
Toxic chemicals and childhood cancer: A review of the evidence

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EXECUTIVE SUMMARY

Childhood cancer is the second largest cause of death to children ages 0-15 in the United States (second only to accidents), and more than 8,000 cases are diagnosed each year. In Massachusetts from 1990-1999, approximately 2,688 children ages 0-19 were diagnosed with cancer and 394 died. The overall rate of childhood cancer in Massachusetts is slightly higher than the national average—16.7 new cases versus 16.1 per 100,000 per year. African American and Latino children in Massachusetts had approximately 25% more diagnosed cancers than white and Asian and Pacific Islander children.

Although childhood cancer is a relatively rare disease, cancer rates increased nearly 21% between 1975 and 1998—approximately 1% each year. Some causes of cancer can be attributed to genetic predisposition, while it is highly likely that environmental exposures, including toxic substances in our environment, food, water, and consumer products, play a role. A panel of experts convened by Mt. Sinai Hospital recently concluded that genetic predisposition accounts for no more than 20% of all childhood cancers and that the environmental attributable fraction of childhood cancer could be between 5% and 90%, depending on the type of cancer. This means that a potentially large percentage of childhood cancers is preventable.

There are some well-established links between environmental exposures and childhood cancer, including: pharmaceuticals such as diethylstilbestrol (DES), an estrogen prescribed from the late 1940s to the early 1970s to prevent miscarriage; ionizing radiation; and chemotherapeutic agents. However, evidence increasingly indicates that parental and childhood exposures to certain toxic chemicals including solvents, pesticides, petrochemicals and certain industrial by-products (dioxins and polycyclic aromatic hydrocarbons) can result in childhood cancer.

This report, commissioned by the Massachusetts Alliance for a Healthy Tomorrow, examines the evidence linking exposures to solvents, pesticides, petrochemicals, and certain industrial by-products with cancer in children. The report is based on examination of the published literature

on epidemiologic studies, animal toxicologic data, reviews of published studies and analyses of studies, case reports, fact sheets, and conference summaries.

Our analysis found the following:

- Epidemiologic studies have consistently found an increased likelihood of certain types of childhood cancer following parental and childhood exposure to pesticides and solvents.

Studies indicate that parental exposure to certain petroleum-based chemicals and parental and childhood exposure to combustion by-products, such as dioxins and polycyclic aromatic hydrocarbons, may increase the likelihood of childhood leukemia and brain and central nervous system cancers.

In one study of pesticide exposures, children with leukemia were 4 to 7 times as likely to have been exposed to pesticides used in the yard or garden compared to children without the disease. Another study found that children with leukemia were 11 times as likely to have mothers who were exposed to pesticide sprays or foggers during pregnancy compared to healthy children. Compared to children of unexposed fathers, children whose fathers were occupationally exposed to benzene and alcohols used in industrial products were nearly 6 times as likely to develop leukemia if the exposure occurred prior to the pregnancy. In Dover Township, New Jersey, researchers found that children with leukemia were 5.4 times as likely as children without leukemia to have drunk water from private wells in groundwater areas with a history of contamination from the Reich Farm Superfund site or wastewater from a nearby industrial facility. In another study, children with acute non-lymphocytic leukemia (ANLL) were 2.4 times as likely as those without ANLL to have parents who were exposed to petroleum products in their jobs.

This evidence is supported by laboratory experiments and data on adult cancers from similar exposures. In most cases, the studies do not provide evidence of cancer from exposure to particular chemicals but rather mixtures or classes of chemicals (e.g., pesticides, solvents, hydrocarbons).

- Exposures that occur prior to conception, in the womb, and in early childhood can increase the likelihood of childhood cancer. Cancer may develop in the fetus if the germ cells (sperm and eggs) of the mother or father are damaged prior to pregnancy. Also, a fetus may be exposed to potentially harmful chemicals *in utero*. In such cases, the toxic substance can cross the placenta and enter the body of a developing fetus, potentially leading to cancer.

Based on the literature, the types of exposures that have the strongest apparent links to childhood cancer include: parental exposure to pesticides from occupational, agricultural, home, and garden uses; parental exposure to solvents in manufacturing and painting; parental occupational exposure to hydrocarbons; maternal exposure to water contaminated with solvents; direct childhood exposure to pesticides from home and garden use; childhood exposure to solvents in drinking water; and childhood exposure to dioxins.

- The evidence supporting the connection between exposure to these toxicants and childhood cancer is strongest for leukemia, brain and central nervous system cancers.

It is difficult to determine the exact magnitude of the contribution of toxic chemicals to the overall burden of childhood cancer. Because the majority of chemicals in commerce—some of which are widely used in everyday products—have not been studied for their potential to cause cancer, we do not have a complete picture of the potential chemical causes of cancer in children. The links with childhood cancer have been adequately studied for only a few chemicals. Mixtures of chemicals mimicking the complex exposures that occur in everyday life have been studied even less.

Since people are exposed to many chemicals and other agents simultaneously, and cancer is a rare disease, it is very difficult to establish causal links. Because of these difficulties and the costs of studies, relatively few epidemiologic studies examining the links have been conducted. Further, many studies that have been conducted have serious limitations and could be expected to provide only weak evidence about causes and childhood cancer. The lack of proof of direct

causal links between toxics and childhood cancer should not be construed as proof of safety. There are far more chemicals in circulation with little or no evidence of harm or safety than there are chemicals tested regularly and shown to be safe.

The evidence presented in this report indicates that preventing parental and childhood exposure to chemicals suspected of causing cancer can have important health benefits. The types of chemicals examined in this report are of concern not only for their ability to cause cancer but other health effects as well—neurological and developmental harms to the fetus, for example. Preventing exposure to chemicals suspected of causing cancer is possible, as recent European policies demonstrate. The European Union will soon require that all chemicals in commercial circulation receive basic testing, and that those that are known or probable carcinogens, mutagens, or reproductive toxicants be used only when there are no safer economically and technically feasible alternatives. This common sense approach to chemical safety is likely to result in significant reductions in childhood exposure to potentially dangerous chemicals.

INTRODUCTION

The Massachusetts Alliance for a Healthy Tomorrow asked the Lowell Center for Sustainable Production to examine the documented links between environmental toxins and cancer in children. This report is based on an examination of the published literature on epidemiologic studies, animal toxicologic data, reviews of published studies and analyses of studies, case reports, fact sheets, and conference summaries. We examine the strength of the evidence on whether exposures to pesticides, solvents, petrochemicals and combustion by-products increase the likelihood of childhood cancer. We focus particularly on leukemia and brain cancer, because they are more common compared to other cancers, and therefore studied more often.

During the last two decades, concerns about the links between environmental factors, including exposure to toxic substances, and childhood cancer have increased. While there is still some debate about the exact magnitude and importance of the observed increases in childhood cancer rates over the last two decades and the causes of the increase, a growing body of evidence from laboratory studies and human epidemiologic studies suggests that toxic substances cannot be ruled out as contributors to childhood cancer.

In this report, we examine the body of evidence on the relationship between toxic substance exposures and certain childhood cancers. This report reviews the evidence for certain chemical exposures for which there is increasing evidence of potential carcinogenicity in children. These chemicals include pesticides, industrial solvents, and some combustion by-products (such as dioxins) and hydrocarbons (petroleum products). We examine the evidence for each class of substance and discuss the strengths and limitations of the literature.

We conclude that there is sufficient human and laboratory evidence that exposure to some common environmental chemicals can result in childhood cancer. Instituting measures to reduce parental and childhood exposures to these and other substances suspected of causing cancer, including development of safer substitutes, should play an important role in a cancer prevention strategy.

Cancer is most common fatal disease in children

Cancer is the most common fatal disease in U.S. children, (second only to accidents among all causes), resulting in approximately 1,500 deaths per year (Zahm and Devesa, 1995). Although cancer mortality has decreased over the years due to improved detection and treatment, more than 8,000 cancer diagnoses are made in U.S. children under the age of 15 annually. Leukemia and cancers of the central nervous system (CNS), including the brain, account for approximately 50% of cancers in children, with diagnosis of leukemia and CNS cancers typically made in children under the age of 2 and 5 respectively (Zahm and Devesa, 1995; Robison, et al., 1995; Carroquino, et al., 1998; Grufferman, 1998; Schmidt, 1998). According to a 2003 U.S. Environmental Protection Agency (U.S. EPA) report, leukemia incidence increased from 24 cases per 1,000,000 children during the 1974-1978 reporting period to 28 cases per 1,000,000 children during the 1994-1998 reporting period.^{1,2} The incidence of CNS tumors increased from 22 per 1,000,000 children during 1979-1983 and peaked at 30 cases per 1,000,000 children by 1993. Fortunately, incidence of CNS tumors has decreased. However, 27 out of every 1,000,000 children were diagnosed with CNS tumors, including brain tumors, between 1994 and 1998 (U.S. EPA, 2003).

Overall, childhood cancer incidence rates in Massachusetts are slightly higher (about 4%, 16.7 versus 16.1 per 100,000) than the national rates which come from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. The Massachusetts rate for leukemia was slightly lower, for lymphoma the rate was slightly higher, and for brain and CNS cancers they were the same as the national rate. Total childhood cancer incidence for females from 1990-1999 went up 1.6% per year, while for males it went down an average of 0.7% per year. For males and females combined the total childhood cancer incidence from 1990-1999 increased approximately 0.5% per year. Childhood cancer death rates are decreasing slightly in the state, though nearly 394 children died from cancer in Massachusetts between the years 1990 and 1999 (MDPH, 2003).

¹ Incidence rate refers to the number of new cases out of a total given population in a given time period.

² U.S. EPA data was computed for children under the age of 20 at time of diagnosis.

From 1995-1999, childhood cancer incidence among Latino and African-American children was approximately 25% higher (20 per 100,000) than that among white and Asian and Pacific Islander children (15 per 100,000) and childhood cancer mortality during the years 1990-1999 among African-American children was approximately 25% higher than that among white, Latino, and Asian and Pacific Islander children (MDPH, 2003).

The incidence of all cancers in children in the U.S. increased nearly 21% between 1975 and 1998—approximately 1% every year for the last two decades (Zahm and Devesa, 1995; Colt and Blair, 1998; Schmidt, 1998). Some cancer researchers argue that improved technology, detection methods, and diagnoses (i.e., computerized axial tomography scans and magnetic resonance imaging) account for the rise, while others argue that if this were the case, one would expect to see cancer incidence rates flattening, which has not yet occurred (Schmidt, 1998; Kaiser, 1999). Others argue that it is impossible to miss brain cancer and leukemia because the symptoms are so painfully obvious (brain cancer) and the tests accurate (leukemia) (Kaiser, 1999).

Given the increasing trend in childhood cancer incidence, and the lack of definitive explanations for it, it is important to consider the evidence for environmental chemical causes. While some researchers postulate that genes and viruses are the main contributors to any observed increase in childhood cancer, other researchers argue that genes, individual susceptibility and the environment are likely to interact in such a way as to disrupt normal cell function, leading to cancer (Zahm and Ward, 1998; Robison, et al., 1995; Carroquino, et al, 1998; Shannon, 1998; Czene, et al., 2002).

A panel of experts convened by Mt. Sinai Hospital concluded that no more than 10%-20% of childhood cancer cases could be attributed to genetic predisposition; non-genetic factors, defined broadly, thus contribute to the other 80%-90%. Given that the specific causes of childhood cancer are largely unknown due to limited study, the panel concluded that the environmental attributable fraction of childhood cancer due to toxic chemical exposures was at least 5-10% and less than 80-90% (Landrigan, et al., 2002).

This means that there are between 400 and 7,200 new cases of childhood cancer per year in the U.S. potentially due to chemical exposures. The Mt. Sinai panel estimated that the annual cost of environmentally related childhood cancer—due to hospitalization and treatment, treatment of secondary cancers, lost parental wages, and decreased IQ due to cancer treatments—ranges from \$132 million to \$663 million (Landrigan, et al., 2002).

Table 1. Number of Cancer Cases and Deaths by Site in Massachusetts Children Younger than 20 Years (1990-1999)³

Cancer or Tumor Site	Cases	Deaths
<i>Leukemia</i>	621	133
<i>Lymphomas and Reticuloendothelial Neoplasms</i>	441	23
<i>Central Nervous System and Miscellaneous Intracranial and Intraspinial Neoplasms (Brain Cancer)</i>	460	78
<i>Renal Tumors (Kidney Cancer)</i>	121	8
<i>Hepatic Tumors (Liver Cancer)</i>	40	10
<i>Malignant Bone Tumors</i>	137	29
<i>Sympathetic Nervous System Tumors</i>	174	113
<i>Retinoblastoma (Eye Cancer)</i>	49	
<i>Soft-Tissue Sarcomas</i>	199	
<i>Germ Cell, Trophoblastic and Other Gonadal Neoplasms (Reproductive Cancer)</i>	175	
<i>Carcinomas and Other Malignant Epithelial Neoplasms (Skin Cancer)</i>	257	
<i>Other and Unspecified Malignant Neoplasms (Cancer)</i>	14	
<i>All Cancer Types</i>	2688	394

³ Adapted from Childhood Cancer in Massachusetts 1990-1999 (2003), Massachusetts Department of Public Health.

Children are particularly vulnerable to chemical exposures in their environment

Children are often more vulnerable to injury caused from toxic chemical exposures than adults due to the combination of disproportionately heavy exposure and biological vulnerability (Landrigan, et al., 2002; Tickner and Poppin, 2000).

- The brains and organs of children continue to grow and develop through adolescence. Exposures to toxins, including pesticides, solvents, combustion by-products and petrochemicals, can disrupt normal cellular processes, resulting in unregulated replication of cells (carcinogenesis).
- Children breathe air at a faster rate and consume more food and water per pound of body-weight compared to adults, resulting in a greater intake of toxic substances.
- Children's bodies are less able to detoxify and excrete toxic substances compared to adults, resulting in a build-up of toxic chemicals, particularly if exposure is constant.
- Children have more hand-to-mouth activity compared to adults and, as a result, may ingest toxic residues from carpets, toys, and furniture that were carried in from outside the home, such as from work clothing, shoes, and pets.
- The breathing zone of children is closer to the ground, which can be cause for concern because concentrations of some chemicals, including pesticides, can be higher the closer one measures to the ground (Zahm and Ward, 1998).

Cancer typically has a long latency period—taking years to decades to develop from the time of exposure. A relatively short latency period is observed for brain cancer and leukemia, which tend to be diagnosed in children under the age of five. Cancer may develop in the fetus if the germ cells (sperm and eggs) of the mother or father are damaged prior to pregnancy. Toxic substance exposures can cause cell damage (mutations) in the germ cells that can then be passed on to the developing embryo, causing cancer later in childhood. Also, a fetus may be exposed to chemicals or pesticides during gestation. Some researchers have found that substances to which pregnant women are exposed can cross the placenta and bind to fetal DNA (forming DNA adducts), causing mutations (damage to genetic material, the start of the cancer process) in the umbilical cord blood of newborns (Perera, et al., 2002).

Thus, exposures to parents prior to conception, to the pregnant mother and fetus, and to the child are all of concern when examining the role of toxic chemical exposures in childhood cancer.

Studying childhood cancer and its causes can be challenging

Although approximately 1 out of 400 U.S. residents will develop cancer by the age of 15, childhood cancer is relatively rare compared to adult cancer, making it difficult to study the causes of the disease (Robison, et al., 1995). This is particularly true if one wishes to study cancers other than leukemia and brain tumors, which account for about half of all diagnoses of cancer in children (Grufferman, 1998).

Most epidemiologic studies of childhood cancer are what are termed “case-control studies”, because they are more effective at demonstrating links between exposures and rare diseases. In a case-control study, individuals with the disease (cases) are identified and individuals without the disease, but with similar demographic characteristics (controls), are matched to the cases. The goal is to see whether those who have the disease are more likely to have had a particular exposure (such as to chemicals) than those without the disease.

A second type of study, called a cohort study, follows an exposed population (for example, farm workers exposed to pesticides) to see whether some health effect is more likely to occur in them or their children compared to an unexposed population. Such studies are used less frequently when studying childhood cancer because very large populations would have to be followed to observe meaningful numbers of cancer cases in the two groups being compared.

Cancer in children also may be studied and described through simple descriptive reports of unusual cases or analyses of cancer clusters. A cluster is defined as an unusual number of cases of disease in a small geographic area. Examples of childhood cancer clusters include Woburn, Massachusetts and Dover Township, New Jersey, which are discussed later in this report. An additional type of study, called an ecologic study examines correlations between cancer rates in geographic areas like counties or towns, and the level of possible exposures in those same areas. Ecologic studies may be useful in providing clues to cancer causes without the high costs of an extensive case-control study. However, ecologic studies tend to provide weaker evidence of

causal links than do cohort and case-control studies because they are not studies of sick children, but instead examine areas with different rates of disease—an indirect way to look for exposure-disease links.

Evidence linking environmental exposures to childhood cancer exists

Links between childhood cancer and *in utero* exposures to certain pharmaceutical agents, such as the drug diethylstilbestrol (DES) are well recognized. DES was given to pregnant women from the late 1940s through the early 1970s to prevent miscarriage. In 1970, seven adolescent girls of women who were prescribed DES were diagnosed with a rare form of vaginal cancer (vaginal clear-cell adenocarcinoma). This tragedy helped scientists realize that the fetus is not fully protected from maternal exposures. That is, when the mother is exposed to an outside agent, the fetus also may be exposed (Ibarreta and Swan, 2001). There are several other well-established examples of environmental exposures and childhood cancer, including chemotherapeutic agents used to treat cancer, ionizing radiation, and increasingly, electromagnetic fields (Spitz and Johnson, 1985; Colt and Blair, 1998; Infante-Rivard, et al., 2000, Feychting, et al., 1998).

Table 2. Potential exposures to toxic chemicals examined in the childhood cancer literature

Chemical Category	Exposure Category			
	Occupational	Residential	<i>In utero</i>	Environmental
Pesticides	X	X	X	X
Solvents	X		X	X
Combustion By-Products/ Petrochemicals	X		X	X

Both parents and children can be exposed to carcinogenic agents; routes of exposure include ingestion of contaminated food and water, inhalation of chemical fumes or contaminated dust particles, and skin absorption of sprays and residues. Nursing infants can be similarly exposed, with breast milk being an additional route of potential exposure. *In utero* exposure can occur through mobilization of toxins in the mother’s blood through the umbilical cord.

This report includes discussion about each of three types of toxic chemicals: 1) pesticides; 2) solvents; and 3) petrochemicals and combustion or industrial by-products (dioxin and polyaromatic hydrocarbons). Often these exposures are defined in broad classes rather than naming specific solvents or pesticides.

Information on each chemical includes:

- 1) An overview of potential routes of exposure, including:
 - occupational exposures to parents;
 - residential (household dust and residues) exposures to parents and children
 - environmental (drinking water and air) exposures to parents and children;
 - exposure to nursing infants and *in utero* exposures.

- 2) A review of the evidence linking toxic exposures and:
 - leukemia;
 - brain cancer, neuroblastoma and CNS cancers;
 - non-Hodgkin's lymphoma; and
 - other cancers in children (liver, soft-tissue sarcoma, Wilms' tumor and carcinomas).

The literature providing evidence of links between exposure to these chemical categories and various types of childhood cancer is summarized in the following tables.

- 3) A review of supporting evidence from laboratory animal toxicology and adult human epidemiologic studies.

The report concludes with an analysis of the strengths and weaknesses of the evidence presented and a discussion of conclusions.

Table 3. Evidence of links between toxic chemical exposures and childhood leukemia

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference
Leukemia	<ul style="list-style-type: none"> • Professional pest control services 	Residential exposures to fetus and children	1 year before and 3 years after birth	Ma, et al., 2002
	<ul style="list-style-type: none"> • Pest strips 	Residential exposures to mothers	During pregnancy	Leiss and Savitz, 1995
	<ul style="list-style-type: none"> • Pesticides 	Residential (farm) exposures to parents and children	Childhood	Lowengart, et al., 1987
	<ul style="list-style-type: none"> • Trichloroethylene • Tetrachloroethylene 	Environmental exposures to children	Childhood	Fagliano, et al., 2003
	<ul style="list-style-type: none"> • Trichloroethylene • Tetrachloroethylene 	Environmental exposures to mothers of girls	During pregnancy	Fagliano, et al., 2003
	<ul style="list-style-type: none"> • Solvent mixture including Trichloroethylene 	Environmental exposures to mothers	During pregnancy	Costas, et al., 2002
	<ul style="list-style-type: none"> • Benzene • Perchloroethylene 	Environmental (air) exposures	Not given	Reynolds, et al., 2002b
	<ul style="list-style-type: none"> • Solvents 	Occupational exposures to fathers	Prior to pregnancy	Feychting, et al., 2001
	<ul style="list-style-type: none"> • Benzene • Alcohols 	Occupational exposures to fathers	Prior to pregnancy	McKinney, et al., 1991
	<ul style="list-style-type: none"> • Chlorinated solvents • Methyl ethyl ketone (MEK) 	Occupational exposures to fathers	Before and during pregnancy and after birth of child	Lowengart, et al., 1987
Leukemia	<ul style="list-style-type: none"> • Diesel exhaust and PAHs 	Environmental (air) exposures to children	Childhood	Lagorio, et al., 2000
	<ul style="list-style-type: none"> • Motor vehicle exhaust (nitrogen dioxide) 	Occupational exposures to fathers	Before pregnancy	Feychting, et al., 1998
	<ul style="list-style-type: none"> • Dioxin 	Environmental (air) exposures to children	Childhood	Bertazzi, et al., 1992
	<ul style="list-style-type: none"> • Hydrocarbon-related occupations 	Occupational exposures to women	During pregnancy	van Steensel-Moll, et al., 1985

Table 4. Evidence of links between toxic chemical exposures and childhood leukemia (specific cell types)

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference	
Acute Lymphocytic Leukemia (ALL)	<ul style="list-style-type: none"> • Pest strips • Insecticides/rodenticides • Garden herbicides and products for tree infestations 	Residential exposures to mothers	During pregnancy	Infante-Rivard, et al., 1999	
		Occupational exposures to mothers	During pregnancy	Shu, et al., 1988	
	<ul style="list-style-type: none"> • Trichloroethylene • Carbon tetrachloride • Perchloroethylene 	Occupational exposures to mothers	Before and during pregnancy and after birth of child	Shu, et al., 1999	
		Environmental exposures to children	Childhood	Shu, et al., 1999	
	<ul style="list-style-type: none"> • Exhaust • PAHs • Gasoline 	Occupational exposures to mothers	Before pregnancy	Shu, et al., 1999	
		Occupational exposures to mothers	Before and during pregnancy	Shu, et al., 1999	
		Occupational exposures to mothers	During pregnancy	Shu, et al., 1988	
	Acute Non-Lymphocytic Leukemia (ANLL)	<ul style="list-style-type: none"> • Pesticides • Pesticides • Pesticides 	Residential exposures to mothers	During pregnancy	Buckley, et al., 1989
			Occupational exposures to fathers	Jobs held more than 1,000 days	Buckley, et al., 1989
Residential exposures to children			Childhood	Buckley, et al., 1989	
<ul style="list-style-type: none"> • Solvents • Benzene 		Occupational exposures to fathers	Not given	Buckley, et al., 1989	
		Occupational exposures to mothers	During pregnancy	Shu, et al., 1988	
<ul style="list-style-type: none"> • Petroleum products • Gasoline 		Occupational exposures to fathers	Not given	Buckley, et al., 1989	
	Occupational exposures to mothers	During pregnancy	Shu, et al., 1988		

Table 5. Evidence of links between toxic chemical exposures and childhood brain and CNS cancer

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference
Nervous System Tumor	• Pesticides	Occupational (farm or forestry) exposures to fathers	Near conception	Feychting, et al., 2001
	• Solvents	Occupational exposures to fathers	Near conception	Feychting, et al., 2001
	• Motor vehicle exhaust (nitrogen dioxide)	Environmental (air) exposures to children	Childhood	Feychting, et al., 1998
Brain Tumor	• Insecticides, including flea and tick products • Sprays and foggers	Residential exposures to mothers	During pregnancy	Pagoda and Preston-Martin, 1997
	• Horticultural and pesticide indicators	Occupational (farm) exposures to parents	Not given	Kristensen, et al., 1996
	• Pesticides	Residential (farm) exposures to mothers	During pregnancy	Bunin, et al., 1994
	• Pesticides	Residential (farm) exposures	Not given	Cordier, et al., 1994
	• Pest strips • Flea collars • Herbicides/Insecticides	Residential exposures to children	Childhood	Davis, et al., 1993
Neuroblastoma	• Pesticides	Residential exposures to children	Not given	Daniels, et al., 2001
	• Horticultural and pesticide indicators	Occupational (farm) exposures to parents	Not given	Kristensen, et al., 1996
	• Benzene • Alcohols • Lacquer thinner • Turpentine	Occupational exposures to fathers	Not given	De Roos, et al., 2001
	• Hydrocarbons, including diesel fuel	Occupational exposures to fathers	Not given	De Roos, et al., 2001
	• Aromatic hydrocarbons • Aliphatic hydrocarbons	Occupational exposures to parents	Not given	Spitz and Johnson, 1985

Table 6. Evidence of links between toxic chemical exposures and other childhood cancers

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference
Non-Hodgkin's Lymphoma (NHL)	• Insecticides, including professional extermination	Residential exposures to children	Childhood	Meinert, et al., 2000
	• Horticultural and pesticide indicators	Occupational (farm) exposures to parents	Not given	Kristensen, et al., 1996
Soft tissue sarcoma (STS)	• Yard pesticides	Residential exposures to children	Childhood	Leiss and Savitz, 1995
Hepatoblastoma	• Hydrocarbons	Occupational exposures to mothers	Not given	Robison, et al., 1995
	• Petroleum products	Occupational exposures to fathers	Not given	Robison, et al., 1995
Wilms' tumor	• Pesticides	Occupational (farm) exposures to parents	Not given	Kristensen, et al., 1996
	• Pesticides	Occupational (farm) exposures to parents	Not given	Sharpe, et al., 1995
	• Pesticides	Residential exposures	Not given	Olshan, et al., 1993
	• Hydrocarbons	Occupational exposures to parents	Not given	Colt and Blair, 1998
	• Hydrocarbons	Occupational exposures to parents	Not given	Wilkins and Sinks, 1984
Urinary tract cancer	• Hydrocarbons	Occupational exposures to parents	Not given	Kwa and Fine, 1980

PESTICIDES

Uses

Pesticides include any substance or mixture intended to prevent, destroy, repel, or mitigate any pest and any substance used as a plant regulator, defoliant, or desiccant (U.S. EPA, 2003). In 1997, more than 800 pesticides and 20,000 pesticide-containing products were registered with the U.S. Environmental Protection Agency (U.S. EPA, 1998b).

The majority of pesticides registered with the U.S. EPA are used in agricultural applications (Zahm and Ward, 1998). However, household residents also are significant users of pesticide products. A 1995 survey revealed that residential households account for an estimated 74 million pounds of pesticides used in the United States (Landrigan, 1999). According to the National Home and Garden Pesticide Use Survey conducted by the U.S. EPA, 82% of households use pesticides with an average of 3 to 4 different pesticide products per home, 75% of which were insecticides used in the home and 22% were insecticides or herbicides used in the yard or garden (Zahm and Devesa, 1995). Sixty-six percent of households treated the home's primary living areas one or more times per year and 37% of households reported insecticide treatments when there was no major insect problem (Zahm and Ward, 1998).

The residential use of pesticides is even higher in urban areas, where 90% of households use pesticides, placing an additional burden on those living in the city, particularly the urban poor and urban ethnic and racial minorities (Gurunathan, et al., 1998; Landrigan, 1999).

Exposures

For years, concerns have been raised over the impacts of agricultural and home and garden applications of pesticides on public health and the environment. Pesticides can contaminate the environment through air dispersion, runoff, over spraying, groundwater contamination, and application drift. People can be exposed to pesticides from drinking water contaminated by runoff; ingesting pesticide residues on fruits and vegetables; through breathing pesticide fumes

during use at home and/or occupationally; and through breathing and ingesting residues transported into the home from shoes and pets (Zahm and Ward, 1998). A recent study found that children whose diets primarily consisted of pesticide treated foods (conventional diets) had concentrations of organophosphate breakdown products in their urine that were six times higher than children whose diets primarily consisted of organic foods, suggesting that organic foods can decrease children's exposures to pesticides to levels below the U.S. EPA's current guidelines (Curl, et al., 2003).

The United States Department of Agriculture estimates that 50 million people obtain drinking water from sources that may be contaminated with pesticides and other agricultural chemicals and the U.S. EPA's National Pesticide Survey of drinking water wells found that one or more pesticides were present in 10.4% of community water systems and 4.2% of rural domestic wells (Zahm and Ward, 1998). In 1994 researchers tested 20,000 samples of tap water and drinking water sources for 5 herbicides and found that 14.1 million people routinely drink water contaminated with the pesticides atrazine, cyanazine, simazin, alachlor and metolachlor, while another investigation by the same group of researchers in 1995 found multiple pesticides in the tap water of 2/3 of cities tested, often at levels that exceed the U.S. EPA health advisory levels (Zahm and Ward, 1998).

In addition to concerns about pesticide exposures related to agriculture, researchers from the National Cancer Institute suggest that the majority of pesticide exposures for children occur from home, lawn, and garden use. They have estimated that household applications of pesticides are 5 times greater than the per-acre application rate of pesticide-treated agricultural lands (Zahm and Ward, 1998). Children may be exposed while pesticides are being applied to a lawn or garden, or by playing on the lawn within 24 hours of application (Zahm and Ward, 1998). Indoor use of pesticides can lead to long-lasting exposures because pesticide residues can remain in carpets, furniture, and plush toys without being affected by degradation processes that exist outdoors (e.g., rain and sun). Pesticides used outdoors can also be tracked into the home on shoes and by pets (Zahm and Ward, 1998).

As previously noted, children can be exposed to pesticides at much higher levels than adults due to their eating habits and close proximity to the ground. In one study, researchers vertically measured residues from a broadcast flea treatment and found that insecticide concentrations were 4 to 6 times greater at a child's breathing level compared with an adult's (Zahm and Ward, 1998). Two other studies found that pesticide residues can be measured on children's toys and other plush surfaces for at least 2 weeks after broadcast indoor spraying of the pesticide chlorpyrifos (Davis and Ahmed, 1998; Landrigan, 1999). One study determined that these residues could expose children at 20-100 times the level the U.S. EPA considers safe for adults (Davis and Ahmed, 1998).

Evidence from epidemiologic studies

Researchers at the NCI reviewed more than 50 studies examining the links between pesticide exposure and childhood cancer, spanning from the mid-1970s through the late 1990s. They found that most of the studies reported an increased likelihood of leukemia and brain cancer from exposure, though the magnitude of the impact varied by study.⁴ Another notable finding was an increased likelihood of non-Hodgkin's lymphoma (NHL) following pesticide exposure, while evidence of associations between pesticide exposure and Wilms' tumor, Ewing's sarcoma, neuroblastoma, and other malignancies in children was weak or inconclusive. The evidence on the connections between pesticide exposure and various types of childhood cancer are summarized below, along with results of key studies. Childhood cancers of concern (leukemia, brain cancer, NHL, soft-tissue sarcoma, and Hodgkin's lymphoma) are generally the same cancers that have been associated with adult exposure to pesticides (Zahm and Ward, 1998).

Leukemia

The links between pesticide exposure and leukemia were first reported through sporadic case reports in the early 1970s. Since those initial case reports, more than 15 studies have been published that support an association between pesticides and childhood leukemia, some of which are presented in the following discussion. Most of these studies found an increased likelihood of

⁴ Some studies used surrogates of exposure, such as occupational category (farming) to estimate potential exposures to pesticides.

leukemia in children of parents who were occupationally exposed to pesticides, lived or worked on a farm, or who applied pesticides in the home and garden. This includes herbicides, insecticides, pesticide bombs and shampoos, and pest strips⁵ compared to those who were not occupationally or residentially exposed to pesticides (Zahm and Ward, 1998). Use of pesticides during pregnancy and direct exposures to children also were associated with an increased likelihood of leukemia in children.

Children who live on, or whose parents work on, a farm have higher levels of pesticides in their homes compared with children who do not live near a farm (Zahm and Ward, 1998). Compared to healthy children, those with acute lymphocytic leukemia (ALL) were 3.5 times as likely to have mothers who had been occupationally exposed to pesticides during pregnancy (Shu, et al., 1988). A study conducted by the Children's Cancer Study Group found that children with acute non-lymphocytic leukemia (ANLL) were more than 2.5 times as likely as children without the disease to have fathers who had used pesticides occupationally for more than 1,000 days. (Buckley, et al, 1989). The same researchers found that the likelihood of developing ANLL increased with the length of time the fathers used pesticides. Children with ANLL were 1.8 times as likely to have fathers who used pesticides at least once per week (Buckley, et al., 1989; Zahm and Ward, 1998).

Household exposures to pesticides are of particular concern due to the potential for prolonged exposure. In one study, children with leukemia were 4 to 7 times as likely to have been exposed to pesticides, compared to children without leukemia (Lowengart, et al., 1987). Another study found that 8 mothers whose children developed leukemia had prolonged exposure to pesticides, while none of the mothers of children without cancer did (Buckley, et al., 1989). These researchers found that children with ANLL were 3.5 times as likely to have been directly exposed to household pesticides on most days (Buckley, et al., 1989). In a more recent study of children ages 0-15 at time of leukemia diagnosis, use of professional pest control services at any time from 1 year before birth to 3 years after was associated with a 2.8-fold increase in the likelihood of developing childhood leukemia when compared to children without leukemia (Ma, et al., 2002).

⁵ Pest strips are pesticide-impregnated resin strips commonly hung in an area to control insects.

In two separate studies, researchers found that children with ALL were 3 to 9 times as likely to have parents who used pesticides during pregnancy or while breast-feeding (Zahm and Ward, 1998; Infante-Rivard, et al., 1999). More specifically, children with ALL were 3.5 times as likely to have mothers who used garden or residential pesticides during pregnancy (Shu, et al., 1988). A more recent study confirmed these findings. Compared to healthy children, children with ALL were 3.7 times as likely to have mothers who used garden or residential herbicides on more than 5 occasions during pregnancy (Infante-Rivard, et al., 1999). Children with leukemia also were more likely to have parents who used pest strips and to have mothers who were exposed to pesticides during pregnancy than children without leukemia (Leiss and Savitz, 1995; Infante-Rivard, et al., 1999).⁶

In one recent study, researchers found that the evidence of childhood cancer was more strongly associated with maternal exposures to pesticides during pregnancy as compared to maternal exposure before pregnancy and direct exposures to children during childhood. Children with ALL were approximately twice as likely to have mothers who used plant insecticides on up to 5 occasions and 4 times as likely to have mothers who used plant insecticides on more than 5 occasions during pregnancy (Infante-Rivard, et al., 1999). Also, children with ALL were 1.7 times as likely as children without ALL to have mothers who used pesticide products for protection of trees between 1 and 5 times during pregnancy (Infante-Rivard, et al., 1999).

Brain cancer

The links between pesticide exposure and CNS and brain cancers were first noted in sporadic case reports in the early 1970s. Since those initial case reports, more than 15 studies have been published that support the role pesticides may play in childhood CNS and brain cancers. Many of these studies were reviewed by researchers at the NCI and are referenced below.

⁶ Pest strips often contain dichlorvos, a pesticide classified by the U.S. EPA as a probable human carcinogen (Leiss and Savitz, 1995; ATSDR, 1997).

Table 7. Exposure to particular pesticide products and evidence of childhood cancer*

Pesticides			
Pesticide Product Exposure	Sources of Exposure	Cancer or Tumor Type	Reference
Professional pest control services	Residential exposures to fetus and children	Leukemia	Ma, et al., 2002
Pesticides	Residential exposures to children	Neuroblastoma	Daniels, et al., 2001
Pesticides	Occupational (farm or forestry) exposures to fathers	Nervous System Tumor	Feychting, et al., 2001
Professional pest extermination in the home	Residential exposures to children	Non-Hodgkin's Lymphoma	Meinert, et al., 2000
Pest strips Insecticides/rodenticides Garden herbicides and products for tree infestations	Residential exposures to mothers during pregnancy	Acute Lymphocytic Leukemia	Infante-Rivard, et al, 1999
Flea and tick spray/fogger	Residential exposures to mothers during pregnancy	Brain tumor	Pagoda and Preston-Martin, 1997
Horticultural pesticide indicators	Occupational (farm) exposures to parents	Neuroblastoma	Kristensen, et al., 1996
Horticultural and pesticide indicators	Occupational (farm) exposures to parents	Wilms' tumor	Kristensen, et al., 1996
Horticultural and pesticide indicators	Occupational (farm) exposures to parents	Non-Hodgkin's Lymphoma	Kristensen, et al., 1996
Horticultural and pesticide indicators	Occupational (farm) exposures to parents	Non-astrocytic neuroepithelial tumors (brain tumors)	Kristensen, et al., 1996
Pest strips	Residential exposures to mothers during pregnancy	Leukemia	Leiss and Savitz, 1995
Yard pesticides	Residential exposures to children	Soft tissue sarcoma	Leiss and Savitz, 1995
Pesticides	Occupational (farm) exposures to parents	Wilms' tumor	Sharpe, et al., 1995
Pesticides	Residential (farm) exposures to mothers during pregnancy	Brain tumor	Bunin, et al., 1994
Pesticides	Residential (farm) exposures to children	Brain tumor	Cordier, et al., 1994

Pesticide Product Exposure	Sources of Exposure	Cancer or Tumor Type	Reference
Flea collars Pest strips Herbicides/Insecticides	Residential exposures to children	Brain tumor	Davis, et al., 1993
Pesticides	Residential exposures	Wilms' tumor	Olshan, et al., 1993
Pesticides	Residential exposures to mothers during pregnancy	Acute Non-Lymphocytic Leukemia	Buckley, et al., 1989
Pesticides	Occupational exposures to fathers	Acute Non-Lymphocytic Leukemia	Buckley, et al., 1989
Pesticides	Residential exposures to children	Acute Non-Lymphocytic Leukemia	Buckley, et al., 1989
Pesticides	Occupational exposures to mothers during pregnancy	Acute Lymphocytic Leukemia	Shu, et al., 1988
Pesticides	Residential (farm) exposures to parents and children	Leukemia	Lowengart, et al., 1987

* Pesticides is a generic term for pesticide products and most often does not refer to any specific pesticide products.

Most of the studies found an association between parents who had applied pesticides in the home and garden and an increased likelihood of brain tumors in their children. *In utero* exposures to pesticides during pregnancy seemed to carry greater risks of brain cancer than exposures after birth (Zahm and Ward, 1998). In one study, researchers found that compared to healthy children, children with brain tumors were about twice as likely to have mothers who were exposed to flea and tick products during pregnancy (Pagoda and Preston-Martin, 1997). This same study found that children with brain cancer were 11 times as likely as children without brain cancer to have mothers who were exposed to sprays or foggers during pregnancy (Pagoda and Preston-Martin, 1997). In another study, researchers found that children with brain cancer were more likely to have been exposed to flea collars on pets, pest strips, termiticides, insecticides in the home, and herbicides in the garden compared to children without brain cancer (Davis, et al 1993).

Children whose parents were occupationally exposed to pesticides were about twice as likely to develop nervous system tumors. Children's risk of developing nonastrocytic neuroepithelial tumors (a type of brain tumor) increased the more their fathers were occupationally exposed to pesticides (Feychting, et al., 2001). A study following children whose fathers were occupationally exposed to pesticides in agricultural work found that these children were 2 to 3 times as likely as the general Norwegian population to develop brain tumors (Kristensen, et al., 1996).

Simply living on a farm also was found to increase the likelihood of childhood cancer risk in several studies (Bunin, et al., 1994; Cordier, et al., 1994; Kristensen, et al., 1996). One study found that children with brain tumors were approximately 4 times as likely to live on a farm, compared to children without cancer, while another study found that children were more than 3 times as likely to develop a brain tumor if their parents owned a farm, although level of pesticide exposures could not be determined (Bunin, et al., 1994; Kristensen, et al., 1996).

Despite this substantial body of evidence linking pesticides to childhood brain cancer, the studies are not entirely consistent. Several studies found no links, or even decreased likelihood of brain cancer from pesticide exposure (Fabia and Thuy, 1974; Howe, et al., 1989; McCredie, et al., 1994).

Other cancers

Early studies conducted on childhood neuroblastoma (a nervous system tumor) by several researchers found no association with parental agricultural work. However, more recent studies, using improved methods, have found an increased likelihood of the disease following parental exposure to pesticides. One such study found that compared to healthy children, those with neuroblastoma were 1.6 times as likely to have parents who used home and garden pesticides at least once (Daniels, et al., 2001). In addition, children with neuroblastoma were nearly twice as likely as children without the disease to have been directly exposed to garden herbicides and slightly more likely to have been directly exposed to insecticides (Daniels, et al., 2001). Another study found that children of parents exposed to pesticides in horticultural work were more likely to have neuroblastoma compared to the general Norwegian population (Kristensen, et al., 1996).

This same study found that children were twice as likely to develop NHL if their parents were exposed to pesticides during horticultural activities (Kristensen, et al., 1996). Another study found that children with NHL were nearly 3 times as likely as healthy children to have been exposed to residentially applied insecticides (Meinert, et al., 2000).

Several studies found inconclusive evidence of an increased likelihood of soft tissue sarcoma (STS) following pesticide exposure. However, one study found that children with STS were 4 times as likely as children without STS to have been exposed to pesticides in the yard (Leiss and Savitz, 1995).

Children of parents who reported use of pesticide spraying equipment were nearly 9 times as likely to develop Wilms' tumor compared to children of parents who did not report use of pesticide spraying equipment (Kristensen, et al., 1996). Children with Wilms' tumor were 2.2 times as likely as children without the disease to live in homes that had been exterminated (Olshan, et al., 1993). In another study, children with Wilms' tumor were many times more likely to have mothers who used pesticides on 10 occasions or more compared to healthy children (Sharpe, et al., 1995). Although the study was small, this result was strong enough to be unlikely due simply to chance.

Evidence from adults, animal and laboratory data

The role of pesticides in childhood cancers is supported by data from studies of adult populations exposed to various pesticides and animal toxicologic data. Increases in the likelihood of leukemia, brain cancer, NHL, Hodgkin's disease, and STS have consistently been associated with pesticide exposures in adults (Dich, et al., 1997).

Female rats and mice fed food contaminated with the pesticide dichlorvos for two years developed leukemia; the pesticide is listed as a probable human carcinogen (ATSDR, 1997). A study of exposure to the herbicide 2,4-D among dogs with leukemia found that they were more likely to have owners who used 2,4-D and commercial lawn care services compared to dogs without leukemia (U.S. EPA, 1994). This finding led the U.S. EPA Science Advisory Board to conclude that 2,4-D use can cause malignant lymphoma in dogs and potentially in humans (U.S.

EPA, 1994). Currently, 2,4-D is listed as a possible human carcinogen based on the study data described above, and on limited evidence of carcinogenicity in male rats.

During the late 1980s and early 1990s, the National Cancer Institute and the National Toxicology Program evaluated 51 pesticides for carcinogenicity and found that 24 demonstrated carcinogenicity in animal toxicology studies (Zahm and Ward, 1998). Many other pesticides have not been reviewed for their carcinogenic potential.

SOLVENTS

Uses

Organic solvents are chemicals characterized by their ability to dissolve other substances. They are widely used in industrial products and are common occupational exposures. Alcohol, toluene, trichloroethylene (TCE), perchloroethylene (Perc), styrene, benzene, ethylene glycol ethers, and xylene are all solvents. Occupations involving solvent exposure include dry cleaning, gluing, auto repair, electronics, painting, printing, and furniture repair, among others. Solvents may be used in the household for painting, adhesives, furniture stripping, and various hobbies. Solvents have been studied individually and as a class.

Exposures

Exposures to solvents typically occur in occupational settings. However, children may be exposed to organic solvents indirectly through their parents' exposure at work, as parents may bring solvent residues home on work clothing and shoes. Solvents can be absorbed into the bodies of workers who use them; high levels of solvent can remain in a worker's breath for up to 16 hours after exposure (Brugnone, et al., 1989). These exposures can then be passed through to the developing fetus or can affect germ cells. Children also may be directly exposed to solvents used in the home (in products such as, adhesives) or from clothing stored in closets that had been dry-cleaned with Perc, a popular dry-cleaning solvent. Various amounts of Perc can be emitted to the air and inhaled by consumers when dry-cleaned clothing is stored in home closets (Wallace and Langlois, 1995). Residents living near dry-cleaning facilities also may be exposed to Perc emitted to the air (U.S. EPA, 1998a).

Evidence from epidemiologic studies

Studies consistently have found an increased likelihood of childhood cancer, particularly leukemia and cancers of the nervous system, among children whose fathers were occupationally exposed to solvents (Colt and Blair, 1998). There also is evidence of an association between childhood leukemia and parental and childhood exposure to solvent-contaminated drinking

water, as has been documented for childhood cancer clusters in Woburn, Massachusetts and Dover Township, New Jersey (Costas, et al., 2002; Fagliano, et al., 2003).

Leukemia

There are a number of studies linking exposure to solvents and childhood leukemia. The two major types of studies that have examined the links between childhood leukemia and exposure to solvents involve parental occupational exposures and environmental exposures from drinking water contamination. One study found that compared to healthy children, those with acute non-lymphocytic leukemia (ANLL) were 2.1 times as likely to have fathers who were occupationally exposed to solvents, while a second and third study found that children with ANLL were 1.25 to 3.5 times as likely to have fathers who were exposed to solvents at work (Buckley, et al, 1989; Feychting, et al., 2001; Lowengart, et al., 1987). Compared to children without the disease, children with leukemia were 3 times as likely to have fathers who were exposed to the solvent methyl ethyl ketone (MEK) and 5.8 times as likely to have fathers who were occupationally exposed to benzene and alcohols prior to pregnancy (Lowengart, et al., 1987; McKinney, et al., 1991).

Similar elevations in the likelihood of cancer were found when maternal exposures were examined. Children with ALL were 1.8 times as likely to have mothers who were exposed to solvents prior to and during pregnancy compared to children without ALL (Shu, et al., 1999). In this same study, children who had ALL were 1.4 times as likely as children without ALL to be directly exposed to trichloroethylene (TCE) and children with ANLL were 4 times as likely as children without ANLL to have mothers who were exposed to benzene during pregnancy (Shu, et al., 1988).

In 1995, the New Jersey Department of Health and Senior Services (NJDHSS) found that the incidence of childhood cancer in Dover Township was significantly higher than would normally be expected in that population for the period 1979 through 1991. Elevated rates existed particularly for leukemia and brain and CNS cancers. In 1997, the NJDHSS and the Agency for Toxic Substances and Disease Registry (ATSDR) began an epidemiologic study to examine the potential exposures associated with the elevated childhood cancer rates in Dover Township.

Table 8. Exposure to solvents and evidence of childhood cancer*

Solvents			
Solvent Exposed	Sources of Exposure	Cancer or Tumor Type	Reference
Trichloroethylene Tetrachloroethylene	Environmental exposures to mothers of girls	Leukemia	Fagliano, et al., 2003
Trichloroethylene Tetrachloroethylene	Environmental exposures to children	Leukemia	Fagliano, et al., 2003
Solvent mixture including Trichloroethylene	Environmental exposures to mothers during pregnancy	Leukemia	Costas, et al., 2002
Benzene Perchloroethylene	Environmental (air) exposures	Leukemia	Reynolds, et al., 2002b
Benzene Alcohols Turpentine Lacquer thinner	Occupational exposures to fathers	Neuroblastoma	De Roos, et al., 2001
Solvents	Occupational exposures to fathers	Nervous System Tumor	Feychting, et al., 2001
Solvents	Occupational exposures to fathers	Leukemia	Feychting, et al., 2001
Trichloroethylene Carbon tetrachloride Perchloroethylene	Occupational exposures to mothers	Acute Lymphocytic Leukemia	Shu, et al., 1999
Trichloroethylene Carbon tetrachloride Perchloroethylene	Environmental exposures to children	Acute Lymphocytic Leukemia	Shu, et al., 1999
Benzene	Occupational exposures to fathers	Leukemia	McKinney, et al., 1991
Solvents	Occupational exposures to fathers	Acute Non-Lymphocytic Leukemia	Buckley, et al., 1989
Benzene	Occupational exposures to mothers during pregnancy	Acute Non-Lymphocytic Leukemia	Shu, et al., 1988
Chlorinated solvents Methyl ethyl ketone (MEK)	Occupational exposures to fathers	Leukemia	Lowengart, et al., 1987

* Solvents is a generic term and often does not refer to any specific chemical unless otherwise noted.

In their investigation they found that girls ages 0-19 with leukemia were 5 times as likely as girls without leukemia to have been prenatally exposed to Parkway Well water, which had been contaminated with TCE and Perc by the Reich Farm Superfund site (Fagliano, et al., 2003). Boys and girls with leukemia were 5.4 times as likely as children without leukemia to have drunk water from private wells in groundwater areas with a history of contamination (from Reich Farm Superfund site or wastewater from a nearby industrial facility) (Fagliano, et al., 2003).

Somewhat similar results were found in a recent study of childhood leukemia in Woburn, Massachusetts. In 1981, the state Department of Public Health confirmed a childhood leukemia cluster in the community. In 1979, two of the city's drinking water wells were contaminated with solvents, including TCE and Perc. A computer model describing Woburn's public water distribution system was developed to determine if childhood cancer could be attributed to exposure to these contaminants in drinking water. Children with leukemia were 8 times as likely to have mothers who likely drank water from contaminated wells during pregnancy compared to children without leukemia (Costas, et al., 2002). Since the number of children with cancer whose mothers were exposed during pregnancy was small, the role of chance could not be ruled out. However, the more contaminated water a mother likely consumed during pregnancy, the more likely her child was to develop leukemia (Costas, et al., 2002). This trend lends support to the plausibility of the solvent-leukemia link.

A recent study of hazardous air pollutants (HAPs) and leukemia found that census tracts with the greatest exposures to HAPs had the highest risk for childhood leukemia; the solvents benzene and Perc were the main contributors to air pollution in these census tracts (Reynolds, et al., 2002b).

Brain cancer and cancers of the CNS

Studies of the links between solvent exposure and brain cancer have yielded more limited evidence of an increased likelihood of cancer. In one study, fathers occupationally exposed to solvents near conception were 1.2 times as likely to have children who developed nervous system cancers compared to the general Swedish population (Feychting, et al., 2001). A study found that compared to a healthy comparison group, children with neuroblastoma were 1.5 times

as likely to have fathers who were exposed to benzene, mineral spirits and alcohols; 3.5 times as likely to have fathers who were exposed to lacquer thinner; and 10.4 times as likely to have fathers who were exposed to turpentine (De Roos, et al., 2001).

Evidence from adult, animal, and laboratory studies

Excesses of leukemia and other types of cancer in adults associated with solvent exposures have been reported over the last several decades. A 1977 study of workers exposed to benzene found that they were 5 to 10 times as likely to develop leukemia as unexposed workers (Infante, 2001). Exposure to Perc in drinking water has been associated with an increased likelihood of adult breast cancer in several studies (Aschengrau, et al., 1998; Aschengrau, et al., 2003). A 1998 U.S. EPA report indicates that the risk of cancer among workers exposed to PCE over a lifetime's work in a dry cleaning facility could be as high as 1 in 100 (U.S. EPA, 1998a).

Animal studies have linked exposures to solvents, such as TCE and Perc, with increased incidence of leukemia in male and female rats and malignant lymphoma in female mice (Burg, 2003; Shu, et al., 1999; Beliles and Totman, 1989). Another study found that male and female rats exposed to Perc developed kidney tumors and male and female mice exposed to Perc developed hepatocellular (liver) adenomas and carcinomas (U.S. EPA, 1998a). In addition, laboratory animal studies provide evidence that chlorinated solvents, including TCE, Perc, toluene and benzene can cause cancers, such as leukemia and lymphoma (Colt and Blair, 1998; Shu, et al, 1999).

PETROCHEMICALS AND COMBUSTION BY-PRODUCTS

Sources

Petrochemicals and combustion by-products refer to broad classes of chemicals (e.g., petroleum products, diesel exhaust, polycyclic aromatic hydrocarbons (PAHs), and dioxins) for which exposures typically occur through air contamination and less frequently through parental occupational or household exposures. We focus particularly on PAHs and dioxin exposures in this section.

Petrochemicals are organic (carbon-based) chemicals derived from natural gas or petroleum and are the building blocks of many other chemical products and synthetic materials used to produce industrial and consumer products including, pesticides, plastics, medicines, and dyes. For example, ethylene is a petrochemical that is the building block of a wide array of other chemical products. Often included in the category of petrochemicals are PAHs. These substances can be purposely produced as building blocks for other products, but human exposures mainly result when PAHs are formed during the incomplete burning of coal, oil and gas (diesel exhaust), household waste, or other organic substances, including tobacco (ATSDR, 1996).

Dioxins are a class of chemicals that are not intentionally produced, but are the by-product of production and combustion processes involving chlorine and carbon-based chemicals. Any time organic materials containing chlorine (such as PVC plastics) are burned, especially during incineration, accidental fires or backyard burning of waste, dioxins can be formed and released into the environment. Municipal solid waste incineration, backyard refuse barrel burning, medical waste incineration, secondary copper smelting, and cement kilns are the most common sources of dioxin emissions to the air in the United States. Dioxins can also be created during chlorine-bleaching processes for whitening paper and wood pulp (CHEJ, 1999).

There are over 100 forms of dioxins, furans and dioxin-like PCBs with a range of toxicity effects in humans and animals. To simplify analyses, all of the various dioxins are compared to one particular form—2,3,7-8 tetrachlorodibenzo-p-dioxin, or TCDD, the most toxic of the class.

Exposures

People are exposed to hydrocarbons primarily by breathing air with hydrocarbon particles in it or ingesting contaminated food, such as grilled meat (ATSDR, 1996; Rothman, et al., 1993).

Exposure to cigarette smoke, wood smoke, and vehicle exhausts are major sources of exposure to PAHs. PAHs can enter water systems through discharges from industrial plants and wastewater treatment facilities. The U.S. EPA has found PAHs in almost half of the 1,430 national priority hazardous waste clean-up sites, and benzo(a)pyrene, benzo(b)fluoranthene, and PAHs are among the top 20 most frequently found toxic substances at these sites (ATSDR, 1996; Nadakavukaren, 2000).

High dioxin exposures can be caused as a result of building fires and chemical accidents. Lower levels of dioxin can be emitted from incinerator stacks and industrial sources and then carried through the air, settling on grasses eaten by grazing animals and in bodies of water where they are ingested by fish. Dioxin enters the human food chain through these routes, and children can be exposed directly through food, from their mothers' blood supply while in the womb, or through breastfeeding (Schettler, et al., 2000).

Evidence from epidemiologic studies

Since the early 1970s epidemiologic studies have provided evidence of the links between parental occupational exposures to hydrocarbons, including benzene—a known human carcinogen—and childhood leukemia and other cancers. Although the human evidence of the links between these chemicals and childhood cancer is weaker than it is for pesticides and solvents, the overall evidence from epidemiologic and toxicologic studies indicates that PAHs and dioxins may contribute to childhood cancer. Several studies indicate that parental exposures in motor vehicle-related occupations (mechanic, gas station attendant, machinist) can increase the likelihood of childhood cancer. A more recent study reveals that PAHs in air pollution to which pregnant women can be exposed can cross the placenta and bind to fetal DNA (forming DNA adducts), causing mutations (damage to genetic material, the start of the cancer process) in the umbilical cord blood of newborns (Perera, et al., 2002).

Leukemia

Some limited evidence on the links between parental occupational exposure to hydrocarbons (diesel fuel and exhaust, petroleum products and PAHs) and leukemia in children exists. An early study (Fabia and Thuy, 1974) found that parental hydrocarbon exposure increased the likelihood of childhood leukemia. A more recent study found that mothers of children with leukemia worked in hydrocarbon-related occupations or with petroleum products more often than mothers whose children did not have leukemia (van Steensel-Moll, et al., 1985). Although more recent studies have not found consistent results, one study of parental occupational exposures revealed that children with leukemia were 2.5 times as likely as healthy children to have mothers who worked in hydrocarbon-related jobs during pregnancy; however, a chance finding could not be completely ruled out in this study (Colt and Blair, 1998; van Steensel-Moll, et al., 1985). Another study revealed that children with ANLL were 2.4 times as likely as healthy children to have parents exposed to petroleum products in their jobs (Buckley, et al., 1989). A more recent study of ALL and parental exposure to PAHs found that children with ALL were 3.1 times as likely to have mothers exposed to PAHs prior to pregnancy compared to children without ALL (Shu, et al., 1999). A study of occupational exposures to mothers revealed that compared to healthy children, children with ALL and ANLL were approximately 2 times as likely to have mothers occupationally exposed to gasoline during pregnancy (Shu, et al., 1988). In addition, children exposed to diesel exhausts and PAHs from air pollution were more likely to develop leukemia than were unexposed children (Lagorio, et al., 2000).

A study of the population of Seveso, Italy, a community where approximately 38,000 people were exposed to a high concentration of TCDD from a 1976 industrial accident, revealed increased childhood mortality rates due to cancer, particularly leukemia, compared to a non-exposed population. Seveso boys aged 1-19 years were twice as likely to die from any type of leukemia and 9.6 times as likely to die from lymphatic leukemia compared to non-exposed boys (Bertazzi, et al., 1992). Seveso girls aged 1-19 years were 2.5 times as likely to die from leukemia compared to non-exposed girls (Bertazzi, et al., 1992). Although consistent with evidence of cancer in Seveso adults, these results were based on small numbers of cancer cases, thus chance could play a role in the elevated rates.

Table 9. Exposure to petrochemicals and combustion by-products and evidence of childhood cancer

Petrochemicals and Combustion By-Products			
Product Exposed	Sources of Exposure	Cancer or Tumor Type	Reference
Hydrocarbons, including diesel fuel	Occupational exposures to fathers	Neuroblastoma	De Roos, et al., 2001
Diesel exhausts PAHs	Environmental (air) exposures to children	Leukemia	Lagorio, et al., 2000
Exhaust	Occupational exposures to mothers before pregnancy	Acute Lymphocytic Leukemia	Shu, et al., 1999
PAHs	Occupational exposures to mothers before and during pregnancy	Acute Lymphocytic Leukemia	Shu, et al., 1999
Hydrocarbons	Occupational exposures to parents	Wilms' tumor	Colt and Blair, 1998
Motor vehicle exhaust (nitrogen dioxide)	Environmental (air) exposures	Leukemia	Feychting, et al., 1998
Motor vehicle exhaust (nitrogen dioxide)	Environmental (air) exposures	Central nervous system cancers	Feychting, et al., 1998
Hydrocarbons	Occupational exposures to mothers	Hepatoblastoma	Robison, et al., 1995
Petroleum products	Occupational exposures to fathers	Hepatoblastoma	Robison, et al., 1995
Dioxin (TCDD)	Environmental (air) exposures	Leukemia	Bertazzi, et al., 1992
Petroleum products	Occupational exposures to fathers	Acute Non-Lymphocytic Leukemia	Buckley, et al., 1989
Gasoline	Occupational exposures to mothers during pregnancy	Acute Lymphocytic Leukemia	Shu, et al., 1988
Gasoline	Occupational exposures to mothers during pregnancy	Acute Non-Lymphocytic Leukemia	Shu, et al., 1988
Aromatic hydrocarbons Aliphatic hydrocarbons	Occupational exposures to parents	Neuroblastoma	Spitz and Johnson, 1985
Hydrocarbon-related occupations	Occupational exposures to mothers	Leukemia	van Steensel-Moll, et al., 1985
Hydrocarbons	Occupational exposures to parents	Wilms' tumor	Wilkins and Sinks, 1984
Hydrocarbons	Occupational exposures to parents	Urinary system cancers	Kwa and Fine, 1980

Neuroblastoma

There is only very limited evidence of a link between hydrocarbon exposure in motor vehicle-related occupations and neuroblastoma. In two early studies researchers found that children with neuroblastoma and children who died of neuroblastoma were 3 times as likely to have parents who were exposed to hydrocarbons in their jobs compared to healthy children (Spitz and Johnson, 1985; Fabia and Thuy, 1974). Although these findings have not been consistently replicated in follow-up studies, a more recent study, which specifically examined diesel fuel exposures, found that children with neuroblastoma were 1.5 times as likely as children without the disease to have parents who were exposed to diesel fuel (De Roos, et al., 2001).

Other cancers

A review of several studies conducted by the Children's Cancer Group found that children with hepatoblastoma (liver cancer) were 3.7 times as likely to have mothers who were exposed to hydrocarbons and 1.9 times as likely to have fathers who were exposed to petroleum products compared to healthy children (Robison, et al., 1995).

Another review of parental occupational exposures and risk of childhood cancer conducted by researchers at the National Cancer Institute concluded that studies have consistently reported an increased likelihood of childhood cancer as a result of parental occupational exposures to hydrocarbons. Compared to healthy children, children with urinary tract cancers were 2.5 times as likely to have parents who were mechanics, gas station attendants, and machinists and those children with Wilms' tumor were up to 1.4 times as likely to have parents who were mechanics, gas station attendants, and machinists, although chance could not be completely ruled out in these studies (Kwa and Fine, 1980; Colt and Blair, 1998; Wilkins and Sinks, 1984).

A recent study of air pollution found that the greater the nitrogen dioxide (NO₂) concentration (from car exhaust) to which a child was exposed, the more likely he or she was to develop cancer. No increased risk of cancer was found among children exposed to less than 49 µg/m³ of NO₂ (Feychting, et al., 1998). However, compared to healthy children, those exposed to 50-79

$\mu\text{g}/\text{m}^3$ of NO_2 were 1.9 times as likely to develop any type of cancer and those exposed to greater than $80 \mu\text{g}/\text{m}^3$ of NO_2 were 3.8 times as likely to develop any type of cancer (Feychting, et al., 1998).

Evidence from adult, animal, and laboratory studies

The International Agency for Research on Cancer (IARC) and the U.S. EPA have classified 2,3,7-8 tetrachlorodibenzo-p-dioxin, or TCDD, a known human carcinogen based on the weight of animal, human evidence, and mechanistic data (U.S. EPA, 2001b). The U.S. EPA has classified other dioxins as likely human carcinogens (U.S. EPA, 2001a). Exposure to aromatic hydrocarbons is a well-established risk factor for kidney cancer in adults (Colt and Blair, 1998).

A National Institute for Occupational Safety and Health (NIOSH) study found that men occupationally exposed to dioxin for more than 1 year were on average 1.5 times as likely as the general U.S. population to develop stomach cancer, lung cancer, NHL, and Hodgkin's disease and 9.2 times as likely as the U.S. population to develop cancer of the soft and connective tissue (CHEJ, 1999; Fingerhut, et al., 1991). A follow-up study concluded that workers exposed to TCDD were more likely to die of all cancers combined compared to the U.S. population (Steenland, et al., 1999).

A study in Germany found that workers exposed to dioxin-contaminated herbicides in an herbicide manufacturing plant for fewer than 20 years were not at increased risk for developing lung cancer. However, workers exposed for more than 20 years were more likely to die from cancer compared to the general West German population (Manz and Berger, 1991). A study conducted in the Netherlands found that workers exposed to herbicides and contaminants were at increased risk for developing respiratory cancer, urinary tract cancer, prostate cancer, and NHL (Hooiveld, et al., 1998).

A study of the adult population of Seveso, Italy revealed an elevated occurrence of gastrointestinal cancer and cancers of lymphatic and hemopoietic tissue (Bertazzi, et al., 1998). Experimental, epidemiologic, and mechanistic data support the hypothesis that increased cancer rates in the community are associated with dioxin exposure (Bertazzi, et al., 1998).

Several studies have been conducted that demonstrate the links between dioxin exposure and cancer in mice, rats and hamsters (Institute of Medicine, 1994; Della Porta, 1987; Rao, et al., 1988).⁷ Hepatocellular carcinoma and hepatocellular adenomas (liver cancer) were observed in female rats and male and female mice exposed to dioxin (Institute of Medicine, 1994; Della Porta, 1987).

Studies conducted during the last several decades reveal that diesel exhaust is definitely carcinogenic (lung cancer) to rats and possibly to mice (Mauderly, 1994; McClellan, 1987). Rats exposed to carbon black developed the same tumors as rats exposed to diesel, which suggests that the particles themselves are carcinogenic in rats (Warren, 2003). Carbon black, a powdered form of elemental carbon formed during partial combustion of hydrocarbons, can be used as a surrogate for diesel exhaust exposure (Nauss, 1997; Warren, 2003; NIOSH, 2003).

A 1994 review of the evidence on adult lung cancer risk and diesel engine exhaust (DE) exposure concluded that the epidemiologic “evidence suggests that heavy occupational exposure to DE probably increases the relative risk for lung cancer in the range of 1.2 to 2.0” (1.2 to 2.0 times more as likely) (Mauderly, 1994). However, in the more than 30 studies reviewed, chance could not always be completely ruled out, direct measures of exposure were not always taken, and cigarette smoking was not always ruled out as a confounding factor (Mauderly, 1994; Warren, 2003). The few studies that did control for smoking, however, researchers still found an association between increased risk of lung cancer and exposure to diesel emissions (Nauss, 1997).

Many animal studies have been conducted on the carcinogenic effects of PAHs, while fewer studies have been conducted in people or on specific PAHs (Tox Probe, 2003). Based on animal toxicology and human epidemiology studies, the U.S. EPA has classified the PAHs, benzo(a)anthracene, benzo(b)fluoranthene, and benzo(a)pyrene as probable human carcinogens, and the U.S. Department of Health and Human Services has classified benzo(a)anthracene,

⁷ According to Rao, et al., (1988) hamsters are the species most resistant to the toxic effects of TCDD; yet they developed squamous cell carcinomas of the skin after TCDD exposure.

benzo(b)fluoranthene, benzo(a)pyrene, among other PAHs, as known animal carcinogens (ATSDR, 1995). In one study, mice fed fairly high doses of benzo(a)pyrene in their feed developed tumors of the lung, forestomach, esophagus, and tongue (Goldstein, et al., 1998).

LIMITATIONS OF THE EVIDENCE

Proving causal relationships between exposures to toxic substances and childhood cancer is difficult for a number of reasons: the rare nature of childhood cancer; difficulties in characterizing exposures, particularly past exposures; the influence of other related exposures on disease (known as confounding); and the difficulty of following exposed individuals over long periods of time.

Almost all of the studies examined in this analysis were retrospective (examining exposures among children with cancer) and based on self-reports about previous exposures from children and their families. In these studies, participants (children and their families) were asked to report on exposures that potentially occurred 5-10 years prior. In such studies, it is always possible that parents of disease victims may remember and report past exposures differently than those without the disease, and this could lead to a bias that would falsely inflate the strength of the association between an exposure and a disease.

Environmental measurements were made in only a few studies, because they are expensive and hard to take years after exposures. Direct exposure measurement is especially difficult when examining substances that are quickly metabolized and excreted. Therefore, in many cases it is not feasible to scientifically validate participants' responses (Grufferman, 1998; Zahm and Ward, 1998).

In general, studying diseases with long latency periods adds to the difficulties in determining the exact cause(s) of disease. With greater periods of time between exposure and disease, there are greater possibilities for additional confounding exposures to take place. On the other hand, cancer development in childhood is usually quicker than in adults, which can make it somewhat easier to study the former than the latter. Information on the timing of exposure to certain chemical compounds can be useful in better understanding and explaining the ability of that exposure to cause childhood malignancies, the interaction of chemicals with cells in the body,

and increases and decreases in vulnerability according to when exposure takes place. Approximately half of the studies—mostly the more recent ones—discussed in this report examined the timing of exposure (pre-pregnancy, pregnancy, childhood).

Because childhood cancer is relatively rare, generally only small numbers of cases can be examined for different malignancies and types of exposure. Studies of childhood cancer with small numbers of cases often produce statistically unstable results, meaning that chance association between exposure and disease cannot be ruled. Such studies must be considered in the context of other studies or other types of information in drawing overall conclusions.

Studies generally focused on generic classes of chemicals, such as solvents, pesticides, or hydrocarbons rather than on specific pesticide or hydrocarbon types (Zahm and Ward, 1998). Comparisons of exposures based on broad classes of chemicals can dilute, or underestimate, the cancer effect of specific chemicals. However, some studies have demonstrated an exposure-response gradient, which gives greater credibility to the results (increasing exposure, increasing likelihood of disease) (Zahm and Ward, 1998).

Many studies focused on occupational category or job title instead of specific job activities. Exposures to employees may be underestimated in that different employees with the same job title may be responsible for different occupational activities and may wear different personal protective equipment (Colt and Blair, 1998).

In general, limitations in the ability to concretely measure exposures would tend to lead to an underestimation of the increase in the likelihood of cancer rather than an overestimation. Thus, the inability to find an increased risk of cancer is often the result of study design (the study did not have sufficient “power” to find the increased risk if it existed) rather than evidence of no harm. Many of the studies examining the links between exposure to toxic substances and childhood cancer, when taken individually, provide only limited or weak evidence of such a link. However, the weight of the evidence examined in this report does provide reason for concern.

Because of the cost and difficulties in establishing causal links between exposure and disease in epidemiologic studies, they should be evaluated along with animal toxicology and *in vitro* cellular studies that can provide additional important information about the substance of concern. Most chemicals have not been studied for their ability to cause cancer. A 1998 U.S. EPA study found that fewer than half of chemicals manufactured above one million pounds per year in this country had been tested for their ability to cause cancer (U.S. EPA, 1998b). Even less is known about smaller volume chemicals or about the effects of chemicals in mixtures. Thus, little research—either epidemiologic or laboratory—has been undertaken to examine the links between exposure to toxic substances and childhood cancer. Despite this lack of knowledge, children are exposed to such substances every day in their air, water, and food, and they are commonly found in products used in households.

CONCLUSIONS

Childhood cancer is the second largest cause of death among children. Evidence indicates that a substantial portion of childhood cancers may be environmentally-related, and thus preventable. In this report, we examined the evidence on the links between toxic substances and childhood cancer. We have focused on three categories of toxic substances—pesticides, solvents, and petrochemicals and production by-products—because they are the groups of chemicals for which evidence has indicated a link to childhood cancer.

Our analysis of the epidemiologic and toxicologic literature found the following:

- Epidemiologic studies indicate that parental and childhood exposures to some pesticides, solvents, petrochemicals and certain industrial by-products can increase the likelihood of cancer in children. In many cases, the studies do not provide evidence of cancer from exposure to particular chemicals but rather mixtures or classes (e.g., pesticides, solvents, hydrocarbons), which are more common in the environment and easier to study.
- Certain chemical exposures that occur prior to conception, in the womb, or in early childhood increased likelihood of childhood cancer. Thus, exposure reduction strategies must address both parental occupational and household exposures as well as childhood exposures.
- The evidence supporting the connection between exposure to these substances and childhood cancer is strongest for leukemia, brain and central nervous system cancers. This is due in part to the fact that these are the most common childhood cancers and thus easiest to study.
- Epidemiologic studies have consistently found an increased likelihood of childhood cancer following parental or childhood exposure to pesticides. Those cancers for which evidence of a link to pesticide exposures exists include: leukemia, brain cancer; neuroblastoma; Wilms' tumor; soft tissue sarcoma; and non-Hodgkin's

lymphoma. Based on a review of the evidence, researchers at the National Cancer Institute concluded: “Although research is underway to characterize the risks of childhood cancer associated with pesticides and identify the specific pesticides responsible, it is prudent to reduce or, where possible, eliminate pesticide exposure to children, given their increased vulnerability and susceptibility. In particular, efforts should be focused to reduce exposure to pesticides used in homes and gardens and on lawns and public lands, which are the major sources of pesticide exposure for most children” (Zahm and Ward, 1998).

- Studies have consistently found an increased likelihood of childhood cancer, particularly leukemia and cancers of the nervous system, following parental exposure to solvents in manufacturing and painting. Based on a review of the evidence, researchers at the National Cancer Institute concluded that “the evidence for an association between childhood leukemia and paternal exposure to solvents is quite strong...despite these limitations [in existing studies], epidemiological studies have provided sufficient evidence that certain parental exposures may be harmful to their children” (Colt and Blair, 1998). Evidence of links between childhood leukemia and solvent-contaminated drinking water (both from maternal and childhood exposure) is also increasing, as has been documented for childhood cancer clusters in Woburn, Massachusetts and Dover Township, New Jersey.
- While generally weaker than the evidence for pesticides and solvents, some studies indicate that parental exposure to hydrocarbon products and parental and childhood exposure to combustion by-products, such as dioxins and polycyclic aromatic hydrocarbons, may increase the likelihood of childhood leukemia and brain and central nervous system cancers. Parental exposures in motor vehicle-related professions (diesel exhaust and particulates), occupations involving exposures to hydrocarbons, and childhood exposures to dioxins are of particular concern.
- Evidence of the carcinogenicity of these classes of chemicals from laboratory toxicology studies and epidemiologic studies of adults provide additional evidence to support the plausibility of links between these chemicals and childhood cancer.

The types of chemicals examined in this report are not only of concern because of their ability to cause cancer but also for their ability to cause other health effects such as neurological and developmental damage and damage to the fetus. Preventing exposure to chemicals suspected of causing cancer is possible, as recent European policies demonstrate. The European Union will soon require that all chemicals in commercial circulation receive basic testing, and that those that are known or probable carcinogens, mutagens, or reproductive toxicants be used only when there are no safer economically and technically feasible alternatives. This common sense approach to chemical safety is likely to result in significant reductions in childhood exposure to potentially dangerous chemicals.

Because the majority of chemicals in commerce—some of which are widely used in everyday products—have not been studied for their potential to cause cancer, we do not have basic carcinogenicity data on the many substances that might cause cancer in children (U.S. EPA, 1998b). Thus the links between only a few toxic chemicals and childhood cancer have been studied. The risks associated with mixtures of chemicals typical of what occurs in everyday life have been studied even less. Therefore, it is difficult to determine the exact magnitude of the contribution of toxic chemicals to the overall burden of childhood cancer.

The lack of proof of direct causal links between toxics and childhood cancer should not be construed as proof of safety. By the time we have good evidence of causal links, many more parents and children will have been exposed. The evidence presented in this report provides sufficient rationale for protecting parents' and children's health by reducing their exposure to chemicals suspected of causing cancer.

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