake Charles "Derivative" medical surveillance program.

EXAMINATION FREQUENCY

Examinations will be given prior to assignment in the Derivatives Area, and at least annually thereafter. Employees who have worked in the area for ten (10) years or longer will have semi-annual examinations (containing the elements in the following section titled SCOPE OF EXAMINATIONS) done in addition to their annual examinations. Employees who are covered must be followed under the corporate Health Care Policy until applicable latency periods have expired.

SCOPE OF EXAMINATIONS

The annual examinations include the following elements from the OSHA Vinyl Chloride Standard (29 CFR 1910.1017):

1. A general physical examination shall be performed, with specific attention to detecting enlargement of liver, spleen or kidneys, or dysfunction in these organs, and for abnormalities in the skin, connective tissue and the pulmonary system,
2. Blood chemistries (see those listed under section titled BLOOD CHEMISTRY PROGRAM),
3. Medical and Work History (see those listed under section titled MEDICAL AND WORK HISTORY).

The examinations provided semiannually to those employees

# PROTOCOL FOR MEDICAL SURVEILLANCE OF EMPLOYEES ASSIGNED TO THE LAKE CHARLES DERIVATIVE AREA

## PURPOSE

PPG Industries' policy is to protect the health and well being of its employees and to be in compliance with all applicable laws, standards, rules and regulations as outlined in the Blueprint. These guidelines are provided for the Lake Charles physicians assessing employees assigned to work in the Derivative Area of that plant. These guidelines are meant to assist the Lake Charles plant physician in implementing the policy. PPG physicians will continue to exercise their clinical judgements and are encouraged to consult with the PPG Corporate Medical Director.

## EMPLOYEES INCLUDED

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2. Blood chemistries (see those listed under section titled BLOOD CHEMISTRY PROGRAM),
3. Medical and Work History (see those listed under section titled MEDICAL AND WORK HISTORY).

The examinations provided semiannually to those employees

with ten (10) or more years of possible exposure to vinyl chloride include the following:

1. Blood chemistries (see those listed under section titled BLOOD CHEMISTRY PROGRAM),
2. A clinical examination that includes a stethoscope examination of the heart and lungs,
3. Palpation of the abdomen and back for abnormalities of liver, spleen and kidneys.
4. Examination of the skin.

BLOOD CHEMISTRY PROGRAM

1. Fasting blood chemistries will be drawn for all examinations per the above criteria. These chemistries must include those mandated by the OSHA Vinyl Chloride Standard. These are:

Total Bilirubin
Alkaline Phosphatase
Aspartate Aminotransferase (AST or SGOT)
Alanine Aminotransferase (ALT or SGPT)
Gamma-Glutamyl Transpeptidase (GGTP)

In addition to these, a triglyceride and cholesterol analysis must also be performed.

2. If any of the screening tests are abnormal (by the limits of the laboratory performing the analysis), a second sample should be obtained within four weeks. If this is normal, an additional confirming sample must be obtained in not less than four nor more than 12 weeks following the first (normal sample).

3. If the analysis of the second sample yields more than one blood chemistry as abnormal (especially if an increasing trend is noted in a test result), or if there is an isolated result that is greater than 2.0 times normal, consideration should be given to restricting the individual from the Derivatives Area. Additional tests which may be useful are included in Appendix A of the OSHA Vinyl Chloride Standard. The blood chemistries are primary screening tests performed to detect abnormal liver function ; however, they are not specific for liver disease and the examining physician must therefore evaluate each employee on an individual basis. If the plant physician feels the need clinically for a second opinion to help arrive at a decision on restriction, a gastroenterologist (who is knowlegable of the OSHA Vinyl Chloride Standard) should be consulted.

MEDICAL and WORK HISTORY

An employee medical and work history must be taken and kept current. The medical history taken shall include those topics identified by the OSHA Vinyl Chloride Standard:

1. alcohol intake;

2. past history of hepatitis;
3. work history and past exposure to hepatotoxic agents; including drugs and chemicals;
4. past history of blood transfusions;
5. past history of hospitalization.

In addition, information as to exposure to hepatotoxins can be obtained from the current industrial hygiene air monitoring data base for the job assigned the employee.

RISK FACTORS

The physicians and his staff will work with each employee on an individual basis to determine and suggest modifications to reduce any risk factors which could be causing or contributing to abnormal blood chemistry results.

WORK RESTRICTIONS

An employee must be restricted from the Derivatives Area whenever the examination reveals clinical findings that, coupled with abnormal blood chemistries, indicate a medical condition which could place the employee at risk. Employees at risk will remain restricted and followed until the condition returns to normal or until the etiology of the condition has been possibly identified and documented.

AIR MONITORING REQUIREMENT

1. A current exposure profile for each job and a copy of the employees individual monitoring results shall also be maintained in the medical records for review by the plant physician.

Date 5/11/89 Signatures _____
Plant Representative

Date 5/11/89 _____
Group Representative

Date 5-11-89 _____
Corporate Medical Director

# PROTOCOL FOR MEDICAL SURVEILLANCE OF EMPLOYEES ASSIGNED TO THE LAKE CHARLES DERIVATIVE AREA

Original Protocol
Now replaced by 5/11/89 update

## PURPOSE

PPG Industries' policy is to protect th
being of its employees and to be in com
applicable laws, standards, rules and r
in the Blueprint. These guidelines are
Charles physicians assessing employees
the Derivative Area of that plant. The
meant to assist the Lake Charles plant
implementing the policy. PPG physician
exercise their clinical judgements and
consult with the PPG Corporate Medical

## EMPLOYEES INCLUDED

Employees assigned, or with the potenti
(shipping and operations employees and
to the Derivative Area, will participate in the Lake Charles
"Derivative" medical surveillance program.

## EXAMINATION FREQUENCY

Examinations will be given prior to assignment in the Derivatives Area, and at least annually thereafter. Employees who have worked in the area for ten (10) years or longer will have semi-annual examinations (containing the elements in the following section titled SCOPE OF EXAMINATIONS) done in addition to their annual examinations. Employees who are covered must be followed under the corporate Health Care Policy until applicable latency periods have expired.

## SCOPE OF EXAMINATIONS

The annual examinations include the following elements from the OSHA Vinyl Chloride Standard (29 CFR 1910.1017):

1. A general physical examination shall be performed, with specific attention to detecting enlargement of liver, spleen or kidneys, or dysfunction in these organs, and for abnormalities in the skin, connective tissue and the pulmonary system,
2. Blood chemistries (see those listed under section titled BLOOD CHEMISTRY PROGRAM),
3. Medical and Work History (see those listed under section titled MEDICAL AND WORK HISTORY).

The examinations provided semiannually to those employees

# PROTOCOL FOR MEDICAL SURVEILLANCE OF EMPLOYEES ASSIGNED TO THE LAKE CHARLES DERIVATIVE AREA

## PURPOSE

PPG Industries' policy is to protect the health and well being of its employees and to be in compliance with all applicable laws, standards, rules and regulations as outlined in the Blueprint. These guidelines are provided for the Lake Charles physicians assessing employees assigned to work in the Derivative Area of that plant. These guidelines are meant to assist the Lake Charles plant physician in implementing the policy. PPG physicians will continue to exercise their clinical judgements and are encouraged to consult with the PPG Corporate Medical Director.

## EMPLOYEES INCLUDED

Employees assigned, or with the potential for assignment (shipping and operations employees and maintenance employees) to the Derivative Area, will participate in the Lake Charles "Derivative" medical surveillance program.

## EXAMINATION FREQUENCY

Examinations will be given prior to assignment in the Derivatives Area, and at least annually thereafter. Employees who have worked in the area for ten (10) years or longer will have semi-annual examinations (containing the elements in the following section titled SCOPE OF EXAMINATIONS) done in addition to their annual examinations. Employees who are covered must be followed under the corporate Health Care Policy until applicable latency periods have expired.

## SCOPE OF EXAMINATIONS

The annual examinations include the following elements from the OSHA Vinyl Chloride Standard (29 CFR 1910.1017):

1. A general physical examination shall be performed, with specific attention to detecting enlargement of liver, spleen or kidneys, or dysfunction in these organs, and for abnormalities in the skin, connective tissue and the pulmonary system,
2. Blood chemistries (see those listed under section titled BLOOD CHEMISTRY PROGRAM),
3. Medical and Work History (see those listed under section titled MEDICAL AND WORK HISTORY).

The examinations provided semiannually to those employees

with ten (10) or more years of possible exposure to vinyl chloride include the following:

1. Blood chemistries (see those listed under section titled BLOOD CHEMISTRY PROGRAM),
2. A clinical examination that includes a stethoscope examination of the heart and lungs,
3. Palpation of the abdomen and back for abnormalities of liver, spleen and kidneys.
4. Examination of the skin.

BLOOD CHEMISTRY PROGRAM

1. Fasting blood chemistries will be drawn for all examinations per the above criteria. These chemistries must include those mandated by the OSHA Vinyl Chloride Standard. These are:

Total Bilirubin
Alkaline Phosphatase
Aspartate Aminotransferase (AST or SGOT)
Alanine Aminotransferase (ALT or SGPT)
Gamma-Glutamyl Transpeptidase (GGTP)

In addition to these, a triglyceride and cholesterol analysis must also be performed.
2. If any of the screening tests are abnormal (by the limits of the laboratory performing the analysis), a second sample should be obtained within four weeks. If this is normal, an additional confirming sample must be obtained in not less than four nor more than 12 weeks following the first (normal sample).
3. If the analysis of the second sample yields more than one blood chemistry as abnormal (especially if an increasing trend is noted in a test result), or if there is an isolated result that is greater than 2.0 times normal, consideration should be given to restricting the individual from the Derivatives Area. Additional tests which may be useful are included in Appendix A of the OSHA Vinyl Chloride Standard. The blood chemistries are primary screening tests performed to detect abnormal liver function ; however, they are not specific for liver disease and the examining physician must therefore evaluate each employee on an individual basis. If the plant physician feels the need clinically for a second opinion to help arrive at a decision on restriction, a gastroenterologist (who is knowlegable of the OSHA Vinyl Chloride Standard) should be consulted.

MEDICAL and WORK HISTORY

An employee medical and work history must be taken and kept current. The medical history taken shall include those topics identified by the OSHA Vinyl Chloride Standard:

1. alcohol intake;

2. past history of hepatitis
3. work history and past exposure to hepatotoxic agents, including drugs and chemicals;
4. past history of blood transfusions;
5. past history of hospitalization.

In addition, information as to exposure to hepatotoxins can be obtained from the current industrial hygiene air monitoring data base for the job assigned the employee.

RISK FACTORS

The physician and his staff will work with each employee on an individual basis to determine and suggest modifications to reduce any risk factors which could be causing or contributing to abnormal blood chemistry results.

WORK RESTRICTIONS

An employee must be restricted from the Derivatives Area whenever the examination reveals clinical findings that, coupled with abnormal blood chemistries, indicate a medical condition which could place the employee at risk. Employees at risk will remain restricted and followed until the condition returns to normal or until the etiology of the condition has been possibly identified and documented.

SPECIAL AIR MONITORING REQUIREMENT

1. Employees with abnormal blood chemistries will have personal monitoring performed weekly as long as the employee remains in the Derivative Area.
2. A current exposure profile for each job and a copy of the employees individual monitoring results shall be maintained in the medical records for review by the plant physician.

Date August 10, 1987 Signature Carl B. Myers, M.D.

Carl B. Myers, M. D.