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# DIOXIN: ENVIRONMENTAL IMPACTS AND POTENTIAL HUMAN HEALTH EFFECTS

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AUTHOR:

Robert Kainz

Environmental Health Fellow

Michael M. Simpson

Science Policy Research Division

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## ISSUE DEFINITION

Animal studies indicate that dioxin is a highly toxic compound; however, there have been no human deaths attributed to exposure to dioxin. Current concerns about dioxin center around the potential adverse environmental impacts as well as the possible harmful human health effects of trace dosages encountered as environmental contaminants. The environmental impact and human health effects of such exposure to dioxin are not clear at this time.

Conflicting statements regarding the effects of dioxin exposure are found in both scientific and popular journals. This controversy stems from the lack of conclusive findings from well-defined exposure studies. Policymakers are consequently confronted with deciding whether or not to take regulatory or other action to address fears about the threat to health and the environment, in the absence of confirmed findings on the risks associated with dioxin.

This issue brief presents a short background on the physical/chemical properties of dioxin, describes several existing sources of possible human exposure, and highlights what is currently known about its environmental impacts and human health effects. Congressional interest is intense at this time because of large numbers of Vietnam veterans' claims for benefits associated with use of herbicides in that war as well as because of certain incidents of potential significance to health involving disposal of wastes containing dioxin. (See also IB83043 -- Agent Orange: Veterans' Complaints and Studies of Health Effects.)

## BACKGROUND AND POLICY ANALYSIS

The compound dioxin was identified when it was synthesized by a research technician in the mid-1950s. The technician was exposed to the dioxin and subsequently developed a severe case of chloracne which required hospitalization. This event provided the first clue as to the potential human health effects of dioxin exposure.

There are many different forms of dioxin; the form most commonly referred to as dioxin is 2,3,7,8,-tetrachlorodibenzo-p-dioxin (TCDD). Dioxin is a contaminant that occurs in the production of TCP (2,4,5,-trichlorophenol). When TCP is used to make other compounds, a dioxin contaminant may be passed along to the new substance. The compound TCP is used in the production of several compounds, including the herbicide 2,4,5,-T (2,4,5,-trichlorophenoxyacetic acid) and the compound hexachlorophene (bis-trichoro-2-hydroxyphenol methane), which is used in soaps and disinfectants.

The level of dioxin contamination in 2,4,5-T until 1970 may have been as high as 1-5 ppm (parts per million). After 1970, levels of dioxin contamination were required to be reduced to less than 0.1 ppm in 2,4,5-T. The U.S. Pharmacopeia has established a maximum detectable limit of 0.05 ppm dioxin for hexachlorophene; the actual content measured in hexachlorophene has been less than 0.005 ppm. (A physical/chemical description of the compound dioxin is provided in the appendix.)

Policymakers have often been called upon to make risk-regulating decisions

in the absence of sufficient scientific data. Frequently such data as may be available are conflicting. In making such policy decisions, Congress considers a number of factors in determining allowable risk to public health and the environment, as well as the economic impact and net social benefits involved. Policy decisions about the regulation of dioxin may affect the general population, several industries, and foreign trade. At present, there are several organizations, activities, agencies, and interest groups concerned about the issue of dioxin. Their positions are reflected by their individual policy statements.

o The Veterans Administration (VA) has a long-standing and continuing concern over the effects of dioxin exposure, stemming from the use of Agent Orange in Vietnam. The VA's review of available literature and ongoing studies indicates that, as yet, no consensus exists within the scientific community concerning the causal relationship between dioxin exposure and those health problems experienced by some Vietnam veterans.

o The Dow Chemical company acknowledges that dioxin is highly toxic and produces ill health effects in laboratory animals; however, at concentrations found in the environment, the company believes dioxin does not pose a health hazard to humans.

o The American Medical Association (AMA) has not confirmed any adverse human health effects related to environmental exposure to dioxin other than chloracne, but has encouraged further research in this area.

o As a result of studies conducted at sites contaminated with dioxin, the Centers for Disease Control (CDC) has established a safe exposure limit for dioxin in the environment at 1.0 parts per billion (ppb). The CDC's position is that below 1.0 ppb the individual is not at risk; above 1.0 ppb, inadequate data exist to determine if any risk is present. CDC is presently conducting research on human exposures to dioxin to better define the limits of risk.

o The Veterans of Foreign Wars (VFW), in its concern for the health of veterans in general, finds that although no confirmed relationship has been established between dioxin exposure and specific adverse health effects, there are sufficient trends reported in the scientific journals to suggest some health risk. The VFW is seeking compensation for any veteran suffering from specific conditions reported to result from dioxin exposure.

o Also supporting the idea of compensation is the Vietnam Veterans of America (VVA). The VVA maintains that scientific evidence supports the association of adverse human health effects and dioxin exposure.

o The Sierra Club and the Environmental Defense Fund (EDF) have taken stronger positions against dioxin. The Club and EDF believe dioxin presents a health hazard and recommend further research to determine the degree of hazard to man. They call for the removal of all uses of chemicals contaminated with dioxin and stricter control over production of chemicals that could have dioxin as a contaminant.

The diversity of these policy positions reflects the lack of conclusive scientific data.

## Dioxin Research

Dioxin research is presently being conducted in several private and Federal research facilities. Federal agencies have budgeted over $10,000,000 for dioxin research during fiscal year 1983 (FY83) and more than $50 million is scheduled to be spent on dioxin research in FY84. The major purpose of this research is to determinate the human health effects and environmental impacts associated with dioxin exposure.

Concern has been expressed concerning the coordination and control of research efforts by individuals, interest groups, researchers, and Federal agencies.

## Sources of Exposure to Dioxin

Public concern about exposure to dioxin has been heightened as a result of increased awareness of several sources of proven or possible exposure: 1) the use of the herbicide "Agent Orange" in aerial spraying operations during the Vietnam conflict (there were also occasional uses of herbicides such as 2,4,5-T for brush control in civilian applications until 1979. Since 1979, uses of 2,4,5-T have been limited to rice crops and rangelands; 2) the Seveso, Italy, chemical plant accident; 3) emissions from municipal incinerators and some fossil fuel power plants; 4) the; spreading of dioxin contaminated oil for dust control in Missouri. and 5) unknown sources of dioxin in Michigan and New Jersey.

### 1. Herbicide Aerial Spraying.

From 1962 to 1971, herbicide aerial spraying operations were conducted by the U.S. in the Republic of Vietnam. The peak periods of spraying were 1968 and 1969. According to the U.S. Air Force, the herbicide most often sprayed was "Agent Orange," a half-and-half mixture of the herbicide 2, 4,-D (2,4-dichlorophenoxyacetic acid) and 2,4,5-T (2,4,5-trichlorophenoxyacetic acid). Dioxin is a contaminant of 2,4,5-T. Average dioxin levels in "agent orange" were estimated at 2 ppm with a high of 47 ppm and a low of 0.02 ppm. The Environmental Protection Agency (EPA) has since recommended the limit for the contaminant dioxin in 2,4,5-T at 0.1 ppm (May 1971). Both U.S. air and ground forces were subjected to possible dioxin exposure while in specific regions of the Republic of Vietnam (see IB83043 -- Agent Orange: Veterans' Complaints and Studies of Health Effects).

### 2. Seveso, Italy, Chemical Plant Accident.

The Seveso, Italy, accident (July 10, 1976) involved an explosion at a chemical plant where TCP was manufactured. A cloud of TCP with the contaminant dioxin escaped from the chemical plant as a result of the explosion. The cloud, estimated to contain roughly 3 grams of dioxin, was dispersed by the wind across a residential area adjacent to the plant. Several hundred people were exposed to the chemical cloud. Within the first year after the accident 187 cases of chloracne were reported; 164 were children and 23 were adults. Eight of the children with chloracne also had severe chemical burns; eleven other children had chloracne and mild chemical burns. Several other children that did not develop chloracne did develop erythema (red skin patches). Very few adults developed chloracne or chemical burns. Studies are still being conducted on the exposed population to determine the chronic health effects.

### 3. Power Plant and Incinerator Emissions.

Dioxin has also been identified as an emission from some fossil fuel power plants and municipal incinerators. The dioxin is produced during the incomplete combustion of fuel or waste that contains such compounds as chlorophenols, chlorinated benzenes, and biphenyl ethers. The amount of discharge (smoke stack emissions) is dependent upon incinerator operation, fuel, and combustion temperature.

4. State of Missouri Contamination.

Dioxin contamination of soil in Missouri dates back to 1971, when dioxin-contaminated waste oil was applied to the soil for dust control. At a horse arena where the dioxin-contaminated waste oil was applied several horses died. Several other sites in the State also were sprayed with the dioxin-contaminated waste oil for dust control. Not all sites have been positively identified or tested. Dioxin contamination sites in the State are estimated to have levels between 1.0 ppm-300 ppb. The problem of dioxin site identification and cleanup has been complicated by rainfall, surface run-off, and flooding which spreads the dioxin contaminated soil. At present, efforts are underway to identify all dioxin sites in the State and either clean up the site or possibly relocate the residents.

5. Michigan and New Jersey Contamination.

Certain sites in Michigan and New Jersey have recently been identified as having been contaminated with dioxin. Dioxin has been detected in rivers around the Dow Chemical Plant in Midland, Michigan, and at three sites near the Diamond Alkali Corp. plant in New Jersey. Both plants are reported to have produced Agent Orange contaminated with dioxin during the Vietnam War. At present only one site has been identified in Michigan. In New Jersey there are 50 additional sites that are scheduled for dioxin contamination testing. The specific source or sources of dioxin contamination remain to be determined in both States. Further investigations will be conducted in each State to identify any additional dioxin contaminated sites.

## Environmental Effects

1. Biological Accumulation and Elimination.

Studies have demonstrated that accumulation and elimination of dioxin occurs in many animal species. It has been reported that dioxin, at concentrations found in the environment, does not accumulate in animal tissue to any significant degree.

It would appear that the rates of accumulation and elimination are dependent upon the environmental concentration, conditions of exposure, and animal species.

Few studies have been conducted to determine whether dioxins are accumulated in plants. Those studies that have addressed this question appear to indicate that very little dioxin accumulation occurs in plants. When accumulation did occur the lowest levels were recorded in the fruits and leaves with the highest levels found on the surface of roots. It is interesting to note that when plants were transplanted from dioxin-contaminated soil to uncontaminated soil, the dioxin levels accumulated in the plant disappeared.

2. Soil Contamination.

Some studies have been conducted to determine if dioxin is persistent in most types of soils. Those studies that evaluate dioxin persistence in soil found that over 90% of the dioxin could be detected in the soil one year after the original contamination occurred. This would indicate that a strong bond is established between dioxin and most soils. The persistence of dioxin in the environment has been attributed to these strong bonds.

3. Water Contamination.

Dioxin is not very soluble in water. The greatest danger of contamination of the rivers and streams is from dioxin-contaminated soil run-off. The eroded dioxin-contaminated soil particles could settle on the bottom of the stream or could be carried with the flow of the stream.

## Disposal Methods

Small quantities of dioxin can be disposed of by physiochemical, chemical, and microbiological means. Physiochemical means include: ultraviolet light; gamma rays; or hydrogen donation. Chemical disposal is possible utilizing ozone and ruthenium salt reactions. Microbiological means depend on microbes to destroy the dioxin. These methods have been field tested with limited success; due to their high cost they are not considered practical for bulk disposal. Larger quantities of dioxin can be disposed of using more traditional means such as: a) incineration; b) perpetual repository storage (not true disposal); c) secure landfill (presently permitted but may still present an environmental hazard later); and d) entombment (concrete mixed with dioxin -- this is not actually disposal).

Dioxin is easily destroyed by natural sunlight in a very short time. The difficulty in this form of disposal results from the fact that natural light destruction of dioxin is only surface active (i.e., it destroys only the layer on the surface directly exposed to the natural sunlight.)

## General Exposure Standards

Two agencies have established exposure standards for dioxin and a third has recommended a maximum exposure limit. The Environmental Protection Agency's Scientific Advisory Panel in 1980 established the "no observable effect level" (NOEL) for dioxin at 0.001 micrograms dioxin per kilogram of body weight per day (mg/kg/day). The NOEL is defined as a dose below which no carcinogenic, teratogenic, or reproductive effect is observed.

The Federal Food and Drug Administration (FDA) set the dioxin levels in edible fish as not to exceed a limit of 50 ppt (parts per trillion). It has been recommended by the Centers for Disease Control (CDC) that individuals not be exposed to levels of dioxin greater than 1 ppb in soil.

The chemical industrial exposure limit for dioxin of 0.0007 mg/kg body weight was set by the EPA to protect workers in the chemical industry and related fields.

## Biological Effects -- Animals

Experiments on laboratory animals show interspecies differences (i.e., no

two species react in the same way) in response to a high concentration acute exposure to dioxin. This response would indicate that dioxin has a different acute toxic effect in each animal species. However, when exposure levels are high enough to cause death, the length of time between exposure and death (the latent period) is similar for each species. How the dioxin causes death in experimental animals is not known. When laboratory animals are exposed to lower concentrations of dioxin, where death is not expected to occur, two sets of symptoms are generally observed. The first set of symptoms, common to all species, includes: a) chloracne; and b) the development of horny skin layer (hyperkeratosis). The second set of symptoms which is specific to each individual species includes: a) in pregnant female mice, dioxin exposure results in the production of some abnormal offspring (teratogenic effect); b) in pregnant female mice and some other species, dioxin exposure causes the death of some of the unborn offspring (fetotoxic effect); c) in chickens a unique lesion is developed (hydropericordium); d) in some animal species an infiltration of tissues with fluid occurs (edema); e) in rabbits liver disturbances are common; f) in monkeys conversion of the meikomian gland occurs (the gland in the eyelid changes from a sebaceous fluid producer to a keratin producer); and g) in guinea pigs suppression of the immune system occurs. Although reproductive disorders were observed in female mice, no reproductive disorders were observed in male mice exposed to dioxin at identical concentrations.

Biological Effects -- Man

No human deaths have been reported after an acute exposure to dioxin. The most prominent effect observed in man from an acute or chronic exposure to dioxin is chloracne. Chloracne's symptons can range in severity and extent. The more severe cases may involve extensive acne-like eruptions of blackheads, abcesses, and cysts initially on the face, giving the appearance of grayish sheets. The most severe cases may involve the total body. Chloracne is not a symptom that is unique to dioxin exposure; it may also occur from exposure to many other chlorinated compounds. The chronic effects of exposure to dioxin (other than chloracne) are not well understood. Although several symptoms have been described by individuals chronically exposed to dioxin, there is not sufficient information to establish a cause-and-effect association. The symptoms that have been reported include: 1) enlarged liver; 2) liver function abnormality; 3) neuromuscular effects; 4) deranged porphyrin (a disturbance in production of porphyrin -- a natural pigment produced by the body); 5) spontaneous abortion; 6) congential malformation; 7) cancer; and 8) chromosomal aberrations.

1. Liver Enlargement.

Enlargement of the liver has been reported in some exposed individuals. However, mortality among the dioxin-exposed individuals who displayed an enlarged liver was not statistically different from that of non-exposed individuals (individuals with normal livers). Any relationship between dioxin exposure and the liver enlargements is unclear at this time.

2. Liver Function Abnormality.

Liver dysfunction has been observed in some individuals who also were accidently exposed to dioxin. Individuals exposed to low levels of dioxin may have an abnormal liver function, yet no temporary or permanent damage may occur. Exposures to very high levels of dioxin may cause an abnormal liver function with some signs of permanent damage. Any relationship between

dioxin exposure and liver function abnormality is unclear at this time.

3. Neuromuscular Effects.

Some individuals exposed to dioxin report a weakness in their lower limbs. This effect has not been observed in any animal trials. The impairment reported seems to be slight, affecting muscular coordination without any other apparent side effects. Any relationship between dioxin exposure and the neuromuscular effect is unclear at this time.

4. Deranged Porphyrin.

Porphyrin derangement, which results in spotting of the skin, is known to have a genetic as well as an environmental cause (e.g., environmental exposure to hexachlorobenzene, polychlorinated biphenyls and dioxin). Any relationship between dioxin exposure and the porphyrin effect is unclear at this time.

5. Spontaneous Abortions.

Spontaneous abortions have been reported as a possible adverse health effect of dioxin exposure. A review of recent studies indicates that there appears to be no difference between the ratio of spontaneous abortions within the dioxin-exposed populations and the non-exposed populations.

6. Congenital Malformations.

It has been reported that as a result of dioxin exposure congenital malformations have occurred. There appears to be no difference in the number of congenital malformations occurring in dioxin exposed and non-exposed populations. This was confirmed in a comparison made between the rate of congenital malformations observed after the Seveso, Italy, accident and the estimated world rate.

7. Cancer.

Cancer has been suggested as an effect of dioxin exposure. It is difficult to demonstrate a cause-and-effect relationship between dioxin exposure and cancer. There appears to be no difference in the overall cancer death rate between the dioxin-exposed and the non-exposed populations. There does appear to be some increase in the incidence of soft tissue sarcoma in dioxin-exposed populations. Evidence at this time is not conclusive.

It has recently been reported that an association may exist between stomach cancer and dioxin exposure. Evidence in support of this association is not sufficient to make a positive confirmation of cause and effect.

8. Chromosomal Aberrations.

Cytogenetic studies (those relating to the function and structure of the cell) to date do not indicate an increase in the frequency of chromosomal aberrations as a result of dioxin exposure. When the prevalence of chromosomal aberrations is compared between the dioxin-exposed individuals and the total population at large no significant difference is observed.

Summary

Studies indicate that dioxin is a highly toxic chemical that may persist for many years in the environment. Plants do not appear to accumulate great amounts of dioxin. Animals appear to accumulate and eliminate dioxin at different rates depending on environmental conditions and animal species. Bodies of water generally become contaminated from dioxin-contaminated soil run-off as a result of erosion. Soil forms a strong bond with dioxin which is mainly responsible for the persistence of the dioxin in the environment.

Dioxin may be disposed of by traditional methods such as incineration, perpetual storage, landfill, and entombment. Dioxin molecules are destroyed by sunlight on exposed surfaces.

Animal exposure studies demonstrate species differences for the effects of dioxin. Chronic exposures appear to result in specific symptoms for each animal species.

Chloracne is the most consistent symptom of dioxin exposure in humans. Other symptoms have been reported, yet no cause-and-effect association has been confirmed.

## Points for Further Consideration

Future issues which may confront policymakers include: (a) identification of cause-effect relationships with regard to the human health effects of dioxin exosure; (b) proposed establishment of dioxin industrial discharge requirements; (c) establishment of final dioxin disposal requirements (changing the chemical character of dioxin); (d) initiation of further chronic exposure studies with animals; (e) development of new waste discharge methodologies; (f) requirement for extensive acute and chronic testing of new chemicals prior to marketing; and (g) the identification of one Federal agency to coordinate all dioxin and Agent Orange research efforts.

## HEARINGS

U.S. Congress. House. Committee on Energy and Commerce. Subcommittee on Oversight and Investigations. Defining health emergencies under the superfunded statute: recent PCB and dioxin cases. Hearing, 97th Congress, 2d session. Nov. 19, 1982. Washington, U.S. Govt. Print. Off., 1983. 370 p.

U.S. Congress. House. Committee on Interstate and Foreign Commerce. Subcommittee on Oversight and Investigations. Agent orange: exposure of Vietnam veterans. Hearing, 96th Congress, 2d session. Sept. 25, 1980. Washington, U.S. Govt. Print. Off., 1981. 249 p.

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U.S. Congress. House. Committee on Veterans Affairs. Subcommittee on Oversight and Investigations. Current status of agent orange studies. May 6, 1981. Washington, U.S. Govt. Print. Off., 1981. 385 p.

U.S. Congress. House. Committee on Veterans Affairs. Subcommittee on Medical Facilities and Benefits. Scientific community report on agent orange. Hearings, 96th Congress, 2d session. Sept. 16, 1980. Washington, U.S. Govt. Print. Off., 1981. 145 p.

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U.S. Congress. House. Committee on Veterans Affairs. Ad Hoc Subcommittee. Status of Vietnam veterans in the Bay area. Hearing, 96th Congress, 2d session. Apr. 10, 1980. Washington, U.S. Govt. Print. Off., 1980. 64 p.

## CHRONOLOGY OF EVENTS

02/00/83 -- Missouri clean up of dioxin spills begins.

11/19/82 -- Hearings held by Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce. Hearing on the hazards of dioxin.

12/03/80 -- P.L. 96-510, Comprehensive Environmental Response Compensation and Liability Act 1980 (CERCLA), "Superfund" -- clean up of hazardous waste sites.

10/21/76 -- P.L. 94-580, Resource Conservation and Recovery Act (RCRA), control of hazardous wastes.

10/11/76 -- P.L. 94-469, Toxic Substance Control Act, the control of all toxic substances not covered by other toxic substances control.

07/10/76 -- Seveso, Italy chemical plant explosion, dioxin contaminant spread over local region.

07/19/75 -- P.L. 94-56, Hazardous Material Transportation Act. (Amended 1976 to cover the transport of toxic materials.)

12/16/74 -- P.L. 93-523, Safe Drinking Water Act. (Amended 1977 to eliminate contaminants from discharge or entry into water sources.)

10/18/72 -- P.L. 92-500, Clean Water Act. (Federal Water Pollution Control Act.) (Amended 1977 to cover discharge of toxic pollutants into water.)

00/00/71 -- Missouri sites were contaminated with dioxin.

12/31/70 -- P.L. 91-604, Clean Air Act. (Amended 1977 to

cover discharge of hazardous pollutants into the air.)

1960-70 -- Agent orange contaminated with dioxin used in Republic of Vietnam for aerial spraying operations.

00/00/56 -- Dioxin identified.

Unknown -- Incinerator production of dioxin.

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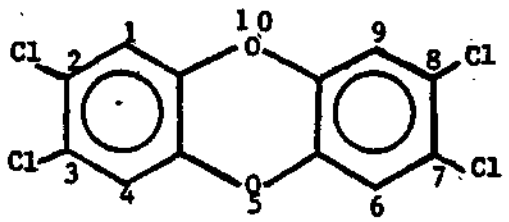
APPENDIX 1

**Structure and physical/chemical characteristics of 2,3,7,8-tetrachlorodibenzo-p-dioxin, TCDD or dioxin.**

Structure




Cl=Chlorine
O=Oxygen
⬡=Benzene

2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

Physical Characteristics

| | | |
|---|---|---|
| molecular weight | 322 | |
| melting point, | 303 - 305°C | 577 - 581°F |
| decomposition point, | 980 - 1,000°C | 1796 - 1832°F |

Chemical Characteristics

Solubility, grams/liter

| | |
|---|---|
| ortho-dichlorobenzene | 1.40 |
| chlorobenzene | 0.72 |
| Orange Herbicide | 0.58 |
| benzene | 0.57 |
| chloroform | 0.37 |
| acetone | 0.11 |
| normal-octanol | 0.05 |
| lard oil | 0.04 |
| methanol | 0.01 |
| water | $2 \times 10^{-7}$ |

REFERENCE:
**Young, A.L., Calcagni, J.A., Thalken, C.E., and Tremblay, J.W. The toxicology environmental fate and human risk of herbicide orange and its associated dioxin. U.S. Air Force Report, OEHL TR-78-92, October 1982.** page I-22

Dioxin research is presently being conducted in several private and Federal research facilities. Federal agencies have budgeted over $10,000,000 for dioxin research during fiscal year 1983 (FY83) and more than $50 million is scheduled to be spent on dioxin research in FY84. The major purpose of this research is to determinate the human health effects and environmental impacts associated with dioxin exposure.

In addition to Federal expenditures, the Dow Chemical Company has made $3,000,000.00 available to researchers to identify the human health effects resulting from dioxin exposure.

Concern has been expressed concerning the coordination and control of research efforts by individuals, interest groups, researchers, and Federal agencies.

## Superfund

At present, funds used to temporarily or permanently relocate residents living in dioxin-contaminated areas come from the Superfund budget. If the trend of buying these contaminated areas continues, additional funding of the Superfund program will become necessary. (See IB83064 -- Superfund: Hazardous Waste Clean-up -- for details of the complete issues associated with the Superfund.)

## Sources of Exposure to Dioxin

Public concern about exposure to dioxin has been heightened as a result of increased awareness of several sources of proven or possible exposure: 1) the use of the herbicide "Agent Orange" in aerial spraying operations during the Vietnam conflict (there were also occasional uses of herbicides such as 2,4,5-T for brush control in civilian applications until 1979. Since 1979, uses of 2,4,5-T have been limited to rice crops and rangelands; 2) the Seveso, Italy, chemical plant accident; 3) emissions from municipal incinerators and some fossil fuel power plants; 4) the; spreading of dioxin contaminated oil for dust control in Missouri. and 5) unknown sources of dioxin in Michigan and New Jersey.

### 1. Herbicide Aerial Spraying.

From 1962 to 1971, herbicide aerial spraying operations were conducted by the U.S. in the Republic of Vietnam. The peak periods of spraying were 1968 and 1969. According to the U.S. Air Force, the herbicide most often sprayed was "Agent Orange," a half-and-half mixture of the herbicide 2, 4,-D (2,4-dichlorophenoxyacetic acid) and 2,4,5-T (2,4,5-trichlorophenoxyacetic acid). Dioxin is a contaminant of 2,4,5-T. Average dioxin levels in "agent orange" were estimated at 2 ppm with a high of 47 ppm and a low of 0.02 ppm. The Environmental Protection Agency (EPA) has since recommended the limit for the contaminant dioxin in 2,4,5-T at 0.1 ppm (May 1971). Both U.S. air and ground forces were subjected to possible dioxin exposure while in specific regions of the Republic of Vietnam (see IB83043 -- Agent Orange: Veterans' Complaints and Studies of Health Effects).

### 2. Seveso, Italy, Chemical Plant Accident.

The Seveso, Italy, accident (July 10, 1976) involved an explosion at a chemical plant where TCP was manufactured. A cloud of TCP with the

contaminant dioxin escaped from the chemical plant as a result of the explosion. The cloud, estimated to contain roughly 3 grams of dioxin, was dispersed by the wind across a residential area adjacent to the plant. Several hundred people were exposed to the chemical cloud. Within the first year after the accident 187 cases of chloracne were reported; 164 were children and 23 were adults. Eight of the children with chloracne also had severe chemical burns; eleven other children had chloracne and mild chemical burns. Several other children that did not develop chloracne did develop erythema (red skin patches). Very few adults developed chloracne or chemical burns. Studies are still being conducted on the exposed population to determine the chronic health effects.

3. Power Plant and Incinerator Emissions.

Dioxin has also been identified as an emission from some fossil fuel power plants and municipal incinerators. The dioxin is produced during the incomplete combustion of fuel or waste that contains such compounds as chlorophenols, chlorinated benzenes, and biphenyl ethers. The amount of discharge (smoke stack emissions) is dependent upon incinerator operation, fuel, and combustion temperature.

4. State of Missouri Contamination.

Dioxin contamination of soil in Missouri dates back to 1971, when dioxin-contaminated waste oil was applied to the soil for dust control. At a horse arena where the dioxin-contaminated waste oil was applied several horses died. Several other sites in the State also were sprayed with the dioxin-contaminated waste oil for dust control. Not all sites have been positively identified or tested. Dioxin contamination sites in the State are estimated to have levels between 1.0 ppm-1,800 ppb. The problem of dioxin site identification and cleanup has been complicated by rainfall, surface run-off, and flooding which spreads the dioxin contaminated soil. At present, efforts are underway to identify all dioxin sites in the State and either clean up the site or possibly relocate the residents.

As a result of the soil being contaminated with dioxin, the EPA has requested the Federal Emergency Management Agency (FEMA) to permanently relocate the residents of Times Beach and 11 families of Imperial, MO. The EPA has also requested FEMA to temporarily relocate three St. James, MO Families.

5. Michigan and New Jersey Contamination.

Certain sites in Michigan and New Jersey have recently been identified as having been contaminated with dioxin. Dioxin has been detected in rivers around the Dow Chemical Plant in Midland, Michigan, and at three sites near the Diamond Alkali Corp. plant in New Jersey. Both plants are reported to have produced Agent Orange contaminated with dioxin during the Vietnam War. At present only one site has been identified in Michigan. In New Jersey there are 50 additional sites that are scheduled for dioxin contamination testing. The specific source or sources of dioxin contamination remain to be determined in both States. Further investigations will be conducted in each State to identify any additional dioxin contaminated sites.

Environmental Effects

1. Biological Accumulation and Elimination.

exposure and cancer. There appears to be no difference in the overall cancer death rate between the dioxin-exposed and the non-exposed populations. There does appear to be some increase in the incidence of soft tissue sarcoma in dioxin-exposed populations. Evidence at this time is not conclusive.

It has recently been reported that an association may exist between stomach cancer and dioxin exposure. Evidence in support of this association is not sufficient to make a positive confirmation of cause and effect.

8. Chromosomal Aberrations.

Cytogenetic studies (those relating to the function and structure of the cell) to date do not indicate an increase in the frequency of chromosomal aberrations as a result of dioxin exposure. When the prevalence of chromosomal aberrations is compared between the dioxin-exposed individuals and the total population at large no significant difference is observed.

## Summary

Studies indicate that dioxin is a highly toxic chemical that may persist for many years in the environment. Plants do not appear to accumulate great amounts of dioxin. Animals appear to accumulate and eliminate dioxin at different rates depending on environmental conditions and animal species. Bodies of water generally become contaminated from dioxin-contaminated soil run-off as a result of erosion. Soil forms a strong bond with dioxin which is mainly responsible for the persistence of the dioxin in the environment.

Dioxin may be disposed of by traditional methods such as incineration, perpetual storage, landfill, and entombment. Dioxin molecules are destroyed by sunlight on exposed surfaces.

Animal exposure studies demonstrate species differences for the effects of dioxin. Chronic exposures appear to result in specific symptoms for each animal species.

Chloracne is the most consistent symptom of dioxin exposure in humans. Other symptoms have been reported, yet no cause-and-effect association has been confirmed.

## Points for Further Consideration

Future issues which may confront policymakers include: (a) identification of cause-effect relationships with regard to the human health effects of dioxin exosure; (b) proposed establishment of dioxin industrial discharge requirements; (c) establishment of final dioxin disposal requirements (changing the chemical character of dioxin); (d) initiation of further chronic exposure studies with animals; (e) development of new waste discharge methodologies; (f) requirement for extensive acute and chronic testing of new chemicals prior to marketing; (g) identification of one Federal agency to coordinate all dioxin and Agent Orange research efforts; and (h) examination of the need for some form of a victim compensation program, based upon a chosen level of acceptable risk, to protect the individual from environmental sources of dioxin.

Congressional Research Service
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DIOXIN

IP0244D

In response to numerous requests for information on dioxin, we have compiled the enclosed material.

Dioxins are contaminants produced in the manufacture of some chemical compounds. There are 22 different forms of dioxin; the type most commonly referred to is TCDD (2,3,7,8-Tetrachlorodibenzo-p-Dioxin). This is formed during the production of TCP (Trichlorophenol), a compound used in some pesticides, soaps, disinfectants, and other compounds. TCDD is found in Agent Orange (a herbicide sprayed in Vietnam) and in such places as Times Beach, Missouri, Michigan, and elsewhere. In some animals, adverse health effects have been reported as a result of dioxin exposure. However, its effects on humans are not yet understood.

This Info Pack includes information on dioxins, the research into their health effects, and the problems which occur as they are identified in other places around the country. Additional information, primarily in newspapers and periodicals, may be found in a local library by consulting the Readers' Guide to Periodical Literature, the General Science Index, and the New York Times Index.

We hope this information will be useful.

Congressional Reference Division

Members of Congress desiring more information on this topic can call CRS at 287-5700.

# HANDBOOK OF TOXIC AND HAZARDOUS CHEMICALS

by

Marshall Sittig

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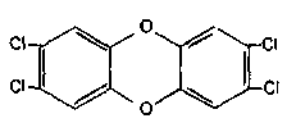
## TETRACHLORODIBENZO-p-DIOXIN

- Carcinogen (EPA-CAG) (A-40)
- Hazardous waste constituent (EPA)
- Priority toxic pollutant (EPA)

**Description:** Polychlorinated dibenzo-p-dioxins are formed in the manufacturing process of all chlorophenols. However, the amount formed is dependent on the degree to which the temperature and pressure are controlled during production.

An especially toxic dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), is formed during the production of 2,4,5-TCP (trichlorophenol) by the alkaline hydrolysis of 1,2,4,5-tetrachlorobenzene. Tetrachlorodibenzo-p-dioxin has the formula $C_{12}H_4Cl_4O_2$. TCDD is a white crystalline solid with a melting point range of 302° to 305°C. Decomposition begins at 500°C and is virtually complete within 21 seconds at a temperature of 800°C. The structural formula is:




As can be anticipated, TCDD has been associated with all synthetic compounds derived from 2,4,5-TCP. This includes the widely used herbicide and defoliant 2,4,5-T (2,4,5-trichlorophenoxyacetic acid).

**Code Numbers:** CAS 1746-01-6 RTECS HP3500000

**DOT Designation:** —

**Synonym:** TCDD.

**Potential Exposures:** TCDD has no uses as such. As noted above, TCDD is an inadvertent contaminant in herbicide precursors and thus in the herbicides themselves. Thus, it is applied in herbicide formulations, but is not used per se. It has been estimated that approximately 2 million acres in the United States have been treated for weed control on one or more occasions with approximately 15 million pounds of TCDD contaminated 2,4,5-T, 2,4-D, or combinations of the two.

In the cases of human exposure to 2,4,5-TCP, the only adverse effects reported were caused by occupational exposure or accidents that occurred during the manufacture of chlorinated phenols or products derived from them.

In 1949, intermediary chemicals of the manufacturing process were released in a U.S. 2,4,5-T plant. This accident led to 117 cases of chloracne among exposed workers.

In 1953 there was an accident in a Middle Rhine factory manufacturing 2,4,5-TCP from 1,2,4,5-tetrachlorobenzene. In addition to contracting chloracne, many workers had liver cirrhosis, heat complaints, and nervous system disorders, and were depressed.

In 1958, 31 employees of a Hamburg, Germany, plant in which 2,4,5-T was made from technical 2,4,5-TCP contracted chloracne and suffered the physical and psychological symptoms associated with it. In 1961 TCDD was conclusively identified as the cause of the chloracne.

An explosion occurred in a 2,4,5-T plant in Amsterdam in 1963. Six months later, 9 of 18 men, who were attempting to decontaminate the plant, developed chloracne. All of the men had worn deep sea diving suits, and all but one wore face masks with goggles while working in the plant. Of these men, three died within 2 years. The man without the face mask or goggles was severely affected. He was unable to walk and required long-term treatment.

In 1964, workers in a 2,4,5-T plant in the United States developed chloracne from exposure to TCDD.

There was an explosion at the Coalite Co.'s 2,4,5-TCP plant in Great Britain in 1968. TCDD had accidentally been produced as the result of an exothermic reaction. Seventy-nine cases of chloracne were reported; many of them were severe.

In 1971 there was an accidental poisoning episode in the United States that affected humans, horses, and other animals. Waste oil contaminated with TCDD had been sprayed on a riding arena to control dust. Later analyses showed that the arena contained TCDD in concentrations of 31.8 to 33.0 μg/g. The most important route of entry of dioxin into the body was the skin. (This does not preclude the effects of ingesting food contaminated with dioxin from handling.)

A 6-year-old girl was the most severely affected. She had an inflammatory reaction of the kidneys and bladder bleeding that was diagnosed as acute hemorrhagic cystitis with signs of focal pyelonephritis. Nine less severely affected persons developed diarrhea, headaches, nausea, polyarthralgias, and persistent skin lesions. The girl most affected was thoroughly reexamined in 1976. Results indicated that all of her original symptoms had completely disappeared. She had grown normally and all tests, including a detailed neurological examination, were normal.

In July 1976, TCDD was accidentally released in the Seveso region of Italy. Most of the inhabitants were adversely affected. The first overt reaction was the appearance of numerous burn-like lesions on many of the inhabitants. These lesions generally receded. They were probably caused by direct contact with the sodium hydroxide and phenolic components in the fallout. However, 2½ months after the explosion, an increasing number of children and young people in the zone most affected began to develop symptoms of chloracne on their faces and bodies, a definite mark of dioxin poisoning. By November 28 people had confirmed cases of chloracne. This number rose to 38 by December and to 130 a year after the explosion. A number of the victims exposed underwent a "complete change of character": they became extremely nervous, tired, moody, and irritable, and had a marked loss of appetite.

There were a number of Seveso women who were pregnant at the time of the accident. The total number of legal and illegal abortions performed as a result of the explosion probably totaled 90. There were 51 spontaneous (as distinct from induced) abortions. A survey conducted by an epidemiological commission has shown that 183 babies were delivered in the 2 months following the accident. Eight cases of birth abnormalities have been noted among babies born to women in the Seveso area who were pregnant at the time of the explosion. However, local physicians have had difficulty relating these abnormalities directly to the explosion because the incidence of birth abnormalities was not significantly higher than the normal incidence of abnormal births.

**Permissible Exposure Limits in Air:** There are no numerical limits; in view of its effects, all contact should be avoided.

**Permissible Concentration in Water:** There are insufficient data to permit the development of criteria for the protection of freshwater or saltwater aquatic life. For the protection of human health, the concentration is preferably zero. An additional lifetime cancer risk of 1 in 100,000 is posed at a concentration of $4.55 \times 10^{-7}$ µg/ℓ as of 1979. EPA did not update this criterion in 1980.

**Determination in Water:** Methylene chloride extraction followed by transfer to benzene and capillary column gas chromatography/mass spectrometry with electron impact ionization (EPA Method 613) or gas chromatography plus mass spectrometry (EPA Method 625).

**Routes of Entry:** Skin absorption, inhalation of vapors.

**Harmful Effects and Symptoms:** TCDD is one of the most toxic substances known. It exhibits a delayed biological response in many species and is highly lethal at low doses to aquatic organisms, birds, and mammals, including man.

It has been shown to be acnegenic, embryolethal, teratogenic, mutagenic (in certain organisms), carcinogenic, and to affect the immune responses in mammals. TCDD has also been shown to persist for 10 years after application to soils and to bioaccumulate in aquatic organisms by factors as high as 8,000-fold. These findings in conjunction with the wide distribution of contaminated products, lead to the conclusion that TCDD represents a potential hazard to both aquatic and terrestrial life.

The toxicity of a dioxin varies with the position and number of chlorines attached to the aromatic rings. Generally, the toxicity increases with increased chlorine substitution. Those dioxins that have halogens at the 2,3, and 7 positions are particularly toxic. TCDD, which has chlorine atoms at the 2,3,7, and 8 positions, is considered the most toxic of the dioxins.

TCDD is an extremely toxic compound exhibiting acute, subchronic and chronic effects in animals and humans. The liver appears to be the target organ of acute exposure. Retention of TCDD by the liver indicates that it apparently undergoes little or no metabolism.

Acute effects of exposure include chloracne, porphyria cutanea tarda, hepatotoxicity, psychological alterations, weight loss, thymic atrophy, thrombocytopenia, suppression of cellular immunity and death. TCDD is teratogenic and fetotoxic. Oral exposure of pregnant rats to 0.125 to 2.0 µg TCDD/kg/day produced fetal mortality, fetal intestinal hemorrhage and both early and late resorptions. There was found an increased incidence of cleft palate when pregnant mice were given TCDD doses of 1.0 µg/kg/day for 10 days during gestation. TCDD has been shown to be mutagenic in three bacterial systems and a potent inducer of hepatic and renal microsomal drug metabolizing enzymes.

The carcinogenic potential of tetrachlorodibenzo-p-dioxin has been established by the findings of two feeding studies. One study found that Sprague-Dawley rats fed dose levels of 5 ppt to ppb TCDD has a significant excess of tumors as compared to the controls. Another feeding study, using the same strain of rats given 0.1, 0.01, 0.001 µg TCDD/kg/day, induced a statistically significant excess of hepatocellular carcinoma in treated rats. Based on these two studies, tetrachlorodibenzo-p-dioxin is likely to be a human carcinogen.

**Points of Attack:** Liver.

**Medical Surveillance:** In short, contact wth TCDD should be avoided but obviously careful preplacement and regular physical exams should be carried out in those cases where worker exposure cannot be avoided with emphasis on liver and kidney function studies (A-39).

**First Aid:** Irrigate eyes with water. Wash contaminated areas of body with soap and water.

**Personal Protective Methods:** As stated above, contact with TCDD should be avoided. When it cannot be avoided, extreme worker protection should be provided.

**Respirator Selection:** Use chemical cartridge respirator.

**References**

(1) U.S. Environmental Protection Agency, *2,3,7,8-Tetrachlorodibenzo-p-Dioxin: Ambient Water Quality Criteria*, Washington, DC (1979).

(2) U.S. Environmental Protection Agency, "Rebuttable Presumption Against Registration of Pesticide Products Containing 2,4,5-Trichlorophenol and Its Salts," *Federal Register* 43, No. 149, 34026-34054 (August 1, 1978).

(3) U.S. Environmental Protection Agency, *TCDD*, Health and Environmental Effects Profile No. 155, Washington, DC, Office of Solid Waste (April 30, 1980).

## Council Report

# Health Effects of Agent Orange and Dioxin Contaminants

Council on Scientific Affairs

The American Medical Association's Council on Scientific Affairs, in response to a request from the medical student section, has reviewed the medical evidence regarding the toxicity and long-term health effects of Agent Orange and its associated contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). This executive summary, which was prepared by the Council on Scientific Affairs Advisory Panel on Toxic Substances, summarizes the findings in its technical report on the subject, which is available on request.

### Background

During the latter stages of the United States' involvement in Vietnam, herbicidal mixtures of 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), otherwise identified by the military as Agent Orange, were sprayed over certain areas of Vietnam for the express purpose of defoliating the jungle and destroying one of the enemy's means of concealment. Similar spray programs have been used in the United States as a means of forestry management. For the past 30 years, mixtures of 2,4-D and 2,4,5-T have been used extensively by homeowners and farmers for ridding lawns and agricultural acreage of unwanted broadleaf vegetation. Large numbers of persons have been exposed to varying amounts of 2,4-D or 2,4,5-T (or both), as well as to the contaminant 2,3,7,8 - tetrachlorodibenzo - *p* - dioxin (TCDD), in the normal course of employment.

Also, during these years, there have been a number of industrial incidents in which workers, as well as civilian populations, have been subjected to accidental exposure to these compounds. A number of litigious actions and government regulatory responses are now pending, based on alleged adverse health effects from such exposures.

The most serious of these allegations by Vietnam veterans and persons involved in accidental industrial exposures are that Agent Orange, or compounds of a like nature, may have caused malignant tumors, sterility, spontaneous abortions, birth defects, disfiguring skin diseases, and other illnesses. In spite of the voluminous data on the biologic effects of the phenoxy-type pesticides and the associated chlorinated dioxins, there is still little substantive evidence for the many claims that have been made against these compounds. Data from experimental animals do indicate that TCDD is a toxic material; however, while suggestive, the data from animal studies are not necessarily applicable to man. Still, a number of those exposures to TCDD of industrial and general populations that have occurred have been sufficiently well documented to offer some insight into the effect of TCDD on man.

Agent Orange, or Herbicide Orange, was a label given by the US military forces to a 50:50 mixture of the *n*-butyl esters of 2,4-D and 2,4,5-T, together with a minor amount (1%) of the free acid of 2,4,5-T and varying amounts of the contaminant TCDD. Agents Green, Pink, and Purple also were used as defoliants by the military forces from 1962 through 1964, a time when few American troops were committed to the field. Another formulation, Herbicide Orange II, was similar to Agent Orange, except that the isooctyl ester of 2,4,5-T was sub-





From the Council on Scientific Affairs, Division of Scientific Activities, American Medical Association, Chicago.

Reprint requests to Council on Scientific Affairs, American Medical Association, 535 N Dearborn St, Chicago, IL 60610 (Richard J. Jones, MD).

stituted for the *n*-butyl ester of 2,4,5-T. In addition to Agent Orange, other spray defoliants used in Vietnam included Herbicide White, whose active ingredient was picloram (or the triisopropanolamine salt of 4-amino-3,5,6-trichloropicolinic acid). This substance is persistent in the environment and highly carcinogenic in rats and mice. Lesser amounts of Herbicide Blue, which contained sodium cacodylate (the sodium salt of cacodylic acid [hydroxydimethylarsine oxide]) (26%) and cacodylic acid (5%), were used. Although the long-term effects in humans of either or both of these compounds are uncertain, picloram and cacodylic acid should be considered along with the aforementioned agents that were encountered in Vietnam.

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin may form as a by-product of the synthesis of 2,4,5-trichlorophenol (TCP), a precursor of 2,4,5-T, when 1,2,4,5-tetrachlorobenzene is subjected to alkaline hydrolysis at elevated temperature and pressure. If the reaction temperature is allowed to rise above 180 °C, the sodium-2-hydroethoxide (formed from the ethylene glycol solvent and caustic soda) decomposes exothermically and promotes the dimerization of sodium trichlorophenate to TCDD. The presence of TCDD as a contaminant of TCP was discovered in 1957, when chloracne developed in workmen involved in the manufacture of TCP.

About 20 years ago, commercially available 2,4,5-T contained anywhere from 1 to 70 ppm of TCDD. When the industry became aware of the contaminant's existence and toxicity, production operations were monitored and altered to reduce the level. Current manufacturing operations are able to control the amount of TCDD in commercial 2,4,5-T formulations to less than 0.01 ppm (with occasional batches as high as 0.05 ppm), a level believed to be nonhazardous to humans and other organisms. Data relating to an acceptable maximum level are presently under regulatory review by the Federal Insecticide, Fungicide and Rodenticide Act; the recommended maximum concentration is now placed at 0.1 ppm.

Commercial formulations of 2,4,5-T and 2,4-D were used safely in agriculture for more than 30 years with no recognized evidence of carcinogenicity or birth defects in humans. The adverse effects that did occur from massive doses of either pure 2,4-D or pure 2,4,5-T were manifested soon after the exposure, and the victims recovered with no signs of long-term damage. When the first symptoms were manifested months or years after the last exposure to these compounds, it was evident that another causal agent had to be responsible. That agent was later suspected to be TCDD. Although 2,4-D is closely related chemically to 2,4,5-T, it is not generally contaminated with TCDD.

### Biologic Effects

Two of the more pronounced biologic effects of some of the chlorinated dioxins are their tendency to cause chloracne (especially in the rabbit, nude mouse, monkey, and man) and the accumulation of fluid in the pericardium and peritoneal cavity of chicks.

Chloracne in man is typified by comedones in a malar distribution; the preauricular and postauricular portions are often accompanied by hirsutism and sometimes by melanosis and secondary inflammation. The disease was first described in 1899; its cause was discovered in 1918 to be due to contact with certain chlorinated hydrocarbons. Chloracne has now become one of the more common forms of occupational dermatitis. Other acute toxic reactions to dioxin include liver and renal damage, porphyria cutanea tarda, hyperpigmentation, hirsutism, polyneuropathies (eg, sensory impairments and weakness in legs), and neurasthenic or depressive syndromes. Thus far, long-term effects, except for persistent chloracne, have not been seen.

Chloracne is not caused by 2,4,5-T and 2,4-D per se; if the condition occurs on exposure to either or both of these compounds, it is most likely that the contaminant TCDD is responsible. Chloracne usually appears within two to three weeks after the first exposure. Mild chloracne clears up within several months after cessation of exposure; severe chloracne, on the other hand, has been known to persist for as long as 30 years following the last exposure. Persons most susceptible are those who are prone to development of acne vulgaris. If exposure to TCDD is severe enough, formation of cysts and, on occasion, inflammation and scarring will occur. If there is no history of chloracne, then the likelihood of a significant exposure to, or adverse health effects from, TCDD is remote. Hence, chloracne is the clinical marker of TCDD exposure.

Long-term exposure to TCDD leads to degeneration of the liver and thymus in experimental animals: one sensitive index of exposure is atrophy of the thymus. Porphyria, altered levels in serum enzymes, and weight loss are also observed. Major organs that are affected are the liver, blood-forming organs, and the reticuloendothelial system. Progressive weight loss, the first clinical sign of toxicity in the monkey, may be accompanied by alopecia, facial edema, and a dry, scaly dermatitis over the rest of the body.

The metabolism of TCDD in man is unknown, and for the present there is only limited information available on the metabolic pathways and metabolites that may occur in other mammals. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin is distributed equally among the fat and liver of mammals, to a lesser extent in the kidneys, and is eliminated via the feces. Samples of fat from beef cattle and samples of milk from cows that had grazed on 2,4,5-T-treated pasture or rangeland, in addition to human milk from an area where 2,4,5-T herbicides were used repeatedly during a 20-year period, had small to undetectable (not more than 10 ppm) amounts of TCDD.

No clearly defined mutagenic effect has been observed in vitro with TCDD. It does induce genetic changes by the Ames test with *Salmonella typhimurium* and *Escherichia coli*, but not with repair-defective strains; there is no evidence (from dominant lethal and cytogenetic evaluations in rodents) that such changes occur in whole animals.

Of perhaps more relevance to man are the in vitro studies on mammalian cells, ie, HeLa cells; Balb-3T3, normal mouse fibroblasts; simian virus (SV) 101, SV 40-transformed 3T3 mouse fibroblasts; human foreskin fibroblasts; and normal human lymphocytes. No significant growth inhibition in the cell cultures nor

discernible ultrastructural changes have been observed by electron microscopy.

The teratogenicity and fetotoxicity of TCDD were discovered in 1969, in the course of a study on the biologic activity of 2,4,5-T. The sample being used was later found to be contaminated with TCDD. The incidence of cleft palate was greater in two particular mouse strains (C57BL/6 and AKR), while the C57BL/6 mouse and the rat had development of a higher incidence of cystic kidney. All doses given the rat led to gastrointestinal tract hemorrhage in the fetus. The increased ratio of fetal liver to body weight in the mouse suggested that TCDD was fetotoxic in this particular species.

A majority of studies using high doses of 2,4,5-T with 0.1 ppm of TCDD or less showed cleft palate in mice, but no other species, and embryotoxicity in the mouse, rat, hamster, sheep, monkey, and rabbit. There is no scientific evidence that 2,4,5-T or TCDD has caused reproductive difficulties or hazards in the human. No conclusive evidence is yet available that phenoxy herbicides or TCDD is mutagenic or teratogenic in man.

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin can induce cancer or serve as a cancer promoter in some strains of rats and mice. In contrast to some other chemical carcinogens, the carcinogenicity is always accompanied by considerable systemic toxicity.

From an environmental viewpoint, TCDD breaks down rapidly on leaves of plants, in water, and on the surface of soil, especially through the action of sunlight. In soil, it generally has a half-life of about 230 days; some soil microorganisms can cause its degradation, especially if other chlorinated hydrocarbons are present.

### Experience in Man

One of the most extensive human experiences with the adverse effects of TCDD in man involves the residents of Seveso, Italy. In July 1976, TCDD was accidentally released from the ICMESA (Industrie Chimiche Meda Societa Anonima) trichlorophenol synthesis plant when a safety disk in a steam-heated reactor vessel ruptured. The plume of reactor contents, including TCDD, rose 18.2 m above the factory and fell in a cone-shaped pattern about 1.6 km long and 0.8 km wide. This is the largest single population to have been exposed to the compound. More than 37,000 persons were potentially exposed to varying doses.

Two years after the incident occurred, the acute and midterm health effects were assessed; the mild chloracne, which occurred mainly in a small group of children, healed quickly. Subclinical peripheral nerve impairment was reported; there was also some liver involvement, but without apparent functional disorder. Neither immunoresponse nor susceptibility to infectious diseases was altered.

The most recent progress report on the long-term epidemiologic survey of the residents of the Seveso area emphasizes the preliminary nature of their findings and reiterates the conclusions of previous investigators. Except for the skin, no organs or body functions were impaired. No derangement of gestation, no fetal lethality and loss, no gross malformations, no growth retardation at term, and no cytogenetic abnormalities have yet occurred.

The first of several accidental releases of TCDD and other dioxins attending the manufacture of TCP or 2,4,5-T occurred in 1949 in the United States. At least 11 other industrial accidents or exposure incidents have occurred since then, both here and abroad. To date, an estimated 579 workers are known to have been exposed, including 156 employees in the ICMESA plant at Seveso.

### Current Studies

There are now a number of studies under way by agencies of the US government and industry, which may resolve questions on the kinds and extent of human damage from exposure to low levels of TCDD.

Through its Department of Environmental and Drug-Induced Pathology, the Armed Forces Institute of Pathology (AFIP) is examining biopsy and autopsy tissue specimens of all Vietnam veterans. To date, only 152 cases have been assessed: the dominant diseases are epidermal inclusion cysts and chronic, nonspecific dermatitis. Thus far, there have been no unusual morphological features or clustering of tumors by diagnosis or site that implicate Agent Orange.

A soft-tissue sarcoma study also has been proposed that will be conducted jointly by the AFIP and the National Cancer Institute.

The Air Force, through Project Ranch Hand, will administer to and examine the 1,200 personnel who were involved in the actual handling and spraying of Agent Orange. They, and the control population of 20,000, are to be followed up during the next 20 years.

The University of California, Los Angeles, was awarded a contract by the Veterans Administration for the design of an epidemiologic study of Vietnam veterans.

Approximately 45,000 Vietnam veterans who expressed concern about the hazards of Agent Orange have been examined by the VA; data for 25,000 of these men have been placed in a special Agent Orange Registry, which may serve later to identify them and to provide medical information as well as indications of health trends during the long term.

The Chloracne Task Force was established to identify those cases of dermatitis that either resemble or are truly chloracne. Cases of the former type will be reexamined by dermatologists who have an expert knowledge of the disease. Thus far, there are only 700 cases of "skin conditions" out of the total of 3,500 filed claims for damage from Agent Orange.

### Recommendations

The Council on Scientific Affairs recommends that (1) the aforementioned studies on exposed or allegedly exposed persons continue to be supported and, if feasible, enlarged to include the cooperative engagement of all internationally known exposure data, as recommended by the International Agency for Research on Cancer; (2) all physicians be alerted through AMA publications to the classic signs of chloracne and the possible signs and adverse effects of TCDD exposure. They should be encouraged to enlist in the present efforts to identify and treat those persons who have had serious exposures to TCDD and to cooperate in the collection of vital information that is needed for the ongoing human epidemiologic studies.

# Dioxin's Uncertain Legacy

## *Animal studies indicate dioxin's toxicity, but clinical data are lacking; this uncertainty compounds the problem of what to do with contaminated sites*

*An article in last week's issue examined how up to 100 sites in Missouri became contaminated with dioxin. Federal and state officials are now faced with difficult decisions on how to reduce further hazards to human health.*

*Times Beach, Missouri.* A weary-looking Douglas King sits near a space heater in the office of the Easy Living Mobile Manor here and notes that since he moved to this blue collar town 10 years ago, four of his dogs have met with mysterious deaths. "They looked like they starved to death," King says. "But I ain't blamin' dioxin." Then he adds that he is concerned about the future health of his two teenage daughters. "But what can you do?" he asks in frustration and bewilderment.

Twelve years ago, waste oil polluted with the extremely toxic chemical dioxin was sprayed along many of the town's roads to control dust. But the contamination was only discovered in December. King is among the 800 families here who are asking rhetorical, yet very real questions about their future in Times Beach. They want to know whether their health has been endangered by dioxin. They want to know if their neighborhoods will be a safe place in which to live. They want to know if dioxin can be eliminated from their community. Or will Times Beach turn into a ghost town?

State and federal officials, to their own frustration, lack clear, precise answers. In terms of health effects, the data available can only provide a qualitative sense of the hazard. Animal studies show that the dioxin isomer found in Times Beach—2,3,7,8-tetrachlorodibenzodioxin—is a potent carcinogen and a teratogen. But good clinical data are scant. Nevertheless, scientists at the Environmental Protection Agency (EPA) wrote in an agency handbook called "Dioxins" that "The slightest trace of 2,3,7,8-TCDD in the environment may have adverse effects on the health of both human and animal populations."

The problem is magnified by the fact that it is exceedingly difficult to rid the environment of dioxin which is chemically very stable. If, as some officials believe, Times Beach is still widely contaminated with up to 100 parts per billion (ppb) of dioxin in the soil, cleanup will pose enormous problems. The Centers for Disease Control (CDC) recommends that human exposure be restricted to less than 1 ppb. Preliminary results from soil samples taken after the flood are to be released in early February.

In the absence of solid data on human exposure to dioxin, CDC officials wrestled with what to tell beleaguered Times Beach residents, already psychologically stressed from the flood disaster. Short of barricading the town off, authorities urged citizens not to go back to their homes. They then issued a long list of precautions for residents who insisted on returning to salvage their sodden belongings. But many, if not most, of the 300 families who returned have not heeded the advice. While EPA technicians slog through the silt in protective clothing and respirators to take soil samples, townspeople can be seen working with their bare hands and without face masks.

Gary Stein, CDC's field coordinator at Times Beach, says, "We're in a gray zone, because the data aren't available to give precise risk estimates." But results from animal and occupational studies give plenty of reasons to support CDC's cautious position.

The animal studies show dioxin's power as a poison. For example, a single oral dose of 0.8 microgram could kill a 14-ounce guinea pig. A small minnow called a mosquito fish is even more sensitive, showing toxicity at 3 parts per trillion.

The EPA dioxin handbook notes that under chronic conditions, the chemical has an "extremely high potential for producing adverse effects. . . ." In one study, rats that ingested 5 parts per trillion of dioxin daily developed cancer after a year and a half. Other experiments have shown marked increases in liver tumors. Dioxin is a tumor promoter as well.

Other chronic effects in animals also make the chemical very worrisome. Several studies in rats and mice have shown dioxin to be teratogenic at incredibly low doses. It affects animals' blood, causing anemia in rhesus monkeys and lowering the number of white blood cells in mice.

Some of the acute and chronic effects seen in animals have also been observed in humans, many of whom were victims of chemical plant accidents over the past three decades. Awareness of the compound's toxicity increased substantially when a chemical plant exploded in Seveso, Italy, in 1976, spreading dioxin dust over 250 acres.

The most obvious and frequent acute symptom of dioxin exposure is chloracne, a severe form of acne that is often disfiguring. According to Renate Kimbrough, a CDC epidemiologist, there is no good treatment for the skin disorder, which may persist for years. But it is an "erroneous assumption," she says, that dioxin exposure always results in chloracne. Other signs of exposure include lassitude, headaches, impotence, loss of weight and hair, anorexia, severe liver damage and nerve disorders.

Epidemiologists, have not yet confirmed dioxin as a cause of cancer in humans. They are, however, seriously concerned that there may be a correlation between dioxin and sarcomas, a rare cancer. A study by Swedish researchers in 1978 reported a five- to six-fold increase in sarcomas in workers exposed to herbicides. The National Institute for Occupational Safety and Health has begun two studies that may shed further light on a possible link. One is examining the causes of death in about 3000 workers involved with the production of the herbicide 2,4,5-T and other chemicals in which dioxin is an unwanted byproduct. Results are due in 1985. Another study is investigating whether the pathology of sarcomas in seven chemical workers reportedly exposed to dioxin has similarities. This study is to be completed within a year.

Given the lack of data on chronic exposure to humans, public health officials are hesitant to draw any conclusions about the future health of Times Beach residents. Kimbrough notes that at Seveso, workers were exposed to a cloud of dioxin. At Times Beach, the dioxin was found in the soil, to which it clings tenaciously. There is little data that reveal how dioxin, bound to soil particles, is absorbed by the body. EPA and CDC scientists say that this kind of data will be very difficult to obtain. Meanwhile, CDC is conducting some preliminary health surveys of Times Beach residents.

Environmental officials face perplexing problems as well. If soil samples show similar levels of contamination that were present before the flood, they will probably have to clean up at least part of Times Beach. During the early 1970's,

scientists believed that the half-life of dioxin was 1 year, but that proved to be wrong. The half-life is now estimated to be up to 10 years. Given its stability, officials may have to treat or excavate potentially thousands of tons of contaminated soil.

Paul E. des Rosiers, a leading expert at EPA on treating dioxin, indicates that few options are available. Italians at Seveso and at least one American firm successfully treated areas of contamination by subjecting them to ultraviolet light in the presence of a hydrogen donor. (The ingenious Italians used a rather abundant hydrogen donor: olive oil.) Treatment by photolysis, however, is only effective at the surface; the contamination at Times Beach apparently extends well beneath the surface.

Des Rosiers says that incineration may prove to be the only good way to eliminate dioxin but the technology is limited to dioxin-laced liquids. Again, Times Beach loses out.

The most practical and economical method to clean up dioxin, he says, is to take the contaminated material to a certified landfill. But this solution has already proved to be fraught with political problems. Landfill disposal may also be impractical for Times Beach, given the immense amount of soil that would have to be moved.

An internal EPA document stated the need to strive for imaginative solutions. Referring to another dioxin-contaminated site in Missouri known as the Minker-Stout site, the document suggested that the area be purchased and then "should be considered for re-sale as a H.W. [hazardous waste] landfill after clean-up." Times Beach residents are unlikely to find that a satisfactory solution.

—MARJORIE SUN

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## Long-term toxicity of dioxin still unclear

The confusing biochemistry of tetrachlorodibenzo-*p*-dioxin (TCDD) has never been more apparent than in a recently compiled report of the American Medical Association on the health effects of agent orange and other herbicides contaminated by polychlorinated dioxins.

The report, prepared by AMA's Advisory Panel on Toxic Substances headed by John R. Beljan of Wright State University, Dayton, Ohio, is intended to inform physicians on what is known about possible human exposure to TCDD and its consequences for human health.

TCDD is the most toxic of the chlorinated dioxin compounds that are present in trace amounts in certain phenoxyacetic herbicides including agent orange, the Defense Department's name for a mixture of the *n*-butyl esters of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid that was used extensively by the U.S. as a defoliant in Vietnam and possibly in Laos during the 1960s. A class action suit has been brought on behalf of veterans who were exposed to TCDD in the agent orange used in Indochina and who have later had various medical complaints including liver damage, cancer, skin rashes, and reproductive problems. The Environmental Protection Agency also has suspended many uses of the commercial phenoxyacetic herbicides 2,4,5-T and silvex because of adverse health effects, chiefly spontaneous abortions, that have been reported among people exposed to these compounds.

There are marked variations in the sensitivity and susceptibility of different animal species to all toxic substances, the AMA report says, but this variation is particularly apparent in the case of TCDD. "Thus, the animal data cannot be translated directly to man," the report says.

Industrial accidents, including the highly publicized explosion of an Acmesa chemical plant in Seveso, Italy, in 1976, have provided a good deal of data on what happens to humans exposed to TCDD, the report says. One of the more pronounced effects is the appearance of chloracne, a severe skin rash. This condition is regarded as the clinical marker of human exposure. Other effects in humans that are likely to occur at high exposure levels include impaired liver function and neurological difficulties, including depression and irritation of the central nervous system. However, these conditions are not progressive and are always cleared with time.

Other adverse effects are well established in test animals, the report says, including damage to the liver, peripheral nerves, blood-forming organs, and reticuloendothelial system. TCDD also alters normal enzyme activity and thus may make other toxins more dangerous. It is not a carcinogen itself, but it does promote or induce cancer in some strains of rats and mice. This carcinogenicity is always accompanied by other forms of toxicity, unlike some other chemical carcinogens. At levels of 0.1 ppm or less, it can cause cleft palate in mice and embryo toxicity in several other animal species, according to the report.

After 30 years of use, "there is still no conclusive evidence that [the commercial herbicides 2,4-D and 2,4,5-T or the TCDD found in the latter] are mutagenic, carcinogenic, or teratogenic in man, nor that they have caused reproductive difficulties in [humans]," the report states. Both herbicides break down rapidly in the soil "and are, therefore, of little environmental concern," according to the report.

The report recommends that studies on exposed persons be continued and enlarged and that all physicians be alerted to the symptoms of chloracne and to the possible signs and adverse effects of TCDD exposure.

Copies of the report, "The Health Effects of 'Agent Orange' and Polychlorinated Dioxin Contaminants" are available for $6.00 from AMA, 535 North Dearborn Street, Chicago, Ill. 60610. □

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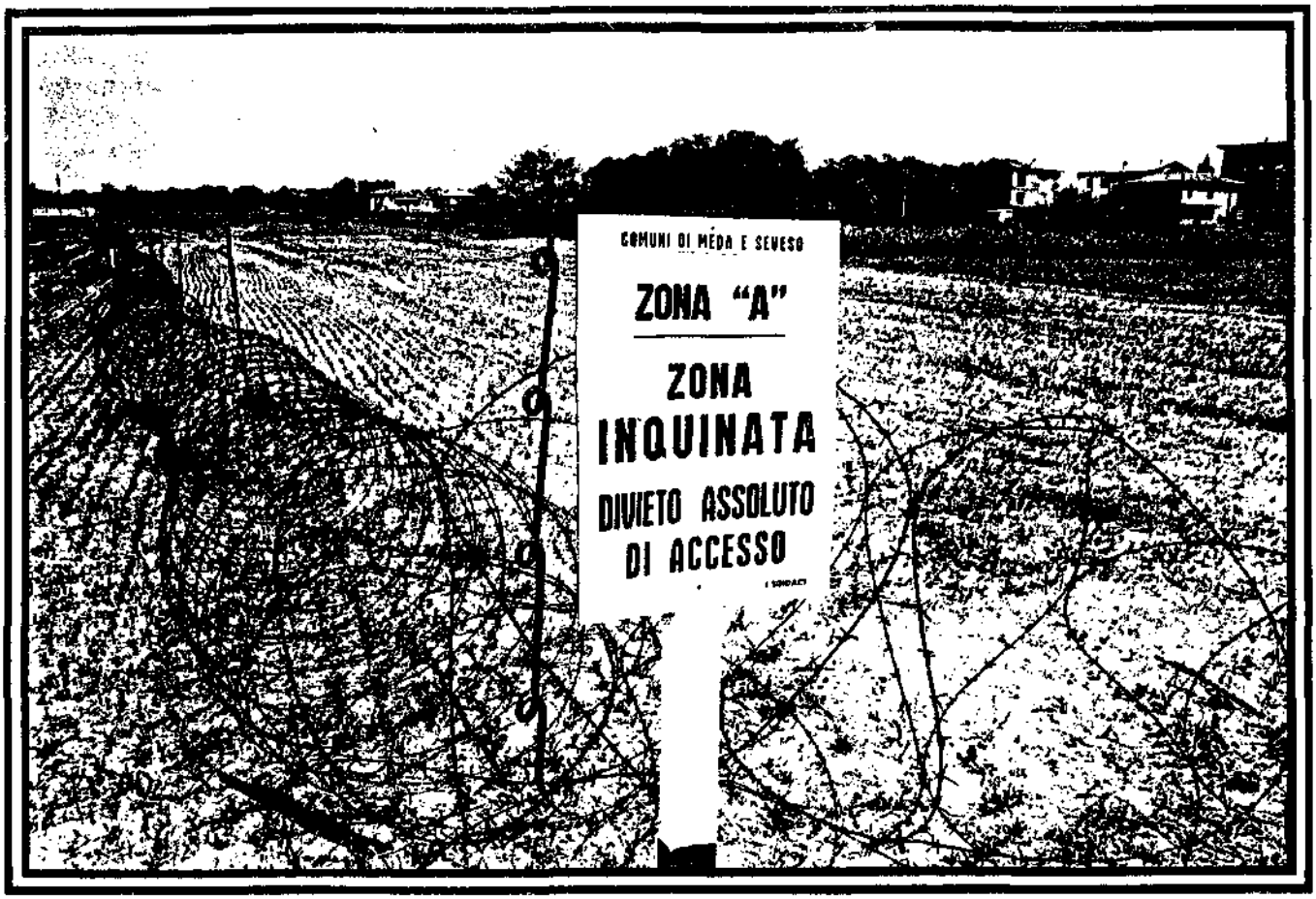



# The Dioxins:
# Toxic and Still Troublesome

BY DAVID KRIEBEL

The dioxins, one small class of highly toxic synthetic pollutants, have never been intentionally manufactured; yet today they are spread around the world. Dioxins occur as contaminants in other chemicals, at concentrations of a few parts per million (ppm) or less—a low level in comparison with many toxic substances which are spread throughout the ecosystem by the millions of pounds. Were it not for the extraordinary toxicity of the dioxins, and particularly 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), they would never have been noticed. But when 2,3,7,8-TCDD is fed to rats at a level of just five parts per trillion (ppt) in food ($5 \times 10^{-12}$), the rats develop cancer and other serious chronic disabilities.[1]

Evidence for the ubiquity of dioxins can be found in the daily newspapers. Some examples:

- In February 1979 the U.S. Environmental Protection Agency temporarily banned the herbicide 2.4.5-trichlorophenoxy-acetic acid (2,4,5-T) for most uses. This herbicide contains traces of dioxin. A major factor in the emergency suspension order halting use of 2,4,5-T was evidence that women in and around the small mountain town of Alsea, Oregon, suffered high miscarriage rates shortly after the annual spraying of 2,4,5-T in the surrounding national forests. The evidence strongly implicated 2,3,7,8-TCDD as the toxin responsible for the miscarriages.[2]
- In November 1978 the Dow Chemical Company, a major manufacturer of 2,4,5-T, claimed that dioxins were formed as a normal part of the combustion process, and that as a result, dioxins were widespread in the environment.[3]
- Dioxins were among the hundreds of toxic chemicals identified in the

**DAVID KRIEBEL** is a Research Associate at the Center for the Biology of Natural Systems, Queens College, Flushing, New York.

acrid runoff from Hooker Chemical Corporation's abandoned dump at Love Canal in Niagara Falls, New York. Residents were evacuated from homes built on the filled dump after complaints about high levels of sickness, miscarriages, and birth defects.[4]

- Thousands of U.S. Vietnam veterans are blaming health problems, including skin rashes, chronic depression, cancer, and birth defects in their children, on a herbicide, Agent Orange, used extensively in the war to defoliate jungles and destroy food crops [see "2,4,5-T: Chemical Time Bomb," *Environment*, June 1979, p. 2]. Agent Orange was a mixture of 2,4,5-T and 2,4-D (a similar herbicide) and contained 2,3,7,8-TCDD and other dioxins at levels as high as 50 ppm (of 2,3,7,8-TCDD).[5] The Veterans Administration so far refuses to acknowledge these complaints as service related and has denied that birth defects in veterans' children could have been caused by any events in Vietnam.
- In Vietnam meanwhile, the dioxins in Agent Orange are suspected of causing an epidemic of liver cancer in the South, and numerous deformities in children born during and after the spraying.[6]
- In July 1976 a chemical reactor used to manufacture 2,4,5-trichlorophenol (the raw material for making 2,4,5-T) in a factory near Seveso, Italy, malfunctioned and vented its contents, including from two to six pounds of pure 2,3,7,8-TCDD over 275 acres of a densely populated region.[7] Not until two weeks later were the residents evacuated. In the meantime, thousands of domestic and wild animals died, and thousands of residents were exposed to unknown levels of the poison. As yet no human fatalities are known to have occurred; however the rate of birth defects in and around Seveso apparently increased in the year following the accident.[8]
- In 1971 three dirt-floor horse rings in northeastern Missouri were sprayed with waste oil to keep down dust. The oil was heavily contaminated with 2,3,7,8-TCDD.[9] Many wild birds, as well as dogs, cats, and horses, died from subsequent contact with the dirt floor and dust. Several people became ill and at least one, a young girl who played on one of the floors, is still disabled. In May 1980 more batches of the same dioxin-laden waste turned up in leaking barrels buried on a farm in Barry County, Missouri.

## Sources of Dioxins

The 75 different molecules (isomers) in the dioxin family are distinguished by the number of chlorine atoms present and by the position of these atoms around the two rings of the molecule (see Figure 1). The prefix before "chloro" in the molecule's name refers to the number of chlorine atoms present. Four (tetra-), five (penta-), six (hexa-), seven (hepta-), and eight (octa-) chlorines are the most common patterns.

A widely used class of industrial chemicals, the *chlorinated phenols*, contains dioxins as contaminants. One phenol, 2,4,5-trichlorophenol, contains the most toxic dioxin, 2,3,7,8-TCDD (a possible route of formation of 2,3,7,8-TCDD is summarized in Figure 1). Other chlorinated phenols contain small amounts of 2,3,7,8-TCDD, and larger quantities of other dioxins. For example, the wood preservative, pentachlorophenol, has been found to contain hexachlorodioxins (9 ppm), heptachlorodioxins (235 ppm), and octachlorodioxins (250 ppm).[10] Chlorophenols are widely used throughout the world as pesticides and feedstocks for many other products. Forty-five million pounds of pentachlorophenol were produced in the United States in 1977.[11] Production statistics on many of the other dioxin-containing products are lacking because the chemicals are produced by just one or two companies and the data are not publicly available.

Manufacturing accidents are one important source of dioxins in the environment. The release at the 2,4,5-trichlorophenol (2,4,5-TCP) factory near Seveso, Italy, in 1976 was not the first such accident. In fact, 13 serious accidents in 2,4,5-TCP factories are known.[12] The first was in 1949 at a Monsanto Company plant in Nitro, West Virginia. In 1963 an explosion in a 2,4,5-TCP plant in Holland caused such severe contamination that the plant was encased in concrete and sent to the bot-

*Dioxins enter the environment in a variety of ways. Although aerial spraying of herbicides on forests and grasslands is probably the most common route of entry, industrial accidents and improper disposal of dioxin-contaminated materials also play a role. These rotting barrels containing dioxin-laden waste oil were discovered on a farm in Barry County, Missouri, in May 1980.*

*A factory accident near Seveso, Italy, in 1976 spread the highly toxic 2, 3, 7, 8-TCDD over 275 acres, necessitating evacuation of nearby residents. In the picture on page 6 military barbed wire surrounds the contaminated "Zone A," to which entry was forbidden. (Photo by C. Cerchioli for Citazione Obbligatoria)*

tom of the Atlantic.[13] Dow Chemical's data strongly suggest that their plant in Midland, Michigan, is a major source of dioxins, presumably through "normal" low-level emissions (no serious accidents are known to have occurred there). Dow is probably the largest producer of dioxin-containing chemicals in the United States.[14]

One other source of dioxins is known: the combustion of chlorinated phenols, and products made from them. Small amounts of 2,3,7,8-TCDD and other dioxins are formed when the herbicide 2,4,5-T is burned under conditions simulating a brush or forest fire.[15] The reaction is quite slow at these temperatures; only about one millionth of the starting material is converted. In this reaction, 2,3,7,8-TCDD, the most toxic dioxin, seems to be the major dioxin produced.[16]

Commercial lumber is frequently treated with pentachlorophenol or other chlorophenols as a preservative. The burning of wood or other combustible materials containing chlorophenols has been studied as a possible source of dioxins.[17] Rappe and his colleagues found more dioxins formed in these experiments than were reported from burning 2,4,5-T.[18] In one test, 2,4,6-trichlorophenol was applied to dried birch leaves and allowed to burn unassisted in an open flask. The residual charcoal contained 2100 ppm of tetrachlorodibenzo-p-dioxins. Prior to burning, less than .02 ppm of TCDD's were present as contaminants in the trichlorophenol. In other words, burning caused a 100,000-fold increase in the level of tetrachlorodibenzo-p-dioxin in the sample. The authors concluded that burning chlorophenol-treated wood was probably a more important source of dioxins in the environment than the burning of phenoxy herbicide-treated forests or fields.

Dioxins have been found in fly ash from municipal incinerators and from an industrial heating plant.[19] However, this fact in itself does not prove that the dioxins were formed during the combustion which also formed the fly ash. Only if the combustion products (fly ash and gasses) have higher dioxin levels than the fuel can the combustion be identified as the source. This apparently has not yet been observed. Buser and his colleagues pyrolyzed (heated to a high temperature) chlorophenols in the laboratory. Dioxins were formed "as expected," and the researchers concluded that "the pattern of the main PCDD's [polychlorinated dioxins] is the same as that found for the two fly ashes[that they tested]."[20] Further work is necessary to definitely prove whether chlorophenols in the combusted materials are the source of the dioxins found in the ash.

## The Dow Report

The most recent contribution to research on the environmental sources of dioxins has been made by scientists at the Dow Chemical Company. In November 1978 the Chlorinated Dioxin Task Force of the Michigan Division of Dow released a report entitled *The Trace Chemistries of Fire–A Source of and Routes for the Entry of Chlorinated Dioxins into the Environment.*[21] The authors state: "Chlorinated dioxins appear to be ubiquitous. Their ubiquity is due to the existence of natural phenomena, trace chemistries of fire."

The authors conclude that refuse incinerators, fossil-fueled power plants, gasoline and diesel-powered autos and trucks, as well as fireplaces, charcoal-grills, and cigarettes are all sources of chlorinated dioxins. But Dow's analytical methods have been challenged by Dr. Christopher Rappe, of the University of Umea, Sweden,[22] who is an expert on the formation and identification of the dioxins.

The Dow scientists measured dioxin levels in a variety of samples from all over the country. If we discount Dr. Rappe's criticisms of Dow's methods and accept the data as reported, the most interesting finding in the report is that soil and dust samples from around Dow's Midland plant contained much higher levels of dioxins than those collected elsewhere.

Table 1 summarizes the data in the Dow paper on soil and dust samples. The presentation of the data is complicated by the small sample sizes and the wide range over which concentrations occur (the ranges also frequently include zero–or, more correctly, levels below

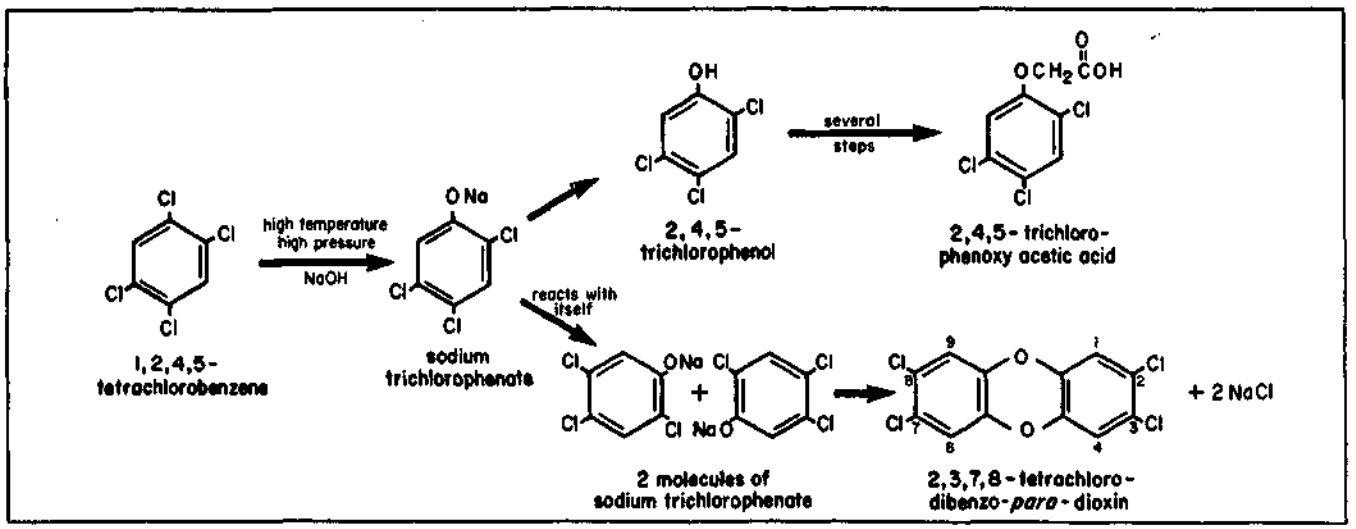



FIGURE 1. A possible route of formation of 2,3,7,8-TCDD and 2,4,5-T.

**Table 1**

**CHLORINATED DIOXIN CONCENTRATIONS IN SOIL AND DUST SAMPLES USED IN THE DOW STUDY**

| Location | Number of Samples | Range of Detectable Concentrations (ppb) TCDD[a] | HCDD[b] | $H_7CDD$[c] | OCDD[d] |
|---|---|---|---|---|---|
| *Soil* | | | | | |
| In and around Dow plant | 5[e] | 1 – 120 | 7 – 280 | 70 – 3200 | 490 – 20000 |
| Metropolitan area | 8 | .005 – .03 | .03 – .3 | .1 – 3 | .4 – 22 |
| Urban area | 5 | [f] | .03 – 1.2 | .03 – 2 | .05 – 2 |
| Rural area | 5 | [f] | [f] | – .05[g] | – .2[g] |
| *Dust* | | | | | |
| In Dow plant | 6 | 1 – 4 | 9 – 35 | 140 – 1200 | 650 – 7500 |
| Midland, Mich. | 2 | .03 – .04 | .2 – .4 | 2 – 4 | 20 – 30 |
| Metropolitan areas | 7 | – .3[g] | – 2[g] | .3 – 34 | .1 – 210 |

(a) Tetrachlorodibenzo-p-dioxin.
(b) Hexachlorodibenzo-p-dioxin.
(c) Heptachlorodibenzo-p-dioxin.
(d) Octochlorodibenzo-p-dioxin.
(e) More than five samples were taken, however data on only the positive samples (5) are reported in Dow's paper. Some negative samples were taken as well.
(f) No sample exceeded the limit of detection for this species.
(g) The maximum reported value. The range included values below the limit of detection.

the limit of detection). In Table 1 the data are presented as the range of positive results. For all four chlorinated dioxin species, the lowest reported concentration in a soil sample from in and around the Dow plant exceeds the highest concentration from any other soil sample by at least a factor of 6. The lowest reported level of any dioxin species in dust from Dow's plant was about three times higher than the highest level in any other dust sample reported.

Nowhere in the paper is this discrepancy between samples from in and around the Dow plant and from elsewhere discussed. Instead, the authors are concerned with identifying the sources of dioxins in the environment, and particularly the role of combustion processes. The experiments necessary for determining the formation of dioxins during combustion would involve measuring dioxin levels in materials, burning them, and then testing the combustion products. An overall gain in the amount of dioxins present would indicate that some dioxins had been formed. Nowhere in Dow's study, which purportedly established that dioxins are formed by "natural phenomena, trace chemistries of fire," is such an experiment reported. Instead, the products of combustion are tested, and dioxins are often found in them. Whether these dioxins were present in the material that was burned *before* combustion took place is not investigated.

Perhaps dioxins *are* formed during combustion. But does this then mean that dioxins have "been with us since the advent of fire," as a Dow official is quoted as having said soon after the report was announced?[23] The studies discussed earlier indicate that chlorophenols—widespread in the environment, can yield dioxins when burned. These *may* be sources of dioxins in combustion—but they have been with us less than a century.

## How Dioxins Spread

Dioxins have been widely distributed through the biosphere. Some of the most important pathways are discussed briefly below. The aerial broadcasting of dioxin-laden herbicides on forests in the United States and on some 6 percent of the land area of Vietnam is the most obvious route of distribution.[24] Until spring 1979, 2,4,5-T and Silvex (a related phenoxy herbicide also containing dioxins) were sprayed on more than 2 million acres annually in the United States. Total U.S. use of these herbicides was about 9.3 million pounds per year.[25]

Between 1961 and 1970 about 100 million pounds of Agent Orange (a 50:50 mixture of 2,4,5-T and the related, but apparently TCDD-free compound 2,4-D) were sprayed over some 2.5 million acres of South Vietnam.[26] Other herbicides also contained dioxins but were used less than Agent Orange. Table 2 summarizes herbicide usage in South Vietnam.

When chlorophenol-treated lumber (the chemical acts as a preservative) is burned (in house fires, wood-waste energy plants, home fireplaces), dioxins are formed and carried off in the fumes and ashes. Fires in sprayed forests and fields may also contribute dioxins to the environment. Ahling and colleagues estimated that as much as one microgram of tetrachlorodioxins per square meter of forest might be formed in a fire immediately following spraying at a typical forest application rate.[27]

Hexachlorophene, a highly effective anti-bacterial agent, contains dioxins, because it is made from 2,4,5-trichlorophenol, the same starting material used for 2,4,5-T. Hexachlorophene soaps are sometimes prescribed for skin rashes. But one condition for which they should clearly not be prescribed is chloracne, a severe form of acne that is the most common symptom of dioxin poisoning.[28]

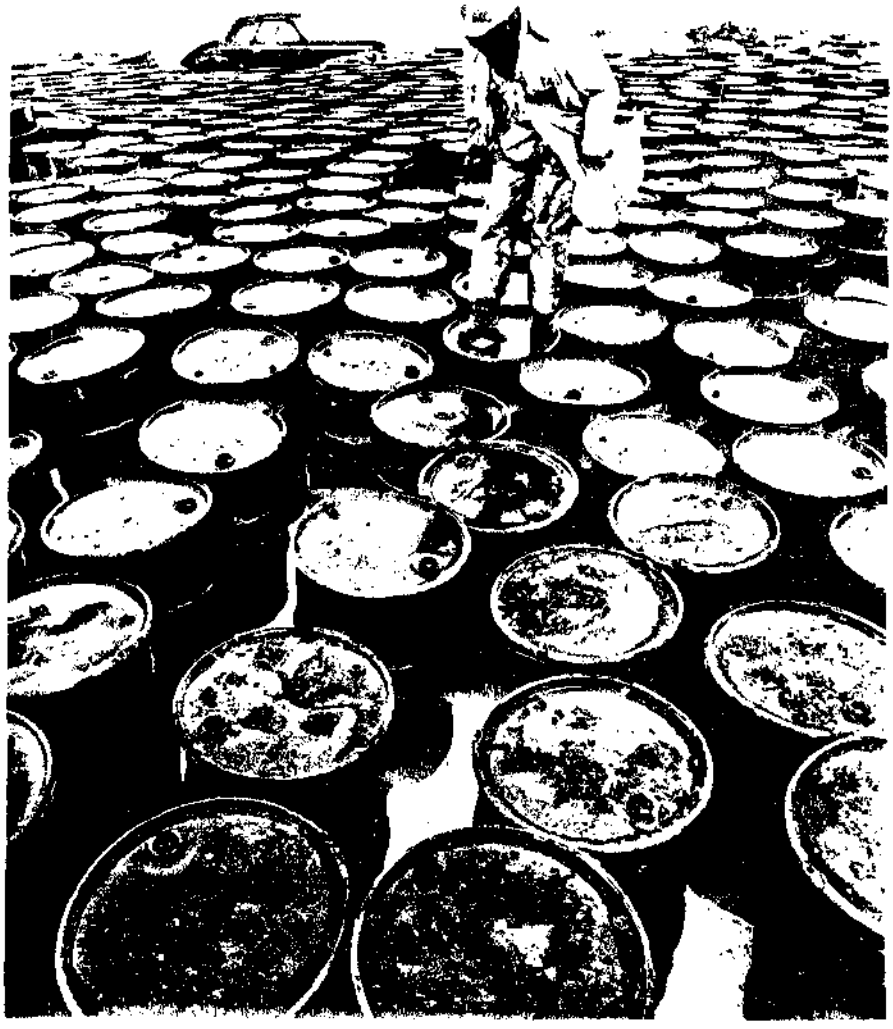
**Table 2**

**HERBICIDES SPRAYED ON SOUTH VIETNAM, 1962 – 1971**

| Chemical | Pounds |
|---|---|
| 2,4-D | 55,940,150 |
| 2,4,5-T* | 44,232,600 |
| Picloram | 3,041,800 |
| Cacodylic acid | 3,548,710 |
| *Total herbicides* | *106,763,260* |

*Approximately 370 pounds of 2,3,7,8-TCDD was sprayed as a contaminant in herbicides using 2,4,5-T as an active ingredient.

SOURCE: Young et al., note 5.



*Steel drums filled with soil contaminated with 20,000 gallons of orthophenol from a railroad tank car spill in Sturgeon, Missouri. A young worker hired to help clean up the spill had to be hospitalized and was later found to have a few parts per trillion of the dioxin 2, 3, 7, 8-TCDD in his blood. (Photo by Nick Kelsh, Columbia, Missouri,* Tribune*)*

Chlorinated phenols are widely used in the chemical industry and, through accidents in manufacture and shipment, low levels of dioxins can be released into the environment. In January 1979 a tank car containing 20,000 gallons of orthochlorophenol spilled its contents in the small town of Sturgeon, Missouri. Dioxins were present in the product at a level of less than 50 ppb. A young worker hired to clean up the spill was reported to have a few parts per trillion of dioxin (2,3,7,8-TCDD) in his blood.[29]

As mentioned earlier, soil samples from in and around Dow Chemical Company's plant in Midland, Michigan, contained up to 100 ppb of 2,3,7,8-TCDD, and much higher levels of the less toxic dioxins.

When a Monsanto Company chemical plant in Sauget, Illinois, was recently found to be contaminated with dioxins, the company was fined $50,000 by the Occupational Safety and Health Administration (OSHA), and required to restrict access to all areas in which chlorophenols were used.[30]

The release of dioxins into the environment can have many different effects, depending on the kind of ecosystem they are placed in. For example, 2,3,7,8-TCDD does not seem to leach out of soil to any measurable extent.[31] One reason is that dioxins are highly insoluble in water. They are soluble to a limited extent in fats, and are found in the fatty tissues of exposed animals.[32] Beef fat from cattle grazed on 2,4,5-T-treated rangeland contained 2,3,7,8-TCDD up to 70 ppt in one study.[33]

Additionally, human breast milk from women living in areas where 2,4,5-T is sprayed has been found to contain traces of 2,3,7,8-TCDD.[34] However, in a more recent study of TCDD levels in 103 milk samples from nursing mothers in California, Oregon and Washington, the EPA found no detectable levels of the dioxin.[35] The limit of detection was approximately three parts per trillion.

The Veterans Administration has measured TCDD levels in the fat of a small number of Vietnam veterans. Of the 22 samples for which results have been released, TCDD was detected in 10 of them at levels of from three to 57 parts per trillion.[36]

Two, 3,7,8-TCDD bioaccumulates in the model ecosystems that have been studied. As an organism is eaten by the next higher organism in the food chain, the dioxin in its body is stored in the predator's fatty tissue, only to be released when the predator dies or is eaten by a predator still higher on the chain. In one study, TCDD was applied to sand at the bottom of an aquarium. The water (and microorganisms) in the aquarium contained 1.3 ppb of 2,3,7,8-TCDD, while mosquito larvae raised in the tank contained 3,700 ppb TCDD, and fish feeding on the larvae were contaminated with 708 ppb of TCDD—a lower, but still substantial concentration.[37] Carp and catfish captured in Vietnamese rivers downstream from a areas sprayed months before contained 2,3,7,8-TCDD, providing tentative field evidence for a dioxin's ability to move up a food chain.[38]

### Environmental Fate of Dioxins

Dioxins are not readily destroyed by many of the routes of decomposition effective for other pollutants. In the environment chemical decomposition typically occurs through reactions with sunlight (photodecomposition), through the action of bacteria (microbial decomposition), or through various chemical reactions. Of these, dioxins seem to be readily broken down only by photodecomposition, and then only under special conditions. When 2,3,7,8-TCDD is suspended in a thin film of some organic solvent (alcohol, benzene, or the petroleum distillates used as the carrier for herbicide sprays) and exposed to direct sunlight, it is rapidly broken

down, having a half-life of as little as one hour.[39] Thus, when dioxin-containing 2,4,5-T is sprayed onto crops, much of the dioxin may be eliminated in a short period of time. No actual field tests have been conducted to confirm this, however. Photodecomposition is slowed and almost stopped when no organic solvent is present (the solvent is thought to serve as a hydrogen donor)—for example, when 2,3,7,8-TCDD is spread on soil or placed in water.[40] The half-life of 2,3,7,8-TCDD is generally thought to be about one year in soils of various types.[41] However, recent studies of TCDD in the soil of Seveso, Italy, have found a much longer half-life—perhaps ten years.[42]

Of 100 microbial strains known to degrade pesticides of various kinds, only five have shown any ability to degrade 2,3,7,8-TCDD.[43] There is no known route of metabolism of the most-studied dioxin, 2,3,7,8-TCDD, in mammals. The half-life of 2,3,7,8-TCDD in the rat is about three weeks to one month.[44]

**Table 3**
**SINGLE ORAL DOSES OF DIOXINS NECESSARY TO KILL 50 PERCENT OF ANIMALS EXPOSED (micrograms per kilogram body weight)**

| Dioxin | Animal Species | $LD_{50}$ (μg/kg bw) |
|---|---|---|
| 2,3,7,8-tetrachloro | Guinea pig | 2 |
| | Rat (male) | 22 |
| | Rabbit | 115 |
| | Mouse | 284 |
| 1,2,3,7,8-pentachloro | Guinea pig | 3 |
| | Mouse | 338 |
| 1,2,3,4,7,8-hexachloro | Guinea pig | 73 |
| | Mouse | 825 |

SOURCE: Hay, note 7; Anon., note 28.

## Toxic Effects

Despite much research over the last ten years, the precise mechanisms of the dioxins' toxicity are unknown. The acute (that is, short-term, high-dose) toxicity of some dioxins is summarized in Table 3. The $LD_{50}$ values (the dose necessary to kill half of the exposed animals) are shown for a variety of species.

**Table 4**
**EFFECTS OF 2,3,7,8-TCDD ON SOME ANIMALS**

| | Mouse | Rat | Guinea Pig | Rhesus Monkey |
|---|---|---|---|---|
| Bone marrow degeneration | ? | ? | + | + |
| Liver degeneration | + | + | – | + |
| Testicular degeneration | + | + | + | + |
| Renal and urinary hyperplasia (abnormal cell proliferation) | – | – | + | + |
| Internal hemorrhage | + | ? | + | + |
| Skin lesions | – | – | – | + |
| Birth defects (after exposure of mother) | + | + | ? | – |
| Cancer | + | + | ? | ? |
| Suppression of immune response | + | + | + | + |

KEY: "+": the effect has been observed; "–": the effect has been observed *not* to occur; "?": conflicting results concerning this effect have been observed.

SOURCE: Miller, Lalich, and Allen, note 1; Federal Register, note 2; Hay, note 7; Anon., note 28; Allen et al., note 45.

The acute and chronic (low-level, long-term) lethal doses for an animal can be quite different. For example, when TCDD is given in one dose, the $LD_{50}$ for rhesus monkeys is 50 to 70 micrograms per kilogram of body weight (μg/Kg/bw), while the same species will succumb from ingesting only 2 to 3 μg/Kg/bw over a nine-month period.[45]

The toxic effects of chronic (low-level, long-term) exposure to dioxins are numerous, and not well understood. Unfortunately, 2,3,7,8-TCDD is the only isomer which has been extensively studied. Table 4 summarizes the toxic effects revealed in a large number of animal studies of this dioxin. Several organ systems have been found to be adversely affected by TCDD. In general, there is substantial agreement among the results obtained from experiments using different species.

As is often the case with environmental toxins, the data on the toxic effects of human exposures are far less abundant, and much more equivocal. The greatest certainty exists about the least severe effects. For example, TCDD can cause a severe skin rash (chloracne), changes in skin color (hyperpigmentation), excessive hair growth (hirsutism), liver damage, and numbness and tingling (polyneuropathies) in the arms and legs.[46] All of these symptoms have been observed in industrial accidents involving exposure of workers to TCDD; chloracne and possibly other of these symptoms have also been seen among U.S. veterans who were exposed to Agent Orange in Vietnam.[47]

## Genetic Toxicity

The possibility that TCDD may also have long-term genetic effects on people is causing great concern in Vietnam and among U.S. veterans of the Vietnam War. Tens of thousands of G.I.s were in or near areas sprayed with Agent Orange,[48] and many of them are blaming that exposure for serious health problems—including cancer, and birth defects among their children. The necessary studies have not been completed to prove these claims, but the evidence is mounting. The following is a brief summary of the data suggesting that TCDD may be capable of damaging human genetic material.

A genetic toxicant is a chemical which is either mutagenic (capable of causing mutations or damaging chromosomes), teratogenic (capable of causing birth defects), or carcinogenic (capable of causing cancer). These three types of toxicity are often grouped together because their mechanisms are thought to be quite similar in many cases. Mutations and many cancers and birth defects are caused by damage to DNA, the molecule carrying the genetic code and contained in the chromosomes. There is ample documentation that

*Bonnie Hill of Alsea, Oregon, who was responsible for first calling attention to a possible relationship between miscarriages in the area and the spraying of nearby forests with 2, 4, 5-T. EPA has since banned most uses of 2, 4, 5-T. (Photo courtesy of the Eugene, Oregon,* Register-Guard*)*

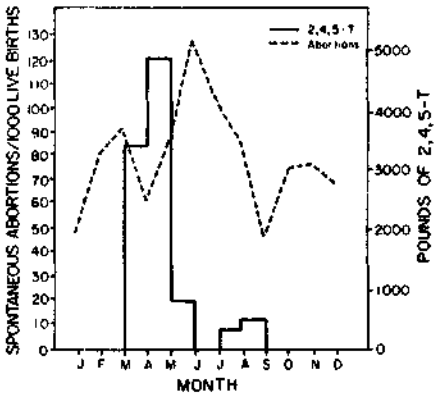



*FIGURE 2. Spraying of 2, 4, 5-T and spontaneous abortions in the region around Alsea, Oregon, accumulated by month, 1972-1977. (SOURCE: EPA)*

TCDD is a genetic toxicant in certain laboratory animals (see Table 4).

At least two studies have reported mutations in people exposed to TCDD. Hungarian chemical workers exposed to TCDD[49] and Vietnamese civilians exposed to Agent Orange[50] have been found to have high rates of chromosome damage.[51]

Birth defects (teratogenicity) have been linked to TCDD by at least three studies:

(*1*) The Environment Protection Agency suspended most uses of the herbicides 2,4,5-T and Silvex on February 28, 1979, largely because they found a significant increase in the rate of spontaneous abortions among women living in and around Alsea, Oregon, an area near many forests routinely sprayed with the herbicides.[52] Both contain TCDD as a trace contaminant. As shown in Figure 2, EPA found that the rate of miscarriages rose from a range of 40 to 80 hospitalized spontaneous abortions per month per 1,000 live births throughout most of the year, to 130 in June and 105 in July—about two months after the spring spraying season. This evidence strongly implicates (but does not confirm) some constituent of the herbicides 2,4,5-T and Silvex as being teratogenic. This study and the one cited just below show that there is a statistical *correlation* between the chemical and the toxic effect, but such studies alone are not sufficient to demonstrate a *causal* link.

(*2*) An Australian study[53] has shown a strong correlation between the rate of use of 2,4,5-T and the frequency of neural-tube defects (birth defects involving the brain or spinal column such as spina bifida, hydrocephaly, and microcephaly) in New South Wales.

(*3*) A recent study from North Vietnam[54] reports a higher incidence of neural tube defects among the children of North Vietnamese veterans of the war in the South (married to North Vietnamese women not exposed to Agent Orange) than among controls. However, the sample size is small, and the authors consider their findings preliminary.

Swedish investigators[55] have recently found strong evidence that exposure to chlorophenols and phenoxy acids (containing TCDD as a contaminant) increases the risk of contracting a rare cancer—soft-tissue sarcoma (a cancer of the connective tissue). They found that 52 people with this cancer more frequently reported exposure to TCDD-containing chemicals than did 208 people matched to the cancer victims by age, sex, and place of residence. The exposure to these chemicals caused a six-fold increase in the risk of contracting soft-tissue sarcoma.

None of the dioxins are yet recognized as human genetic toxicants, despite the evidence cited here. Large-scale epidemiological studies of workers exposed to dioxins and of Vietnam veterans are necessary before the issue can be settled.

* * * *

Literally thousands of scientific papers have been written on dioxins (most of them on 2,3,7,8-TCDD) and the products contaminated with them. That the dioxins are a class of extremely toxic chemicals is one point of general consensus in this literature. Among the critically important but still unresolved issues are: Are dioxins being created in significant quantities through combustion? What is the fate of the unknown quantities already dispersed throughout the environment? Are dioxins causing genetic damage to the human population? This paper has touched on each of these issues, but much more research must be conducted before they can be put to rest.

Meanwhile, public policy decisions regarding dioxin-containing products must be made. As is often the case, the scientific information available cannot provide unequivocal guidance to the policy makers, and the decision to regulate must ultimately be a social one—informed but not dictated by the scientific information at hand.

**ACKNOWLEDGMENT**

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(Hearings on whether EPA should make the temporary suspension of 2,4,5-T permanent have been going on for many months and will probably continue for about another year. Although a recent press release from the Dow Chemical Company [the principal producers of 2,4,5-T] claims that the Alsea studies have been "abandoned" by EPA, sources at EPA deny that this is in fact the case. Dr. Robert Duncan, Director of the Division of Biostatistics in the Department of Epidemiology at the University of Miami Medical School, was one of the authors of the original Alsea II study. In a telephone conversation with Environment, Professor Duncan reported that he has reworked his original data, taking into account some new data developed by Oregon State University and the various criticisms made of his study, and that the original correlation between the number of abortions per 1,000 live births and the time and amount of spraying of 2,4,5-T still continues to hold true.)

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IP244



# Dow Planning $3 Million Program to Allay Fears Over Dioxins

By Ward Sinclair
Washington Post Staff Writer

MIDLAND, Mich., June 1—The Dow Chemical Co. announced yesterday that it will spend $3 million on independent studies to show what it already believes—that there is no danger to humans from trace levels of dioxins, poisonous byproducts of the production of some chemicals.

President Paul F. Oreffice, presiding at a heavily attended briefing in the Dow headquarters television studio, conceded that the program is aimed as much at quieting public fears as it is in producing new science.

"Our perspectives and judgments about the dioxin controversy remain unchanged," Oreffice said. "What has changed is that with all the publicity dioxin has received, the general public cannot be expected to take our word for it without corroboration. We invite and are encouraging third-party evaluation and verification of our own scientific conclusions."

Dow in recent months has been at the center of an outcry in Michigan and other parts of the country over the health effects of dioxins, compounds highly toxic to laboratory animals.

Dow's Agent Orange, a jungle defoliant used in Vietnam, and 2,4,5-T, a herbicide no longer manufactured here, generated dioxin as a byproduct. Both are the subject of potentially expensive litigation seeking to hold the company liable for health impairment allegedly caused by its products.

Oreffice and other Dow officials have maintained consistently that there is no health threat from dioxins, and have rejected allegations that the company has poisoned the soil around Midland and the water of the Tittabawassee River with its industrial processes.

Yesterday's news conference, which drew print and electronic media reporters from across the country, was part of an intensified Dow public relations campaign to allay public fears about its products and to counter charges of secrecy and corporate arrogance.

Oreffice complained that "fame breeds fame, and the spotlight on dioxin in Midland has attracted a steady stream of reporters, camera crews, government officials and others .... Sometimes we have been asked questions for which there are no absolute answers. For this we have been accused of equivocation or talking out of both sides of our mouth.

"When we respond unequivocally, we are accused of arrogance or self-righteousness. I guess we can accept these accusations. But what we cannot and will not accept is the level of anxiety and concern the publicity surrounding this issue has generated in the country, in this state, and for some in this community.

"We believe we have come up with an approach for addressing the understandably human concerns that people throughout the state and perhaps nationally are feeling about dioxin in Michigan."

Oreffice said Dow's $3 million investment will cover these elements:

- A state and federal study of soil contamination inside the plant, in the city of Midland and other sites; an investigation of dioxin sources inside the plant; a state study of soft tissue cancer, which in Midland County exceeds national averages, and a University of Michigan research study on ways to reduce dioxin in the Dow waste water effluent stream.
- Expansion of Dow's analytical laboratory, doubling its ability to detect dioxin in the regional environment, and a study by an independent scientific organization that Oreffice declined to identify to determine if trace amounts of dioxin pose a health hazard to humans.

Oreffice said he believed Dow's effort, to be completed within two years, will help answer concerns about the perils of dioxin. And he also said that Dow supports the proposed $12 million national dioxin study by the Environmental Protection Agency.

The company president, however, indicated he expected no surprises as a result of Dow's investment. He said he anticipated the studies would show "that all our science is correct and that there is no danger .... We will accept the results."

The company announcement was greeted skeptically by at least one of Dow's local critics. Environmentalist Andrea K. Wilson said, "I'm glad there will be more studies but we'd like to be assured there will be independent third-party review of the findings. We're thinking this may be an attempt to defuse our request for a full scale EPA investigation .... All of Dow's focus is on the dioxin, but there are real serious concerns here about other environmental and public health issues."

PAUL F. OREFFICE
..."We will accept the results"