COI-/VCM
INFO TO DON P.

LAW OFFICES
KELLER AND HECKMAN
1150 17TH STREET, N.W.
SUITE 1000
WASHINGTON, D.C. 20036
(202) 956-5600

December 7, 1989

Roy T. Gottesman, Ph.D.
The Vinyl Institute
155 Route 46 West
Wayne, New Jersey 07470

Re: NTP Fifth Annual Report on Carcinogens

Dear Roy:

The National Toxicology Program's Fifth Annual Report on Carcinogens has recently been made available. Since you may receive inquiries on this matter, I am enclosing the introductory portion and the sections describing vinyl chloride and di(2-ethylhexyl)phthalate (DEHP).

By way of background, the Fourth Annual Report was issued in 1985 (so obviously the Fifth Annual Report is dated 1989). Both vinyl chloride and DEHP were listed as carcinogens in the Fourth Annual Report, but I thought you might appreciate having a copy of the most recent version for your files.

Cordially yours,

Peter

Peter L. de la Cruz

Enclosures

cc: Larry Thomas (w/o enc.)
Robert W. Sherman (w/o enc.)
Hugh Patrick Toner (w/o enc.)

SL 089495

FIFTH ANNUAL REPORT ON CARCINOGENS 1989

U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
Public Health Service

National Toxicology Program

Pursuant to Section 301(b)(4)
of the Public Health Service Act
as Amended by Section 262, PL 95-622

FIFTH ANNUAL REPORT ON CARCINOGENS 1989

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Toxicology Program

Prepared for the
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
Research Triangle Park, North Carolina 27709
By
Technical Resources, Inc.
Rockville, Maryland 20852
Under Contract Number
N01 ES 3 5025

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NOTE TO THE READER

Listing of a substance in the *Annual Report on Carcinogens* is mandated by Public Law 95-622 and is for informational purposes. The evaluation of substances listed in the *Annual Report* is performed by scientists from the National Toxicology Program and other Federal health research and regulatory agencies. This listing is the first step in hazard identification, is qualitative in nature, and represents only one step in the total risk assessment process. The evaluation of the degree of potential human risk from the substances included in the *Annual Report* requires a wider analysis than has been made in preparing this document. That is properly the purview of the Federal, State, and local health regulatory and research agencies authorized to implement the laws relating to carcinogens.

For the purpose of this Report, "known carcinogens" are defined as those substances for which there is sufficient evidence of carcinogenicity from studies in humans to indicate a causal relationship between the agent and human cancer. "Reasonably anticipated to be carcinogens" are those substances for which there is limited evidence of carcinogenicity in humans and/or sufficient evidence of carcinogenicity in experimental animals. Sufficient evidence in animals is demonstrated by positive carcinogenicity findings in multiple strains and species of animals, in multiple experiments, or to an unusual degree with regard to incidence, site or type of tumor, or age of onset. Only substances for which the evidence of carcinogenicity has been peer-reviewed are evaluated for possible inclusion in the Annual Reports.

Anyone who is aware of published data that may alter the listing of a substance in the *Annual Report* is encouraged to make this information available to the National Toxicology Program.

Although every effort is made to prepare the *Annual Report* as accurately as possible, mistakes may occur. Readers are requested to communicate any errors to Annual Reports on Carcinogens, c/o National Toxicology Program, P.O. Box 12233, Research Triangle Park, North Carolina 27709, in order that corrections can be reported in future Annual Reports.

I. EXECUTIVE SUMMARY

EXECUTIVE SUMMARY

The *Fifth Annual Report on Carcinogens*, prepared by the National Toxicology Program (NTP), U.S. Public Health Service, is issued by the Secretary of the Department of Health and Human Services (DHHS), pursuant to Public Law 95-622 of November 9, 1978.* This law requires the Secretary to publish an annual report that contains "a list of all substances (i) which either are known to be carcinogens or which may reasonably be anticipated to be carcinogens and (ii) to which a significant number of persons residing in the United States are exposed;..." Annual Reports should also provide available information on the nature of exposures, the estimated number of persons potentially exposed, and the extent to which the implementation of Federal regulations decreases the risk to public health from exposure to these substances.

For the purpose of this Report, "known carcinogens" are defined as those substances for which the evidence from human studies indicates that there is a causal relationship between exposure to the substance and human cancer. Substances "which may reasonably be anticipated to be carcinogens" are defined as those for which there is limited evidence of carcinogenicity in humans or sufficient evidence of carcinogenicity in experimental animals.

Substances in the above categories, for which potential exposure of persons residing in the United States has been demonstrated, are included in the Report. In the *Fifth Annual Report*, attempts are made to list substances that are currently being used, or for which there is some evidence for continuing exposures in the workplace or in the general environments of persons residing in the United States. In Section IX, there is a list of chemicals now banned or no longer produced in the United States, and/or for which there is no evidence for continuing exposure of persons residing in the United States. These chemicals have formerly appeared in Annual Reports, and information about them is provided in these earlier editions for all who are interested. The *Fifth Annual Report* does not contain all known or reasonably anticipated carcinogens. Additional substances with identified carcinogenic properties as defined above will be included in subsequent Annual Reports.

Several problems are encountered in developing the information required for the *Annual Report on Carcinogens*. Estimating the number of people potentially exposed to a substance and identifying the nature, route, and intensity of this potential exposure are difficult tasks. It is often impossible to obtain accurate production volumes and use patterns for most chemicals. The information that is being collected by the U.S. Environmental Protection Agency under the Toxic Substances Control Act, at least that part which is public record, may assist in obtaining more recent and accurate data on domestic production and importation of substances in the Reports. In addition, data compiled from the National Occupational Exposure Survey (NOES) conducted by the National Institute for Occupational Safety and Health (NIOSH) from 1980 to 1983 provides new information on the numbers of workers

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* Section 262, Paragraph (4).

Section V is a glossary of frequently used terms, a list of commonly used acronyms, and some common units of measurement. Section VI is an index of Chemical Abstracts Service (CAS) registry numbers for chemical substances, and the page number where the substance appears in the *Fifth Annual Report*. Section VII is a list of participating agencies and their staff who collaborated in the preparation of the *Fifth Annual Report*, and Section VIII contains a cumulative list of the Code of Federal Regulations and Federal Register citations for this Report.

Corrections or suggestions for the Report, as well as any additional information that the reader may have, should be sent to Annual Reports on Carcinogens, c/o National Toxicology Program, P.O. Box 12233, Research Triangle Park, North Carolina 27709.

Summaries of this Report may be obtained from the Public Information Office, National Toxicology Program, B2-04, P.O. Box 12233, Research Triangle Park, North Carolina 27709. Copies of the complete Report are available for a fee from the National Technical Information Service, 5285 Port Royal Road, Springfield, Virginia 22161.

II. INTRODUCTION

INTRODUCTION

Cancer is the second most common cause of death in the United States. One in every four Americans will suffer from cancer sometime during their lifetime; one in every five will die from cancer. In 1984, more than 450,000 Americans died of cancer (NCHS, 1986). In addition to the physical and emotional suffering caused by cancer, this disease may cost the Nation as much as $39 billion each year in lost production and income, medical expenses, and research resources. For these reasons, the American public is concerned about cancer and cancer hazards, especially about ways to prevent the occurrence or decrease the incidence of cancers.

Contrary to popular belief, cancer is not one but many diseases which may have different causes. Many scientists believe that from one-third to two-thirds of all cancers may be associated with the environment in which we live and work. In this context, the environment is understood as "anything that interacts with humans, including substances eaten, drunk, and smoked; natural and medical radiation; workplace exposures; drugs; aspects of sexual behavior; and substances in air, water, and soil (OTA, 1981)." Some cultural and behavioral patterns, apart from defined habits of smoking and alcohol consumption, may significantly influence the development of tumors in the gastrointestinal tract, breast, uterus, and prostate. These aspects of social environment, personal behavior, and habits are sometimes called "lifestyle." Although we rarely know the environmental factors and conditions which are responsible for the development of specific cancers, in some cases we are beginning to have some understanding. For example, we now know that the way foods are prepared and cooked, or how they are stored and preserved, can greatly affect the incidence of cancers in any population. It is the hope of many scientists in these fields that much of the cancer associated with the environment may be avoidable -- perhaps by some changes in "lifestyle."

Development of cancer also depends on "host factors." Host factors are attributes of human organisms associated with individual differences in the risk of developing a specified cancer. A host factor may be associated with reduced risk of a cancer, not only with increased risk (Cole, 1982). Examples of host factors are immunological and endocrine functions, nutritional status, genetic constitution, age, and sex, all of which can interact with one another and with the way the host handles the carcinogen -- i.e., how the host absorbs, distributes or stores, metabolizes, and excretes the carcinogen (Bartsch & Armstrong, 1982).

Americans, concerned with the relationships between their environment and cancer, have asked for information about substances that cause or might cause cancer.

Section 262 of Public Law 95-622 of November 9, 1978* reflects the requests for this information. Paragraph (4) of this section stipulates that

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* Community Mental Health Centers Act, Amendments.

Participants

Within the Department of Health and Human Services, the responsibility for preparing these Annual Reports has been given to the National Toxicology Program.* Agencies participating in this effort through the NTP Working Group for the Annual Reports on Carcinogens are:

Centers for Disease Control/National Institute for Occupational Safety and Health (CDC/NIOSH)

Consumer Product Safety Commission (CPSC)

U.S. Environmental Protection Agency (EPA)

Food and Drug Administration (FDA)

National Institutes of Health/National Cancer Institute (NIH/NCI)

National Institutes of Health/National Institute of Environmental Health Sciences (NIH/NIEHS)

National Institutes of Health/National Library of Medicine (NIH/NLM)

U.S. Department of Labor/Occupational Safety and Health Administration (DOL/OSHA)

Four of these agencies -- CPSC, EPA, FDA, and OSHA -- are responsible for regulating hazardous substances and limiting the exposure to and use of such substances.

Most of the information in each entry of the Annual Report on Carcinogens on "Use", "Production", and "Exposure" is provided by participants from the regulatory agencies given above.

Identifying Carcinogens

For many years, government research agencies, industries, universities, and other research organizations have studied various substances to ascertain those that might cause cancer. Other Federal agencies have been developing information on possible exposure and potential hazards and making rules and regulations to control substances which have been identified as carcinogens.

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* DHHS member agencies participating in NTP are NIH/NCI; NIH/NIEHS; FDA/National Center for Toxicological Research (FDA/NCTR); CDC/NIOSH; and Agency for Toxic Substances and Disease Registry (ATSDR).

2) Reasonably anticipated to be carcinogens:

A. There is "limited evidence of carcinogenicity" from studies in humans, "which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias or confounding, could not adequately be excluded," or

B. There is "sufficient evidence of carcinogenicity" from studies in experimental animals "which indicates that there is an increased incidence of malignant tumors: (a) in multiple species or strains, or (b) in multiple experiments (preferably with different routes of administration or using different dose levels), or (c) to an unusual degree with regard to incidence, site or type of tumor, or age at onset. Additional evidence may be provided by data concerning dose response effects, as well as information on mutagenicity or chemical structure."

The reader is reminded that the *Fifth Annual Report on Carcinogens* (and all previous editions) is a condensation of large amounts of data and conclusions made by bodies which peer review the data submitted as evidence about cancer and its relation to specific exposures. As such, the *Fifth Annual Report on Carcinogens* must be less detailed about the actual tests and their drawbacks. The original monographs on each listing are given in the references, and the reader is advised to turn to these for the specific arguments, both pro and con, which went into the listing decision.

Human and Animal Studies

Both human and animal studies, where available, are used in identifying chemicals as possible carcinogens for humans. The strongest evidence for relationships between exposure to any given chemical and cancer in humans comes from carefully conducted epidemiological studies. Good epidemiology studies of cancer must consider the latent period of most cancer development since the exposure to the carcinogen often occurs many years (sometimes 20 to 30 years or more) before the first sign of cancer appears. As an alternative to what is usually missing in epidemiological studies of suspected carcinogens for humans (accurate information about dose and duration of exposure, and interactions of the suspected carcinogen with other chemicals or modifiers), scientists can use well-designed animal studies. In these, the suspected carcinogen is administered to large numbers of animals in (usually at least) two species over a range of doses and times with all parameters chosen to maximize the possibility of producing cancer (e.g., the doses of suspected carcinogen are usually large).

The *Fifth Annual Report on Carcinogens* contains entries on the carcinogenicity of seven metals (arsenic, beryllium, cadmium, chromium, lead, nickel, and thorium). Many different salts or compounds of these metals exist and, with any particular metal, only a few of these have been evaluated in animals for carcinogenicity. However, some general principles may apply. The toxicologic (and carcinogenic) hazard from a metal may often be a property less of the form of the metal administered than of the metal per se, although the toxicity and carcinogenicity (e.g., potency) of any compound can also be a function of its bioavailability. The anion or ligand of the metal often seems to determine the physico-chemical properties which then affect bioavailability characteristics such as solubility, absorption, and distribution to sites believed to be involved in carcinogenesis, etc. In the absence of data (e.g., about bioavailability), all compounds or salts of any metal shown to be carcinogenic in one of its forms may be reasonably anticipated to be carcinogens. This caveat may also apply to the elemental metal (OHEA, 1986).

Ionizing radiation, ultra-violet radiation (including sunlight), tobacco, alcoholic beverages, and some viruses are known or suspected to be carcinogens. They have not been included in this Report (unless acting in conjunction with a chemical) because ionizing radiation is discussed thoroughly in a General Accounting Office Report, and a Surgeon General's Report reviews the overwhelming relationship between tobacco and cancer (GAO, 1981; OSH, 1982). Several publications issued by the National Cancer Institute explain the relationship of alcoholic beverages, ultra-violet radiation, and viruses to cancer (e.g., Shimkin, 1980).

Certain manufacturing processes and mixtures of chemicals have been considered by the International Agency for Research on Cancer (IARC) and have been classified by IARC as sources which are associated with increased incidences of cancer in workers in these settings. Among these are:

1. Boot and Shoe Manufacture and Repair (IARC S.4, 1982; IARC V.25, 1981)
2. Certain Combined Chemotherapy for Lymphomas (IARC S.4, 1982; IARC V.25, 1981)
3. Furniture Manufacture (IARC S.4, 1982; IARC V.1, 1972)
4. Hematite Underground Mining (IARC S.4, 1982; IARC V.1, 1972)
5. Isopropyl Alcohol Manufacturing (Strong-Acid Process) (IARC S.4, 1982; IARC V.15, 1977)
6. Manufacture of Auramine (IARC S.4, 1982; IARC V.1, 1972)
7. Nickel Refining (IARC S.4, 1982; IARC V.2, 1973; IARC V.11, 1976)
8. Rubber Industry (IARC S.4, 1982; IARC V.28, 1982).

This list of substances with key references is then published in the Federal Register for comment. Final decisions on the substances to be included in the Annual Report and on other issues raised are made after the two review groups have evaluated the submitted comments on each of the issues.

Once decisions have been made on the chemicals to be included in the Annual Report, the support contractor prepares the initial draft of the Report, which contains an entry on each of the substances judged to be known carcinogens or reasonably anticipated to be carcinogens. As mandated by Congress, these entries include data on the nature of exposure to the substances and the estimated numbers of persons exposed, and information on the Federal regulations promulgated on the substances; in addition, they contain summaries of the relevant carcinogenicity data. The information on Federal regulations and other Federal activities is supplied by the agencies that serve on the Working Group for the Annual Report on Carcinogens. These agencies also contribute data on levels of exposure to the substances under the use situations for which they have jurisdiction.

Following extensive review by NIEHS scientific staff, the draft Report is revised and submitted first to the Working Group for the Annual Reports on Carcinogens and then to the NTP Executive Committee for evaluation. Modifications suggested by member Agencies are incorporated into the document which is then transmitted to the Secretary, Department of Health and Human Services, for final review, approval, and publication.

Because of increased levels of interest in the Annual Reports on Carcinogens, a further opportunity for public comment was added to the process for preparation of the *Fifth Annual Report on Carcinogens*. An open meeting was held on April 21, 1987, in Washington, DC, to discuss the process by which the Annual Reports on Carcinogens are prepared, and to receive oral and written comments. Seventeen oral presentations were given, all but one of which were supported by written submissions. Fourteen other written comments were submitted by individuals and groups unable to attend the meeting. In response to requests for more information on the process for preparation of the Annual Reports, the above description has been added to this Report and will appear in subsequent Reports.

Estimating Exposure

According to clause (ii) of subparagraph (4)(A), this Report is required to include those substances "to which a significant number of people residing in the United States are exposed." Substances to which only a few people are exposed are not included for the most part. Yet some substances that have been banned or restricted in use are contained in the Report (e.g., safrole, arsenical pesticides, mirex), either because people who were previously exposed remain potentially at risk, or because these substances are still present in the environment.

OSHA has recently taken regulatory action which affects the permissible exposure limits for the following substances: amitrole, beryllium and certain beryllium compounds, chromic acid and chromates including zinc chromate, carbon tetrachloride, DDT (dichlorodiphenyltrichloroethane), 1,4-dichlorobenzene, 1,2-dichloroethane, 1,3-dichloropropene, di(2-ethylhexyl)phthalate, dimethyl sulfate, 1,4-dioxane, epichlorohydrin, ethyl acrylate, hydrazine and hydrazine sulfate, 4,4'-methylenebis(2-chloroaniline), certain nickel compounds, 2-nitropropane, propylene oxide, tetrachloroethylene, 2,4-toluene diisocyanate, o-toluidine and toluidine hydrochloride, and toxaphene. For information on current OSHA regulations for these substances, the reader should obtain 54 FR 2329 (January 19, 1988) or OSHA Publication 3112, Air Contaminants -- Permissible Exposure Limits (29 CFR 1910.1000).

Estimating Risk Reduction

Clause (ii) in subparagraph (4)(C) requires a statement identifying "for each effluent, ambient, or exposure standard established by a Federal agency with respect to a substance contained in the list under subparagraph (A), the extent to which, on the basis of available medical, scientific, or other data, such standard, and the implementation of such standard by the agency, decreases the risk to public health from exposure to the substance;..." This requires quantified information on the amount of protection from cancer that the public receives from established Federal standards.

Estimating the amount of health protection is perhaps the most difficult task in preparing the Annual Reports. One reason is that most Federal laws concerned with reducing cancer risk have been enacted within the last 15 years. Given the long period between the initial exposure to a carcinogen and the onset of disease, it is still too early to evaluate to what extent Federal standards and other regulations have decreased the human cancer risk. Another reason is that information on past exposure levels, which could serve as a baseline for estimating future risk reduction, often is not available or accurate.

The risk -- the probability of developing cancer -- depends on many things, including the intensity, route, and duration of exposure to a carcinogen. Individuals may respond differently to similar exposures, depending on host factors such as age, sex, nutritional status, overall health, and inherited characteristics. Only in a few instances, where studies of long-term human exposures and cancer incidence in restricted environments are available, can risk be estimated with any confidence.

The regulation of asbestos in the workplace provides a good example. In 1969, under the Walsh-Healey Act, which then regulated only firms with government contracts, the standard for permissible exposure was 12 fibers of asbestos per cubic centimeter (cm^3) of air. Under the Occupational Safety and Health Act, this standard was reduced to 5 fibers/cm^3 in 1972 and to 2 fibers/cm^3 in 1976. On April 17, 1980, a joint NIOSH/OSHA Working Group recommended the elimination of all nonessential uses of asbestos and the implementation of a public health program to reduce human exposures. On April 10, 1984, OSHA proposed a rule lowering the permissible exposure to 0.2 or 0.5 fibers/cm^3 (5 micrometers in length) and requiring other provisions for employee protection.

Other Information

Section V is a glossary of terms, acronyms, and units of measurement used frequently in the *Fifth Annual Report*. Section VI is a list of Chemical Abstracts Service (CAS) registry numbers of chemical substances in this Report, and the page number where a profile of the substance appears in the *Fifth Annual Report*. Section VII is a list of participating agencies and their representatives who collaborated in preparing the *Fifth Annual Report*. Section VIII contains a cumulative list of Federal Regulations and Federal Register citations for this report. Section IX is a list of chemicals which have been delisted from the Annual Report because they are now banned or no longer produced in the United States.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. Supplement 4. 292 pp. Lyon, France: IARC, 1982.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity. Supplement 7. 440 pp. Lyon, France: IARC, 1987.

NCHS. National Center for Health Statistics. Advance Report of Final Mortality Statistics, 1984. Vol. 35, No. 6. 44 pp. Washington, DC: U.S. Department of Health and Human Services, 1986.

OHEA. "Health Assessment Document for Nickel and Nickel Compounds"; Final Report; especially section 2 (pages 7 and 11); section 5 (page 14); and section 8 (pages 113, 155, and 225). EPA Office of Health and Environmental Assessment, EPA/600/8-83/012ff, September 1986.

OSH. Office on Smoking and Health. The Health Consequences of Smoking: Cancer, a Report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, 1982.

OTA. Office of Technology Assessment, Congress of the United States. Assessment of Technologies for Determining Cancer Risks from the Environment. U.S. Government Printing Office, Washington, DC, 1981.

Shimkin, M.B. Science and Cancer. NIH Publication No. 80-568, Third Revision. National Cancer Institute, National Institutes of Health. Bethesda, MD: U.S. Department of Health and Human Services, 1980.

III. SUBSTANCES LISTED

XX

SL 089512

A. List of Substances

LIST OF SUBSTANCES*

1. Substances or groups of substances, occupational exposures associated with a technological process, and medical treatments that are known to be carcinogenic.**

	Page
4-Aminobiphenyl	8
Analgesic Mixtures Containing Phenacetin	11
Arsenic and Certain Arsenic Compounds	14
Asbestos	28
Azathioprine	41
Benzene	43
Benzidine	50
Bis(chloromethyl)ether and Technical Grade Chloromethyl Methyl Ether	56
1,4-Butanediol Dimethylsulfonate (Myleran)	62
Chlorambucil	64
Chromium and Certain Chromium Compounds	67
Coke Oven Emissions	619+
Conjugated Estrogens	79
Cyclophosphamide	82
Diethylstilbestrol	86
Melphalan	91

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* Several manufacturing processes or mixtures of chemicals/drugs have been considered by IARC/ARC as carcinogenic. Please see page xi in the Introduction for a discussion and listing of these.

** For the purpose of this Report, "known carcinogens" are defined as those substances for which the evidence from human studies indicates that there is a causal relationship between exposure to the substance and human cancer.

\+ This occupational exposure is included in section IIIC.

Methoxsalen with Ultra-violet A Therapy (PUVA)	
Mustard Gas	
2-Naphthylamine	1
Soots, Tars, and Mineral Oils	6
Thorium Dioxide	1
Vinyl Chloride	1

* This occupational exposure is included in section IIIC.

2. Substances or groups of substances, and medical treatments which may reasonably be anticipated to be carcinogens.*

	Page
2-Acetylaminofluorene	114
Acrylonitrile	117
Adriamycin	124
Aflatoxins	126
2-Aminoanthraquinone	129
o-Aminoazotoluene	131
1-Amino-2-methylanthraquinone	133
Amitrole	135
o-Anisidine Hydrochloride	138
Benzotrichloride	141
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1,3-Butadiene	156
Cadmium and Certain Cadmium Compounds	161
Carbon Tetrachloride	174
Chlorendic Acid	181
Chlorinated Paraffins (C_{12}, 60% Chlorine)	184
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)	188
Chloroform	190
3-Chloro-2-methylpropene	196
4-Chloro-o-phenylenediamine	198
C.I. Basic Red 9 Monohydrochloride	201
p-Cresidine	203
Cupferron	206
Dacarbazine	208

* For the purpose of this Report, substances "which may reasonably be anticipated to be carcinogens" are defined as those for which there is a limited evidence of carcinogenicity in humans or sufficient evidence of carcinogenicity in experimental animals.

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1,2-Dibromoethane (EDB)	228
1,4-Dichlorobenzene	238
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1,2-Dichloroethane	249
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Thioacetamide	580
Thiourea	583
Toluene Diisocyanate	587
o-Toluidine and o-Toluidine Hydrochloride	593
Toxaphene	598
2,4,6-Trichlorophenol	603
Tris(1-aziridinyl)phosphine Sulfide	607
Tris(2,3-dibromopropyl)phosphate	610
Urethane	614

VINYL CHLORIDE
CAS No. 75-01-4

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of vinyl chloride in experimental animals (IARC V.19, 1979; IARC S.4, 1982). When administered by inhalation, vinyl chloride induced kidney and pulmonary adenomas, mammary adenomas and carcinomas, liver angiosarcomas, and angiosarcomas and adenocarcinomas in other organs in mice of both sexes. Inhalation of vinyl chloride induced epidermoid, mucoepidermoid, and Zymbal gland carcinomas, osteochondromas, nephroblastomas, brain neuroblastomas, liver angiosarcomas, angiosarcomas and papillomas in other organs, and lung tumors in rats of both sexes. Male hamsters developed liver angiosarcomas, skin trichoepitheliomas, melanomas, acanthomas, lymphomas, and forestomach papillomas, and rabbits developed lung adenocarcinomas and skin acanthomas; newborn rats developed angiosarcomas and hepatomas when exposed to vinyl chloride by inhalation. The tumorigenic effect of vinyl chloride was increased when it was administered by inhalation prior to and concurrent with ethanol in the drinking water. This route of administration induced liver angiosarcomas, neoplastic nodules, and hepatocellular carcinomas, lung angiosarcomas, kidney fibromas and angiosarcomas, and skin fibromas in rats (Radike et al., 1977). Subcutaneous injections of vinyl chloride in olive oil induced nephroblastomas in rats. When injected intraperitoneally, vinyl chloride induced angiosarcomas and nephroblastomas in rats. When administered by gastric intubation, vinyl chloride dissolved in olive oil induced liver angiosarcomas, Zymbal gland carcinomas, nephroblastomas, and thymic and intraabdominal angiosarcomas in rats of both sexes (IARC V.19, 1979; IARC V.7, 1974).

There is sufficient evidence for the carcinogenicity of vinyl chloride in humans (IARC S.4, 1982). Although evidence of a carcinogenic effect of vinyl chloride in humans has come from groups occupationally exposed to high doses of vinyl chloride, there is no evidence that there is an exposure level below which no increased risk of cancer would occur in humans. Case reports in epidemiology have shown increased incidences of liver angiosarcomas and hemangiomas, lung angiosarcomas and adenocarcinomas, brain angiosarcomas, other lymphomas, and lymphopoietic system tumors in humans occupationally exposed to vinyl chloride (IARC V.19, 1979).

PROPERTIES

Vinyl chloride is a colorless, flammable gas with a faintly sweet odor. The gas polymerizes in light and liquifies in a freezing mixture. It is slightly soluble in water, soluble in ethanol, and very soluble in ether, carbon tetrachloride, and benzene. In the form of vapor, vinyl chloride is a dangerous fire and severe explosion hazard when exposed to heat, flame, or oxidizers. On standing, it forms peroxides in air and can then explode. On combustion, it is degraded mainly to carbon dioxide, carbon monoxide, hydrogen chloride, and traces of phosgene. Technical grade vinyl chloride is commercially supplied as a 99.9% pure liquid under pressure.

USE

Vinyl chloride is industrially important because of the inherent flame retardant properties of its polymer, its wide variety of end use products, and the low cost of producing polymers from it (ATSDR, 1988). Vinyl chloride monomer is the parent compound of polyvinyl chloride (PVC), a plastic resin used in innumerable consumer and industrial products, including containers, wrapping film, battery cell separators, refrigerant gas, electrical insulation, water distribution systems (water and drain pipes, hose), flooring, windows, phonograph records, videodiscs, irrigation systems, and credit cards. Vinyl chloride-vinyl acetate copolymers are used extensively to produce vinyl asbestos floor tiles (IARC V.7 1974; IARC V.19, 1979; NCI DCCR 1978; ATSDR, 1988).

PRODUCTION

Vinyl chloride is produced at 10 locations in the U.S. Imports of vinyl chloride were approximately 200 million lb in 1987. Domestic production of vinyl chloride in 1986 was estimated to be between 8.5 billion and 8.6 billion lb. This was approximately 94 to 98% of the available production capacity in 1986 (ATSDR, 1988). This figure represents a decrease from the 1985 production of 9.4 billion lb (Chem. Engr. News, 1987a). In 1985, vinyl chloride imports approached 130 million lb, and exports exceeded 1 billion lb (Chem. Week, 1986b). The USITC identified nine companies that produced a total of 7.5 billion lb of vinyl chloride in 1984, representing a substantial increase in production over the 6.8 billion lb produced in 1983 (USITC, 1984; USITC, 1985). The U.S. imported over 128 million lb of vinyl chloride in 1983 (USITCa, 1984). The 1979 TSCA Inventory identified 17 companies producing 6.9 billion lb of vinyl chloride in 1977, with some site limitations. The CBI Aggregate was more than 1 billion lb (TSCA, 1979).

EXPOSURE

The primary routes of potential human exposure to vinyl chloride are inhalation and dermal contact. Potential human exposure to vinyl chloride occurs in the workplace, through general air and water pollution, and to a limited extent, from the use of fabricated products (NCI DCCR, 1978). The major source of releases of vinyl chloride into the environment is believed to be emissions and effluents from plastic industries. Most of the vinyl chloride released into the environment will eventually locate in the atmosphere while much smaller amounts will eventually locate in ground water. Segments of the general population living in the vicinity of emission sources are potentially exposed to vinyl chloride by inhalation of contaminated air. Average daily intake of vinyl chloride by these people ranges from trace amounts to 2,100 ug/day. The average daily intake of vinyl chloride by inhalation is expected to be essentially zero for the remainder of the population; however, new car owners are potentially exposed to relatively high levels due to volatilization

of vinyl chloride from vinyl polymers within the car interior. Vinyl chloride has been detected at concentrations as high as 9.8 ug/l in surface water, 380 ug/l in ground water, and 10 ug/l in drinking water in the U.S. It has been reported that migration of vinyl chloride from rigid PVC water pipes into drinking water occurs and that it is directly proportional to the residual level of vinyl chloride in the pipe itself. The majority of the general population is not expected to be exposed to vinyl chloride through ingestion of drinking water. However, people who have PVC water pipes that have not been treated adequately to remove vinyl chloride monomer may ingest 0.06 to 2.8 ug/day of vinyl chloride from drinking water (ATSDR, 1988). The average daily intake of vinyl chloride through the diet is predicted to be essentially zero. Although large quantities of vinyl chloride are produced each year in the U.S., it is not in the production of the chemical itself that the greatest potential for harmful exposure exists. Occupational exposures generally occur after production, as the finished monomer is piped to storage or transportation, or during maintenance. The greatest potential for harmful hazard is when the chemical is polymerized to form other materials, nearly all of which are PVC resins, during which process vinyl chloride escapes into the air (NCI DCCR, 1978). This has been the major emission source and the process in which the highest occupational exposures have been reported. NIOSH estimated that 27,000 workers are exposed to vinyl chloride and that as many as 2.2 million workers are potentially exposed (NIOSH 28, 1978). Workplace air in some PVC manufacturing plants was found to contain 100 to 800 mg/m^3 vinyl chloride. A NIOSH survey of three vinyl chloride manufacturers reported time-weighted average (TWA) exposures of 0.18 to 69 mg/m^3 vinyl chloride in workplace air (ATSDR, 1988). Vinyl chloride has been detected in domestic and foreign cigarettes and little cigars, in concentrations of 5.6 to 27 ng/cigarette, and in a marijuana cigarette at 5.4 ng/cigarette (IARC V.19, 1979).

REGULATIONS

CPSC, EPA, and FDA each banned the use of vinyl chloride as an aerosol propellant, eliminating the potential exposure of 1 million to 5 million people annually. Under the Clean Air Act (CAA), National Emission Standards for Hazardous Air Pollutants (NESHAP) addresses vinyl chloride emissions from production and manufacturing facilities. A statutory reportable quantity (RQ) of 10 lb has been proposed for this chemical under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Under the Clean Water Act (CWA), EPA published a water quality criteria document addressing vinyl chloride for the protection of human health. EPA regulates vinyl chloride as a hazardous constituent of waste under the Resource Conservation and Recovery Act (RCRA). Under the Safe Drinking Water Act (SDWA), EPA established a maximum contaminant level (MCL) of 0.002 mg/l for vinyl chloride. FDA eliminated the use of vinyl chloride in drug products and proposed to alert food manufacturers to the need for monitoring packaging materials that may contain it. FDA's Center for Food Safety and Applied Nutrition reevaluated its position and has withdrawn the proposal. OSHA has adopted a permissible exposure limit (PEL) of.1 ppm for vinyl chloride as an 8-

hr TWA, with a 5-ppm ceiling for any 15-minute period; OSHA requires medical surveillance, training for workers, use of protective clothing and respirators, warning signs, product labeling, and periodic monitoring for vinyl chloride in the workplace.

REGULATIONS

	Regulatory Action	Effect of Regulation/Other Comments
CPSC	16 CFR 1500.17(a)(10). Promulgated 8/21/74. Ban of self-pressurized household products that contain vinyl chloride monomer as an ingredient or in the propellant.	As a result of bans by CPSC, FDA, and EPA, 1 million to 5 million persons no longer are exposed.
EPA	40 CFR 61.60 - 61.71. Promulgated 10/21/76, 12/3/76, 6/7/77. CAA 112: NESHAP addressed vinyl chloride emissions from vinyl chloride monomer production and polymerization, and certain ethylene dichloride manufacturing facilities.	Imposes engineering controls that have been shown to reduce emissions by 95% over precontrol levels.
	45 FR 79318. Published 11/28/80. CWA 304: Water quality criteria published.	Under review for possible revision.
	48 FR 23552. Proposed 5/25/83. CERCLA 101(14): Designates and establishes statutory RQ of 1 lb.	This substance is being assessed for both carcinogenicity and other toxic effects; statutory RQ applies.
	52 FR 8140. Proposed 3/16/87. CERCLA 101(14): NPRM proposing adjustment of RQ from 1 lb to 10 lb based on specific scientific and technical criteria.	Would, if promulgated, provide control over releases of vinyl chloride into the environment.
	3/75. FIFRA 3: Cancellation/suspension of all vinyl chloride monomer-containing pesticides registered for use in homes, food handling establishments, hospitals, and enclosed areas.	

(Continued)

REGULATIONS

	Regulatory Action	Effect of Regulation/Other Comments
E P A	40 CFR 261.11, 261.33. Promulgated 5/19/80. RCRA 3001-3004: Subjects waste products, off-specification batches, and spill residues in excess of 1,000 kg to handling and report/recordkeeping requirements. Also designates vinyl chloride as a hazardous constituent of waste, and subjects wastes known to contain it to the same requirements.	Based on toxic effects other than acute. The Carcinogen Assessment Group at EPA has included this chemical on its list of potential carcinogens. As a result of this listing, vinyl chloride is regulated under the hazardous waste disposal rule of RCRA. This action was based on evidence that inhalation of high concentrations of vinyl chloride resulted in acute toxicity that was manifested by an array of symptoms, included unconsciousness, cardiac effects, bone changes, and degenerative changes in the brain, liver, and kidneys.
	40 CFR 141. Promulgated 7/8/87. SDWA: MCL of 0.002 mg/l established for vinyl chloride.	Effective date 1/9/89. Will apply to all community water systems that regularly serve 25 persons for at least 8 months/year. MCL equivalent to an estimated cancer risk of 10^{-5}.
F D A	39 FR 30830. Published 8/26/74. Center for Drugs and Biologics, Center for Devices and Radiological Health, FD&CA: Prohibits the use of vinyl chloride as a propellant in aerosol cosmetic products and requires that manufacturers obtain an approved new drug application before using vinyl chloride as a propellant in aerosol drug products.	Has eliminated use of vinyl chloride in drug products and as a propellant vehicle in aerosol products.

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REGULATIONS

	Regulatory Action	Effect of Regulation/Other Comments
F D A	40 FR 40529. Published 9/3/75. Center for Food Safety and Applied Nutrition, FD&CA: NPRM proposing to regulate vinyl chloride monomer in packaging materials, but rules were not finalized. Any drug products containing vinyl chloride must pass through the New Drugs Application Process.	This has alerted manufacturers to the need to monitor their packaging materials for vinyl chloride monomer. The Bureau of Alcohol, Tobacco, and Firearms has banned polyvinyl chloride containers for alcoholic beverages, based on FDA work.
	51 FR 4173. Published 2/3/86. Center for Drugs and Biologics, Center for Devices and Radiological Health, FD&CA: Would provide for the safe use of vinyl chloride polymers by establishing limits on the amount of residual vinyl chloride monomer that products may contain, would codify all known prior sactions for vinyl chloride polymers. Would provide for the use of certain previously unregulated vinyl chloride polymers in manufacturing vinyl chloride bottles. Would delete vinyl chloride-vinylidene chloride copolymers from the list of materials that may be used as coatings on fresh fruits.	Withdraws previous NPRM.
N I O S H	3/11/74. Recommends that exposure to vinyl chloride be reduced to the minimum detectable level of 1 ppm (sampled over a 15-minute period).	

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REGULATIONS

	Regulatory Action	Effect of Regulation/Other Comments
OSHA	29 CFR 1910.19. Amended 10/4/74 to include paragraph (b). OSH Act: Implements application of 1910.1017 to Construction, Ship Repair, Ship Building, Ship Breaking, and Longshoring and Marine Terminals. 29 CFR 1910.1017. Promulgated 10/4/74. OSH Act: PEL $\leq$ 1 ppm, 8-hr TWA, 5 ppm ceiling/15 min; no direct contact with liquid. Protective clothing, respirators, training, medical surveillance requirements for workers; monitoring requirements; sign requirements for regulated areas; labeling requirements for containers.	Regulatory History: 1952. Walsh-Healey, 500 ppm maximum allowable concentration. 8/27/71. OSHA Takeover Standard -- 500 ppm (1300 mg/m^3) ceiling. 4/5/74. Emergency Temporary Standard -- 50 ppm ceiling (39 CFR 12341). 10/5/74. Final Standard -- current limit effective in all industries (39 FR 35892).

DI(2-ETHYLHEXYL)PHTHALATE
CAS No. 117-81-7

CARCINOGENICITY

There is sufficient evidence for the carcinogenicity of di(2-ethylhexyl)phthalate in experimental animals (IARC V.29, 1982; IARC S.4, 1982; IARC S.7, 1987). When administered in the diet, di(2-ethylhexyl)phthalate induced hepatocellular carcinomas in female rats and in mice of both sexes (NTP 217, 1982).

An IARC Working Group reported there were no data available to evaluate the carcinogenicity of di(2-ethylhexyl)phthalate in humans (IARC V.29, 1982; IARC S.7, 1987).

PROPERTIES

Di(2-ethylhexyl)phthalate is a colorless liquid with a slight odor. It is insoluble in water, miscible with mineral oil and hexane, and soluble in most organic solvents. Di(2-ethylhexyl)phthalate is easily dissolved in body fluids such as saliva and plasma. Di(2-ethylhexyl)phthalate is available in the U.S. in a variety of technical grades. Typical product specifications are: 99.0 to 99.6% minimal ester content; 0.1% maximal moisture content; and 0.007 to 0.01% acidity (as acetic acid or phthalic acid).

USE

Di(2-ethylhexyl)phthalate is used primarily as one of several plasticizers in polyvinyl chloride (PVC) resins for fabricating flexible vinyl products. According to CPSC, EPA, and FDA, these PVC resins are used to manufacture many products, including teething rings, pacifiers, soft squeeze toys, balls, vinyl upholstery, tablecloths, shower curtains, raincoats, adhesives, polymeric coatings, components of paper and paperboard, defoaming agents, enclosures for food containers, animal glue, surface lubricants, flexible devices for administering parenteral solutions, and other products that must stay flexible and noninjurious for the lifetime of their use. Di(2-ethylhexyl)phthalate also is used to manufacture vinyl gloves used for medical examinations and surgery (about 500 million pairs annually).

The only significant nonplasticizer use for di(2-ethylhexyl)phthalate is as a replacement for polychlorinated biphenyls in dielectric fluids for electric capacitors. The following miscellaneous uses for di(2-ethylhexyl)-phthalate have been reported: as a solvent in erasable ink; as an acaricide for use in orchards; as an inert ingredient in pesticides; as a component of cosmetic products; as a vacuum pump oil; in detecting leaks in respirators; and in the testing of air filtration systems. Several of these reported applications are believed to be no longer practiced or never to have been carried out on a commercial scale (IARC V.29, 1982).

PRODUCTION

There are currently no separate data available on the production of di(2-ethylhexyl)phthalate in the U.S. In 1985, the USITC identified 10 companies reporting total production not exceeding 300 million lb for all dioctyl phthalates (USITC, 1986). NCI estimated that U.S. companies produced 257 million lb of di(2-ethylhexyl)phthalate in 1980. The Society of Plastics reported that 302 million lb of the chemical was consumed in the U.S. during 1980. The 1979 TSCA Inventory identified ten companies producing 307 million lb of di(2-ethylhexyl)phthalate in 1977 and eight companies importing 1,500 lb. The CBI Aggregate was between 100 million and 1 billion lb (TSCA, 1979). There were no data available on exports of di(2-ethylhexyl)phthalate. Di(2-ethylhexyl)phthalate was patented in 1933 and became commercially available in the U.S. in 1939 (IARC V.29, 1982).

EXPOSURE

The primary routes of potential human exposure to di(2-ethylhexyl)-phthalate are inhalation, ingestion, and dermal contact. The entire population is exposed to low levels of this widely used plasticizer. About 300 million lb of di(2-ethylhexyl)phthalate are used each year to manufacture plastic products for commercial, medical, and consumer use. Plasticizers such as di(2-ethylhexyl)phthalate do not become a permanent part of the plastic matrix during the manufacturing process; thus, under certain use or disposal conditions, they can migrate from plastic products into the environment (ATSDR, 1987i).

A high risk segment of the population consists of individuals receiving dialysis treatments or large quantities of blood that have contacted di(2-ethylhexyl)phthalate-containing tubing or containers. Among this population are hemophiliacs and dialysis patients. Large-volume parenteral formulations that are administered intravenously as replenishers (i.e., fluids, nutrients, electrolytes) are packaged in flexible containers made from polyvinyl chloride that contain phthalate as a plasticizer; the estimated concentration of di(2-ethylhexyl)phthalate in replenishers is less than 5 ppm. Another high risk population includes workers exposed to di(2-ethylhexyl)phthalate during the formulation and processing of plastics. The total pool of such workers numbers about 600,000 in the U.S., although only a small percentage receives high exposures (ATSDR, 1987i).

Di(2-ethylhexyl)phthalate is known to be widely distributed in the environment, and has been detected in soil samples, animal and human tissues, and various forms of marine life. The chemical is biodegradable, but tends to partition into sediment where it is relatively persistent. In general, concentrations of di(2-ethylhexyl)phthalate in fresh waters lie within a range of a fraction of a ug/l to 10 ug/l, although occasionally much higher values have been observed. Another potential source of exposure is the leaching of the chemical from plastic articles placed in landfills (ATSDR, 1987i; IARC V.29, 1982).

Because of its low solubility in water and its low vapor pressure, exposure to di(2-ethylhexyl)phthalate in either water or air appears to be minimal for most individuals. For the general population, the most likely route of exposure is through contaminated food, which provides an average of about 0.3 mg/day and a maximum of about 2 mg/day per individual. The greatest risk of exposure for the general population is the contact of food with high fat or oil content with containers and wrappings containing di(2-ethylhexyl)-phthalate. Because of the compound's high lipophilicity, such foods tend to extract it, thereby enabling exposure to humans ingesting the food. The highest levels have been detected in milk and cheese (ATSDR, 1987i).

REGULATIONS

CPSC has received the final report of an independent, nonfederal scientific panel which was convened to review the available chronic toxicity and exposure information on di(2-ethylhexyl)phthalate as used in consumer products. The Commission staff has evaluated the panel's report and agrees, in general, that di(2-ethylhexyl)phthalate should be regarded as a potential human carcinogen. The Toy Manufacturers of America (TMA), representing pacifier and toy manufacturers, has stated that most manufacturers already have discontinued the use of di(2-ethylhexyl)phthalate in their products. The Commission staff has determined that domestic manufacturers are not using di(2-ethylhexyl)-phthalate in vinyl pacifiers, and importers appear to be acquiring non-di(2-ethylhexyl)phthalate-containing pacifiers. The staff has therefore concluded that the estimated cancer risk from di(2-ethylhexyl)phthalate, which was primarily from pacifier use, has substantially declined. Commission staff is working with the TMA to determine the scope of a voluntary standard to limit the use of di(2-ethylhexyl)phthalate in vinyl pacifiers. The TMA voluntary standard limits the amount of di(2-ethylhexyl)phthalate to less than 3% in pacifiers and teethers.

EPA regulates di(2-ethylhexyl)phthalate under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Superfund Amendments and Reauthorization Act (SARA), and Toxic Substances Control Act (TSCA). Di(2-ethylhexyl)phthalate is included on lists of chemicals for which water quality criteria have been established under CWA. A statutory reportable quantity (RQ) of 100 lb has been proposed for this chemical under CERCLA. Under RCRA, SARA, and TSCA, di(2-ethylhexyl)phthalate is subject to report/recordkeeping requirements. SARA sets threshold amounts for di(2-ethylhexyl)phthalate used, manufactured, or processed at a facility. Manufacturers, importers, and processors of di(2-ethylhexyl)phthalate are required to submit to EPA copies and lists of unpublished health and safety studies under TSCA. FDA regulates di(2-ethylhexyl)phthalate as an indirect food additive. OSHA established a permissible exposure limit (PEL) of 5 mg/m^3 as an 8-hr time-weighted average (TWA) for the compound. Di(2-ethylhexyl)phthalate is the subject of a NIOSH Special Hazard Review because of a National Toxicology Program bioassay in which the chemical was found to be carcinogenic in rats and mice; its use in testing respirators for leaks causes additional concern. NIOSH has submitted the preliminary hazard review to OSHA.

REGULATIONS

	Regulatory Action	Effect of Regulation/Other Comments
E P A	45 FR 79318. Published 11/28/80. CWA 304(a): Water quality criteria for di(2-ethylhexyl)phthalate published.	Under review for possible revision. Decision anticipated during 1985.
	48 FR 23552. Published 5/25/83. CERCLA 101(14): Proposed adjustment of statutory RQ from 1 lb to 5,000 lb.	
	52 FR 8140. Published 3/16/87. CERCLA 101(14): NPRM proposing adjustment of RQ to 100 lb based on specific scientific and technical criteria.	Would, if promulgated, provide additional control over releases of di(2-ethylhexyl)phthalate into the environment.
	52 FR 13305. Published 4/22/87. FD&CA 408: Di(2-ethylhexyl)phthalate identified as an inert ingredient of toxicological concern in pesticides. Requires data and labeling.	Encourages the use of the least toxic ingredient available and requires the development of data necessary to determine the conditions of safe use of products containing toxic ingredients.
	40 CFR 261.11, 261.33. Promulgated 5/19/80. RCRA 3001-3004: Subjects off-specification batches, waste products, and spill residues in excess of 1,000 kg to handling and report/recordkeeping requirements. Also designates di(2-ethylhexyl)-phthalate as a hazardous constituent of waste, and subjects wastes known to contain it to the same requirements.	Based on toxic effects other than acute. The Carcinogen Assessment Group at EPA has included this chemical on its list of potential carcinogens. As a result of this listing, di(2-ethylhexyl)phthalate is regulated under the hazardous waste disposal rule of RCRA.
	52 FR 3479. Published 2/4/87. SARA 313: Establishes list of toxic chemicals and groups of chemicals subject to reporting requirements.	General threshold amounts are currently set at 10,000 lb/yr for toxic chemicals used at a facility and 75,000 lb/yr if manufactured or processed at a facility.

(Continued)

REGULATIONS

	Regulatory Action	Effect of Regulation/Other Comments
E P A	52 FR 12866. Published 4/17/87. SARA 110: Establishes priority list of CERCLA hazardous substances subject to reporting requirements.	Amends CERCLA 104(i). Establishes requirements for preparation of: a list of hazardous substances found at National Priority List sites; toxicological profiles of those substances; and a research program to fill data gaps associated with the substances.
	47 FR 335. Published 1/5/82. TSCA 4(b): Notice of negotiated testing agreement.	
	40 CFR 712. Promulgated 6/22/82. TSCA 8(a): Final rule to require production and use data.	Based on ITC testing recommendation. Would provide added means to estimate exposure potential.
	40 CFR 716. Promulgated 10/4/82. TSCA 8(d): Requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies.	
F D A	21 CFR 175.105, 175.300, 175.380, 176.170, 176.210, 177.1010, 177.1210, 177.1400, 178.3120, 178.3910, 181.27. FD&CA: Regulated as indirect food additive.	Used in: adhesives, resinous and polymeric coatings, xylene formaldehyde resins condensed with 4,4'-isopropylidenediphenolepichlorohydrin epoxy resins, components of paper and paperboard in contact with aqueous and fatty foods, defoaming agents used in manufacture of paper and paperboard, semirigid and rigid acrylic and modified acrylic plastics, closures with sealing gaskets for food containers, water-insoluble hydroxethyl cellulose film, animal glue, surface lubricants used in the manufacture of metallic articles, and plasticizers.

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REGULATIONS

	Regulatory Action	Effect of Regulation/Other Comments
NIOSH	3/83. NIOSH published a Special Occupational Hazard Review which recommended alternatives to the use of di(2-ethylhexyl)phthalate in respirator fit testing.	These recommendations were necessary because of potential carcinogenic risk identification from 1982 National Toxicological Program animal studies.
OSHA	29 CFR 1910.1000. Promulgated 5/29/71. OSH Act: PEL $\leq$ 5 mg/m^3 (2 ppm) TWA.	Regulatory History: 5/29/71. OSHA Takeover Standard -- current limit in effect. Standard adopted for toxic effects other than cancer.