2008–2009 Annual Report President's Cancer Panel

REDUCING ENVIRONMENTAL CANCER RISK

What We Can Do Now

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES National Institutes of Health **National Cancer Institute**

The President's Cancer Panel

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This report is submitted to the President of the United States in fulfillment of the obligations of the President's Cancer Panel to appraise the National Cancer Program as established in accordance with the National Cancer Act of 1971 (P.L. 92-218), the Health Research Extension Act of 1987 (P.L. 99-158), the National Institutes of Health Revitalization Act of 1993 (P.L. 103-43), and Title V, Part A, Public Health Service Act (42 U.S.C. 281 *et seq.*).

April 2010
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Suzanne H. Reuben
for
The President's Cancer Panel

April 2010

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Cancer Institute

The President
The White House
Washington, DC 20500

Dear Mr. President:

Though overall cancer incidence and mortality have continued to decline in recent years, the disease continues to devastate the lives of far too many Americans. In 2009 alone, approximately 1.5 million American men, women, and children were diagnosed with cancer, and 562,000 died from the disease. With the growing body of evidence linking environmental exposures to cancer, the public is becoming increasingly aware of the unacceptable burden of cancer resulting from environmental and occupational exposures that could have been prevented through appropriate national action. The Administration's commitment to the cancer community and recent focus on critically needed reform of the Toxic Substances Control Act is praiseworthy. However, our Nation still has much work ahead to identify the many existing but unrecognized environmental carcinogens and eliminate those that are known from our workplaces, schools, and homes.

To jumpstart this national effort, the President's Cancer Panel (the Panel) dedicated its 2008–2009 activities to examining the impact of environmental factors on cancer risk. The Panel considered industrial, occupational, and agricultural exposures as well as exposures related to medical practice, military activities, modern lifestyles, and natural sources. In addition, key regulatory, political, industrial, and cultural barriers to understanding and reducing environmental and occupational carcinogenic exposures were identified. The attached report presents the Panel's recommendations to mitigate or eliminate these barriers.

The Panel was particularly concerned to find that the true burden of environmentally induced cancer has been grossly underestimated. With nearly 80,000 chemicals on the market in the United States, many of which are used by millions of Americans in their daily lives and are un- or understudied and largely unregulated, exposure to potential environmental carcinogens is widespread. One such ubiquitous chemical, bisphenol A (BPA), is still found in many consumer products and remains unregulated in the United States, despite the growing link between BPA and several diseases, including various cancers.

While BPA has received considerable media coverage, the public remains unaware of many common environmental carcinogens such as naturally occurring radon and manufacturing and combustion by-products such as formaldehyde and benzene. Most also are unaware that children are far more vulnerable to environmental toxins and radiation than adults. Efforts to inform the public of such harmful exposures and how to prevent them must be increased. All levels of government, from federal to local, must work to protect every American from needless disease through rigorous regulation of environmental pollutants.

Environmental exposures that increase the national cancer burden do not represent a new front in the ongoing war on cancer. However, the grievous harm from this group of carcinogens has not been addressed adequately by the National Cancer Program. The American people—even before they are born—are bombarded continually with myriad combinations of these dangerous exposures. The Panel urges you most strongly to use the power of your office to remove the carcinogens and other toxins from our food, water, and air that needlessly increase health care costs, cripple our Nation's productivity, and devastate American lives.

Sincerely,

LaSalle D. Leffall, Jr., M.D., F.A.C.S.
Chair

Margaret L. Kripke, Ph.D.

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Executive Summary

Despite overall decreases in incidence and mortality, cancer continues to shatter and steal the lives of Americans. Approximately 41 percent of Americans will be diagnosed with cancer at some point in their lives, and about 21 percent will die from cancer. The incidence of some cancers, including some most common among children, is increasing for unexplained reasons.

Public and governmental awareness of environmental influences on cancer risk and other health issues has increased substantially in recent years as scientific and health care communities, policymakers, and individuals strive to understand and ameliorate the causes and toll of human disease. A growing body of research documents myriad established and suspected environmental factors linked to genetic, immune, and endocrine dysfunction that can lead to cancer and other diseases.

Between September 2008 and January 2009, the President's Cancer Panel (the Panel) convened four meetings to assess the state of environmental cancer research, policy, and programs addressing known and potential effects of environmental exposures on cancer. The Panel received testimony from 45 invited experts from academia, government, industry, the environmental and cancer advocacy communities, and the public.

This report summarizes the Panel's findings and conclusions based on the testimony received and additional information gathering. The Panel's recommendations delineate concrete actions that governments; industry; the research, health care, and advocacy communities; and individuals can take to reduce cancer risk related to environmental contaminants, excess radiation, and other harmful exposures.

Key Issues for Reducing Environmental Cancer Risk

Issues impeding control of environmental cancer risks include those related to limited research on environmental influences on cancer; conflicting or inadequate exposure measurement, assessment, and classification; and ineffective regulation of environmental chemical and other hazardous exposures.

Environmental Cancer Research

Research on environmental causes of cancer has been limited by low priority and inadequate funding. As a result, the cadre of environmental oncologists is relatively small, and both the consequences of cumulative lifetime exposure to known carcinogens and the interaction of specific environmental contaminants remain largely unstudied. There is a lack of emphasis on environmental research as a route to primary cancer prevention, particularly compared with research emphases on genetic and molecular mechanisms in cancer.

Environmental Exposure Measurement, Methodologic, Assessment, and Classification Issues

Efforts to identify, quantify, and control environmental exposures that raise cancer risk, including both single agents and combinations of exposures, have been complicated by the use of different measures, exposure limits, assessment processes, and classification structures across agencies in the U.S. and among nations. In addition, efforts have been compromised by a lack of effective measurement methods and tools; delay in adopting available newer technologies; inadequate computational models; and weak, flawed, or uncorroborated studies.

Some scientists maintain that current toxicity testing and exposure limit-setting methods fail to accurately represent the nature of human exposure to potentially harmful chemicals. Current toxicity testing relies heavily on animal studies that utilize doses substantially higher than those likely to be encountered by humans. These data—and the exposure limits extrapolated from them—fail to take into account harmful effects that may occur only at very low doses. Further, chemicals typically are administered when laboratory animals are in their adolescence, a methodology that fails to assess the impact of *in utero*, childhood, and lifelong exposures. In addition, agents are tested singly rather than in combination.

Regulation of Environmental Contaminants

The prevailing regulatory approach in the United States is reactionary rather than precautionary. That is, instead of taking preventive action when uncertainty exists about the potential harm a chemical or other environmental contaminant may cause, a hazard must be incontrovertibly demonstrated before action to ameliorate it is initiated. Moreover, instead of requiring industry or other proponents of specific chemicals, devices, or activities to prove their safety, the public bears the burden of proving that a given environmental exposure is harmful. Only a few hundred of the more than 80,000 chemicals in use in the United States have been tested for safety.

U.S. regulation of environmental contaminants is rendered ineffective by five major problems: (1) inadequate funding and insufficient staffing, (2) fragmented and overlapping authorities coupled with uneven and decentralized enforcement, (3) excessive regulatory complexity, (4) weak laws and regulations, and (5) undue industry influence. Too often, these factors, either singly or in combination, result in agency dysfunction and a lack of will to identify and remove hazards.

Sources and Types of Environmental Contaminants

The line between occupational and environmental contaminants is fine and often difficult to demarcate. Many known or suspected carcinogens first identified through studies of industrial and agricultural occupational exposures have since found their way into soil, air, water, and numerous consumer products. People from disadvantaged populations are more likely to be employed in occupations with higher levels of exposure (e.g., mining, construction, manufacturing, agriculture, certain service sector occupations) and to live in more highly contaminated communities. The reality of this unequal burden is not just a health issue, but an issue of environmental justice.

While all Americans now carry many foreign chemicals in their bodies, women often have higher levels of many toxic and hormone-disrupting substances than do men. Some of these chemicals have been found in maternal blood, placental tissue, and breast milk samples from pregnant women and mothers who recently gave birth. Thus, chemical contaminants are being passed on to the next generation, both prenatally and during breastfeeding. Some chemicals indirectly increase cancer risk by contributing to immune and endocrine dysfunction that can influence the effect of carcinogens.

Children of all ages are considerably more vulnerable than adults to increased cancer risk and other adverse effects from virtually all harmful environmental exposures. In addition, some toxics have adverse effects not only on those exposed directly (including *in utero*), but on the offspring of exposed individuals.

Exposure to Contaminants from Industrial and Manufacturing Sources

Manufacturing and other industrial products and processes are responsible for a great many of the hazardous occupational and environmental exposures experienced by Americans. Many of these contaminants—even substances banned more than 30 years ago—remain ubiquitous in the environment because they break down very slowly, if at all. Other industrial chemicals or processes have hazardous by-products or metabolites. Numerous chemicals used in manufacturing remain in or on the product as residues, while others are integral components of the products themselves. Further, in the ongoing quest for more effective and efficient ways of making industrial and consumer products, new chemicals and other substances are being created continually and existing substances are being put to new uses. Limited research to date on unintended health effects of nanomaterials, for example, suggests that unanticipated environmental hazards may emerge from the push for progress.

Exposure to Contaminants from Agricultural Sources

The entire U.S. population is exposed on a daily basis to numerous agricultural chemicals, some of which also are used in residential and commercial landscaping. Many of these chemicals have known or suspected carcinogenic or endocrine-disrupting properties. Pesticides (insecticides, herbicides, and fungicides) approved for use by the U.S. Environmental Protection Agency (EPA) contain nearly 900 active ingredients, many of which are toxic. Many of the solvents, fillers, and other

chemicals listed as inert ingredients on pesticide labels also are toxic, but are not required to be tested for their potential to cause chronic diseases such as cancer. In addition to pesticides, agricultural fertilizers and veterinary pharmaceuticals are major contributors to water pollution, both directly and as a result of chemical processes that form toxic by-products when these substances enter the water supply. Farmers and their families, including migrant workers, are at highest risk from agricultural exposures. Because agricultural chemicals often are applied as mixtures, it has been difficult to clearly distinguish cancer risks associated with individual agents.

Environmental Exposures Related to Modern Lifestyles

Conveniences of modern life—automobile and airplane travel, dry cleaning, potable tap water, electricity, and cellular communications, to name a few—have made daily life easier for virtually all Americans. Some of these conveniences, however, have come at a considerable price to the environment and human health, and the true health impact of others is unconfirmed. For example, mobile source air emissions (e.g., from cars, trucks, other passenger vehicles, ships), especially diesel particulate pollution, are responsible for approximately 30 percent of cancer resulting from air pollution. Disinfection of public water supplies has dramatically reduced the incidence of waterborne illnesses and related mortality in the United States, but research indicates that long-term exposure to disinfection by-products such as trihalomethanes may increase cancer risk. Chemicals used for household pest control can become a component of carpet dust, posing a risk to children when they play on the floor.

Sharp controversy exists in the scientific community as to possible adverse health effects from exposure to low frequency electromagnetic energy. The use of cell phones and other wireless technology is of great concern, particularly since these devices are being used regularly by ever larger and younger segments of the population. At this time, there is no evidence to support a link between cell phone use and cancer. However, the research on cancer and other disease risk among long-term and heavy users of contemporary wireless devices is extremely limited. Similarly, current and potential harms from extremely low frequency radiation are unclear and require further study. In addition, ultraviolet radiation from excess sun exposure and tanning devices has been proven to substantially increase skin cancer risk.

Exposure to Hazards from Medical Sources

In the past two decades, improved imaging technologies, nuclear medicine examinations, and new pharmaceutical interventions have made possible significant strides in our ability to diagnose and treat human disease, including cancer. It is becoming increasingly clear, however, that some of these same technologies and drugs that have contributed so greatly to health status and longevity also carry risks.

While ionizing radiation exposures from radon, occupational, and other sources have remained essentially stable over the past 30 years, Americans now are estimated to receive nearly half of their total radiation exposure from medical imaging and other medical sources, compared with only 15 percent in the early 1980s. The increase in medical radiation has nearly doubled the total average effective radiation dose per

individual in the United States. Computed tomography (CT) and nuclear medicine tests alone now contribute 36 percent of the total radiation exposure and 75 percent of the medical radiation exposure of the U.S. population. Medical imaging of children is of special concern; compared with adults, children have many more years of life during which a malignancy initiated by medical radiation can develop. Many referring physicians, radiology professionals, and the public are unaware of the radiation dose associated with various tests or the total radiation dose and related increased cancer risk individuals may accumulate over a lifetime. People who receive multiple scans or other tests that require radiation may accumulate doses equal to or exceeding that of Hiroshima atomic bomb survivors. It is believed that a single large dose of ionizing radiation and numerous low doses equal to the single large dose have much the same effect on the body over time.

Moreover, radiation dose for the same test can vary dramatically depending on the equipment used, technologist skill, application of dose-reduction strategies, and patient size, age, and gender. Licensure of imaging and radiation therapy technologists varies depending on the type of test performed by the technologist. Some states have only partial regulation; six states and the District of Columbia have no licensure or regulatory provisions of any kind.

In addition, pharmaceuticals have become a considerable source of environmental contamination. Drugs of all types enter the water supply when they are excreted or improperly disposed of; the health impact of long-term exposure to varying mixtures of these compounds is unknown.

Exposure to Contaminants and Other Hazards from Military Sources

The military is a major source of toxic occupational and environmental exposures that can increase cancer risk. Information is available about some military activities that have directly or indirectly exposed military and civilian personnel to carcinogens and contaminated soil and water in numerous locations in the United States and abroad. However, we may never know the full extent of environmental contamination from military sources. Nearly 900 Superfund sites are abandoned military facilities or facilities that produced materials and products for or otherwise supported military needs. Some of these sites and the areas surrounding them became heavily contaminated due to improper storage and disposal of known or suspected carcinogens including solvents, machining oils, metalworking fluids, and metals. In some cases, these contaminants have spread far beyond their points of origin because they have been transported by wind currents or have leached into drinking water supplies.

Hundreds of thousands of military personnel and civilians in the United States received significant radiation doses as a result of their participation in nuclear weapons testing and supporting occupations and industries, including nuclear fuel and weapons production, and uranium mining, milling, and ore transport. Hundreds of thousands more were irradiated at levels sufficient to cause cancer and other diseases. These populations include the families of military and civilian workers, and people—known as "downwinders"—living or working in communities surrounding or downstream from testing and related activities, and in

relatively distant areas to which nuclear fallout or other radioactive material spread. Federal responses to the plight of affected individuals have been unsatisfactory. Those affected lack knowledge about the extent of their exposure or potential health problems they may face. Similarly, most health care providers are not aware of cancer and other latent radiation effects and therefore are unlikely to adequately monitor patients for these health conditions. Exposure to ionizing radiation related to nuclear weapons testing is an underappreciated issue worldwide.

Exposure to Environmental Hazards from Natural Sources

Most environmental hazards with the potential to raise cancer risk are the product of human activity, but some environmental carcinogens come from natural sources. For example, radon gas, which forms naturally from the breakdown of uranium mineral deposits, is the second leading cause of lung cancer in the United States and the leading cause of lung cancer among people who have never smoked. Radon-induced lung cancer is responsible for an estimated average of 21,000 deaths annually. People who smoke and also are exposed to radon have a higher risk of lung cancer than from either exposure alone.

Although human activities such as mining, ore processing, use of arsenic-containing pesticides, and burning of fossil fuels are major contributors to waterborne arsenic in the U.S., most inorganic arsenic in drinking water is from natural sources. Inorganic arsenic in drinking water has been linked to skin, lung, bladder, and kidney cancer in both sexes and with prostate cancer in men, as well as numerous non-cancerous conditions including endocrine, reproductive, and developmental effects.

Reducing Environmental Cancer Risk: A Call to Action

The burgeoning number and complexity of known or suspected environmental carcinogens compel us to act to protect public health, even though we may lack irrefutable proof of harm. Action is possible at several levels: conducting scientific research to enhance our understanding and by extension, our ability to prevent and respond to environmental carcinogens; enforcing existing policies and regulations that protect workers and the public; implementing policy and regulatory changes that support public health and reduce the burden of cancer; and taking personal action.

The Panel concludes that:

We Need to Determine the Full Extent of Environmental Influences on Cancer.

At this time, we do not know how much environmental exposures influence cancer risk and related immune and endocrine dysfunction. Environmental contamination varies greatly by type and magnitude across the nation, and the lifetime effects of exposure to combinations of chemicals and other agents are largely unstudied. Similarly, the cancer impact of exposures during key "windows of vulnerability" such as the prenatal period, early life, and puberty are not well understood. Nonetheless, while these diverse effects often are difficult to quantify with existing technologies and research methods, in a great many instances, we know enough to act.

The Nation Needs a Comprehensive, Cohesive Policy Agenda Regarding Environmental Contaminants and Protection of Human Health.

Environmental health, including cancer risk, has been largely excluded from overall national policy on protecting and improving the health of Americans. It is more effective to prevent disease than to treat it, but cancer prevention efforts have focused narrowly on smoking, other lifestyle behaviors, and chemopreventive interventions. Scientific evidence on individual and multiple environmental exposure effects on disease initiation and outcomes, and consequent health system and societal costs, are not being adequately integrated into national policy decisions and strategies for disease prevention, health care access, and health system reform.

Children Are at Special Risk for Cancer Due to Environmental Contaminants and Should Be Protected.

Opportunities for eliminating or minimizing cancer-causing and cancer-promoting environmental exposures must be acted upon to protect all Americans, but especially children. They are at special risk due to their smaller body mass and rapid physical development, both of which magnify their vulnerability to known or suspected carcinogens, including radiation. Numerous environmental contaminants can cross the placental barrier; to a disturbing extent, babies are born "pre-polluted." Children also can be harmed by genetic or other damage resulting from environmental exposures sustained by the mother (and in some cases, the father). There is a critical lack of knowledge and appreciation of environmental threats to children's health and a severe shortage of researchers and clinicians trained in children's environmental health.

Continued Epidemiologic and Other Environmental Cancer Research Is Needed.

Available evidence on the level of potential harm and increased cancer risk from many environmental exposures is insufficient or equivocal. The Panel is particularly concerned that the impact, mechanisms of action, and potential interactions of some known and suspected carcinogens are poorly defined.

Meaningful measurement and assessment of the cancer risk associated with many environmental exposures are hampered by a lack of accurate measurement tools and methodologies. This is particularly true regarding cumulative exposure to specific established or possible carcinogens, gene-environment interactions, emerging technologies, and the effects of multiple agent exposures. Single-agent toxicity testing and reliance on animal testing are inadequate to address the backlog of untested chemicals already in use and the plethora of new chemicals introduced every year. Some high-throughput screening (HTS) technologies are available to enable testing of many chemicals and other contaminants simultaneously, but many remain to be developed to meet chemical testing needs. Support also is needed to develop methods for interpreting the wealth of data that HTS technologies generate. At this time, incentives to encourage development of this research are nearly non-existent.

Support for large, longitudinal studies to clarify the nature and magnitude of cancer risk attributable to environmental contaminants must continue. The capacity to collect biologic samples at the inception

of studies is essential; even if current technologies do not allow these samples to be fully utilized at this time, it must be assumed that such technologies will evolve and enable use of collected biosamples to provide essential study baseline data. Personal health data privacy issues that currently limit research access to data and biosamples will need to be addressed.

Cancer risk assessment also is hampered by lack of access to existing exposure data, especially for occupational/industrial exposures, and regarding levels of radon, asbestos, and other contaminants in schools and day care centers.

An Environmental Health Paradigm for Long-Latency Disease Is Needed.

Recognizing that results of laboratory and animal studies do not always predict human responses, an environmental health paradigm for long-latency diseases is needed to enable regulatory action based on compelling animal and *in vitro* evidence before cause and effect in humans has been proven.

Existing Regulations for Environmental Contaminants Need to Be Enforced and Updated; Stronger Regulation Is Needed.

Weak laws and regulations, inefficient enforcement, regulatory complexity, and fragmented authority allow avoidable exposures to known or suspected cancer-causing and cancer-promoting agents to continue and proliferate in the workplace and the community. Existing regulations, and the exposure assessments on which they are based, are outdated in most cases, and many known or suspected carcinogens are completely unregulated. Enforcement of most existing regulations is poor. In virtually all cases, regulations fail to take multiple exposures and exposure interactions into account. In addition, regulations for workplace environments are focused more on safety than on health.

Industry has exploited regulatory weaknesses, such as government's reactionary (rather than precautionary) approach to regulation. Likewise, industry has exploited government's use of an outdated methodology for assessing "attributable fractions" of the cancer burden due to specific environmental exposures. This methodology has been used effectively by industry to justify introducing untested chemicals into the environment.

Radiation Exposure from Medical Sources Is Underappreciated.

The use of radiation-emitting medical tests is growing rapidly. Efforts are needed to eliminate unnecessary testing and improve both equipment capability and operator skill to ensure that radiation doses are as low as reasonably achievable without sacrificing image or test data quality. At least one initiative is underway to improve and disseminate radiation reduction strategies and educate physicians, device manufacturers, their training staff, and others about radiation doses associated with specific tests. No mechanism currently exists to enable individuals to estimate their personal cumulative radiation exposure, which would help patients and physicians weigh the benefits and potential harm of contemplated imaging and nuclear medicine tests.

Medical Professionals Need to Consider Occupational and Environmental Factors When Diagnosing Patient Illness.

Physicians and other medical professionals ask infrequently about patient workplace and home environments when taking a medical history. Such information can be invaluable in discovering underlying causes of disease. Moreover, gathering this information would contribute substantially to the body of knowledge on environmental cancer risk.

Workers, Other Populations with Known Exposures, and the General Public Require Full Disclosure of Knowledge about Environmental Cancer Risks.

Individuals and communities are not being provided all available information about environmental exposures they have experienced, the cumulative effects of such exposures, and how to minimize harmful exposures. The disproportionate burden of exposure to known or suspected carcinogens experienced by specific populations (e.g., agricultural and chemical workers and their families, radiation-exposed groups such as uranium mine workers, nuclear industry workers, nuclear test site workers and "downwinders," residents of cancer "hot spots" or other contaminated areas) has not been fully acknowledged.

The Military Needs to Aggressively Address the Toxic Environmental Exposures It Has Caused.

Toxic materials produced for and used by the military have caused widespread air, soil, and water pollution across the United States and beyond our borders, including chemical and radiation contamination in and around current and former military installations, materiel production facilities, and mines. These contaminants, many of which may have serious long-term and latent effects including cancer, are a danger both to military personnel and civilians. Overall, the military has not responded adequately to health problems associated with its operations absent substantial pressure from those affected, advocacy groups, or the media. Of special concern, the U.S. has not met its obligation to provide for ongoing health needs of the people of the Republic of the Marshall Islands resulting from radiation exposures they received during U.S. nuclear weapons testing in the Pacific from 1946–1958.

Safer Alternatives to Many Currently Used Chemicals Are Urgently Needed.

The requisite knowledge and technologies exist to develop alternatives to many currently used chemical agents known or believed to cause or promote cancer. Many chemists require additional training to understand environmental hazards and reformulate products. Importantly, "green chemistry" alternative products themselves require longitudinal study to ensure that they do not pose unexpected health hazards.

The Panel believes that just as there are many opportunities for harmful environmental exposures, ample opportunities also exist to intervene in, ameliorate, and prevent environmental health hazards. Governments, industry, the academic and medical communities, and individuals all have untapped power to protect the health of current and future generations of Americans and reduce the national burden of cancer.

Policy, Research, and Program Recommendations

Based on its conclusions, the Panel recommends:

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
1. A precautionary, prevention-oriented approach should replace current reactionary approaches to environmental contaminants in which human harm must be proven before action is taken to reduce or eliminate exposure. Though not applicable in every instance, this approach should be the cornerstone of a new national cancer prevention strategy that emphasizes primary prevention, redirects accordingly both research and policy agendas, and sets tangible goals for reducing or eliminating toxic environmental exposures implicated in cancer causation. The proposed Kid Safe Chemicals Act introduced in the 110th Congress, or similar legislation, has the potential to be an important first step toward a precautionary chemicals management policy and regulatory approach to reducing environmental cancer risk. Optimally, it should shift the burden of proving safety to manufacturers prior to new chemical approval, in mandatory post-market studies for new and existing agents, and in renewal applications for chemical approval.	President/Administration Congress Environmental Protection Agency (EPA) Department of Labor (DOL)/ Occupational Safety and Health Administration (OSHA) Department of Health and Human Services (HHS): • Food and Drug Administration (FDA) • National Institutes of Health (NIH) Department of Agriculture (USDA) State governments Industry

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
2. A thorough new assessment of workplace chemical and other exposures is needed to quantify current health risks. Previous estimates of occupational cancer risk are outdated and should no longer be used by government or industry.	Congress National Academy of Science/ Institute of Medicine National Science Foundation (NSF) General Accountability Office Other multidisciplinary group appointed for this task HHS/National Institute for Occupational Safety and Health (NIOSH) DOL: • OSHA • Mine Safety and Health Administration (MSHA)
3. In large measure, adequate environmental health regulatory agencies and infrastructures already exist, but agencies responsible for promulgating and enforcing regulations related to environmental exposures are failing to carry out their responsibilities. The following are needed:	
• A more integrated, coordinated, and transparent system for promulgating and enforcing environmental contaminant policy and regulations, driven by science and free of political or industry influence, must be developed to protect public health.	EPA HHS/FDA USDA DOL: • OSHA • MSHA
• Better concordance of exposure measures and standards is needed to facilitate interagency and international regulatory policy and enforcement and to identify research needs.	HHS/National Institute of Environmental Health Services (NIEHS) EPA DOL/OSHA
• The United States should carefully consider the potential impact on consumers and commerce of the Globally Harmonized System for classifying carcinogens.	President/Administration Congress

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
• Information sharing among the public, researchers, regulatory agencies, industry, and other stakeholders must be a bedrock component of the environmental health regulatory system mission.	EPA DOL: • OSHA • MSHA HHS: • FDA • Center for Disease Control and Prevention (CDC) USDA Department of Defense (DoD) Department of Energy (DOE) Environmental and cancer research communities Industry Media
• Environmental and public health advocates should be included in developing the environmental cancer research and policy agendas and in information dissemination.	Advocates EPA HHS: • FDA • CDC DOE
4. Epidemiologic and hazard assessment research must be continued and strengthened in areas in which the evidence is unclear, especially research on workplace exposures, the impact of *in utero* and childhood exposures, and exposures that appear to have multigenerational effects. Current funding for federally supported occupational and environmental epidemiologic cancer research is inadequate.	Congress EPA HHS: • National Cancer Institute (NCI) • NIEHS • National Institute for Child Health and Human Development • NIOSH EPA NSF Nongovernmental research funders

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
5. Measurement tool development and exposure assessment research, including the development of new research models and endpoints, should be accelerated to enable better quantification of exposures at individual, occupational, and population levels.	
• High-throughput screening technologies and related data interpretation models should be developed and used to evaluate multiple exposures simultaneously. It may be possible to screen apparently similar suspect chemicals together and regulate these as a group as indicated by findings.	HHS • NIEHS • NIOSH NSF DoD/Applied Research Projects Agency Industry
• Methods for long-term monitoring and quantification of electromagnetic energy exposures related to cell phones and wireless technologies are urgently needed given the escalating use of these devices by larger and younger segments of the population and the higher radiofrequencies newer devices produce.	DOE HHS/NIOSH EPA National Council on Radiation Protection and Measurements (NCRP)
6. The cancer risk attributable to residential radon exposure has been clearly demonstrated and must be better addressed. The following are needed:	
• The Environmental Protection Agency (EPA) should consider lowering its current action level (4 pCi/L) for radon exposure, taking into account data on radon-related cancer risk developed since the existing action level was established.	EPA
• Public and health care provider education should be developed and broadly disseminated to raise awareness of radon-related cancer risk.	HHS Health care provider professional organizations Media
• Improved testing methods for residential radon exposure and better methods for assessing cumulative exposure should be developed. Tax deductions or other incentives should be implemented to encourage radon mitigation retrofitting of existing housing. Building code changes should be made to require radon reduction venting in new construction.	Industry Congress Internal Revenue Service State and local governments
• All schools, day care centers, and workplaces should be tested at regular intervals for radon. Radon level data must be made available to the public. Buildings found to have levels in excess of the EPA action level should be mitigated.	State and local governments

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
7. Actions must be taken to minimize radiation exposure from medical sources. Specifically:	
• Health care providers, radiology technicians, and the public must be informed about the extent of radiation exposure from commonly used imaging and nuclear medicine examinations and the potential health risks of these procedures. Referring physicians are responsible for discussing with the patient the balance of benefit and risk associated with each imaging or nuclear medicine procedure being recommended. An educational/ decision-making tool that considers each patient's cumulative lifetime radiation exposure should be developed to facilitate these provider-patient communications.	Physicians and other health care providers Health professional organizations Advocates Media HHS: • Agency for Healthcare Research and Quality • NCI
• The estimated effective radiation dose of all imaging and nuclear medicine tests performed should be a required element in patient records and should be a core data element in all electronic health records systems. In addition, patients should be assisted to reconstruct an estimate of the total medical radiation dose they have received.	Joint Commission for Accreditation of Healthcare Organizations (JCAHO) HHS: • FDA • Centers for Medicare and Medicaid Services (CMS) • CDC • Health Resources and Services Administration (HRSA) • Indian Health Service (IHS) • Office of the National Coordinator for Health Information Technology (ONCHIT) Department of Veterans Affairs (VA) DoD Physicians and other health care providers
• Radiation dose-lowering techniques must be implemented consistently and to the maximum extent feasible.	Physicians and other health care providers
• Inspection of radiation-emitting medical equipment and pharmaceuticals must become more stringent, and uniform credentialing of technicians who administer scans is needed.	JCAHO Radiation technologist professional organizations HHS/FDA

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
8. The unequal burden of exposure to known and suspected carcinogens must be addressed.	
• Individuals exposed to nuclear fallout and other nuclear contamination by biologically important radionuclides must be provided all available information on these exposures. A system must be developed to enable affected individuals to reconstruct and add radiation doses received so that they can adequately assess their cumulative exposure and potential health risks, including cancer.	DoD DOE Nuclear Regulatory Commission HHS/NCI VA NCRP
• The Advisory Committee on Energy-related Epidemiologic Research (ACERER) should be rechartered, or a similar body convened, to enable individuals exposed to nuclear testing fallout and other nuclear exposures to participate in policy making and other decisions that will affect their access to health care and compensation related to those exposures.	DOE
• Geographic areas and vulnerable populations (including but not limited to children, migrant and other farm workers, and residents of high-poverty areas and cancer "hot spots") should be studied to determine environmental influences on cancer risk; identified risks must be remediated to the maximum extent possible.	EPA HHS/NIEHS DoD USDA
• The U.S. Government should honor and make payments according to the judgment of the Marshall Islands Tribunal.	President/Administration Congress

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
9. Physicians and other medical personnel should routinely query patients about their previous and current workplace and home environments as part of the standard medical history. This information will increase the likelihood that environmental factors in cancer and other illnesses are considered and will strengthen the body of information on environmental exposures and disease. Data on workplace and home environmental history should be incorporated into existing and developing automated medical records systems.	Physicians and other health care providers HHS: • ONCHIT • NCI: Surveillance, Epidemiology, and End Results Program • CDC: National Program of Cancer Registries • CMS • HRSA • IHS DoD: TRICARE VA: Veterans Health Information System and Technology Architecture Private insurer patient databases
10. "Green chemistry" initiatives and research, including process redesign, should be pursued and supported more aggressively, but new products must be well-studied prior to and following their introduction into the environment and stringently regulated to ensure their short- and long-term safety.	HHS/NIEHS EPA NSF
11. Public health messages should be developed and disseminated to raise awareness of environmental cancer risks and encourage people to reduce or eliminate exposures whenever possible.	HHS: • FDA • CDC • HRSA • CMS USDA DOE Federal Communications Commission Advocates Media

* The Panel recognizes that entities other than those listed may have a vital role or interest in implementation of the recommendations.

What Individuals Can Do: Recommendations

Much remains to be learned about the effects of environmental exposures on cancer risk. Based on what is known, however, there is much that government and industry can do now to address environmental cancer risk. The Panel's recommendations in this regard are detailed above. At the same time, individuals can take important steps in their own lives to reduce their exposure to environmental elements that increase risk for cancer and other diseases. And collectively, individual small actions can drastically reduce the number and levels of environmental contaminants.

CHILDREN
1. It is vitally important to recognize that children are far more susceptible to damage from environmental carcinogens and endocrine-disrupting compounds than adults. To the extent possible, parents and child care providers should choose foods, house and garden products, play spaces, toys, medicines, and medical tests that will minimize children's exposure to toxics. Ideally, both mothers and fathers should avoid exposure to endocrine-disrupting chemicals and known or suspected carcinogens prior to a child's conception and throughout pregnancy and early life, when risk of damage is greatest.
CHEMICAL EXPOSURES
2. Individuals and families have many opportunities to reduce or eliminate chemical exposures. For example: • Family exposure to numerous occupational chemicals can be reduced by removing shoes before entering the home and washing work clothes separately from the other family laundry. • Filtering home tap or well water can decrease exposure to numerous known or suspected carcinogens and endocrine-disrupting chemicals. Unless the home water source is known to be contaminated, it is preferable to use filtered tap water instead of commercially bottled water. • Storing and carrying water in stainless steel, glass, or BPA- and phthalate-free containers will reduce exposure to endocrine-disrupting and other chemicals that may leach into water from plastics. This action also will decrease the need for plastic bottles, the manufacture of which produces toxic by-products, and reduce the need to dispose of and recycle plastic bottles. Similarly, microwaving food and beverages in ceramic or glass instead of plastic containers will reduce exposure to endocrine-disrupting chemicals that may leach into food when containers are heated.

- Exposure to pesticides can be decreased by choosing, to the extent possible, food grown without pesticides or chemical fertilizers and washing conventionally grown produce to remove residues. Similarly, exposure to antibiotics, growth hormones, and toxic run-off from livestock feed lots can be minimized by eating free-range meat raised without these medications if it is available. Avoiding or minimizing consumption of processed, charred, and well-done meats will reduce exposure to carcinogenic heterocyclic amines and polyaromatic hydrocarbons.
- Individuals can consult information sources such as the Household Products Database to help them make informed decisions about the products they buy and use.
- Properly disposing of pharmaceuticals, household chemicals, paints, and other materials will minimize drinking water and soil contamination. Individuals also can choose products made with non-toxic substances or environmentally safe chemicals. Similarly, reducing or ceasing landscaping pesticide and fertilizer use will help keep these chemicals from contaminating drinking water supplies.
- Turning off lights and electrical devices when not in use reduces exposure to petroleum combustion by-products because doing so reduces the need for electricity, much of which is generated using fossil fuels. Driving a fuel-efficient car, biking or walking when possible, or using public transportation also cuts the amount of toxic auto exhaust in the air.
- Individuals can reduce or eliminate exposure to secondhand tobacco smoke in the home, auto, and public places. Most counseling and medications to help smokers quit are covered by health insurance or available at little or no cost.

RADIATION

3. Adults and children can reduce their exposure to electromagnetic energy by wearing a headset when using a cell phone, texting instead of calling, and keeping calls brief.

4. It is advisable to periodically check home radon levels. Home buyers should conduct a radon test in any home they are considering purchasing.

5. To reduce exposure to radiation from medical sources, patients should discuss with their health care providers the need for medical tests or procedures that involve radiation exposure. Key considerations include personal history of radiation exposure, the expected benefit of the test, and alternative ways of obtaining the same information. In addition, to help limit cumulative medical radiation exposure, individuals can create a record of all imaging or nuclear medicine tests received and, if known, the estimated radiation dose for each test.

6. Adults and children can avoid overexposure to ultraviolet light by wearing protective clothing and sunscreens when outdoors and avoiding exposure when the sunlight is most intense.

SELF-ADVOCACY

7. Each person can become an active voice in his or her community. To a greater extent than many realize, individuals have the power to affect public policy by letting policymakers know that they strongly support environmental cancer research and measures that will reduce or remove from the environment toxics that are known or suspected carcinogens or endocrine-disrupting chemicals. Individuals also can influence industry by selecting non-toxic products and, where these do not exist, communicating with manufacturers and trade organizations about their desire for safer products.

Preface

Since its creation in 1971, the President's Cancer Panel (PCP, the Panel) has fulfilled its charge to monitor and appraise the development and execution of the National Cancer Program and report directly to the President of the United States regarding barriers or impediments to the fullest and most rapid execution of the Program. The Panel meets not less than four times per year and reports its findings annually or more frequently, as needed.

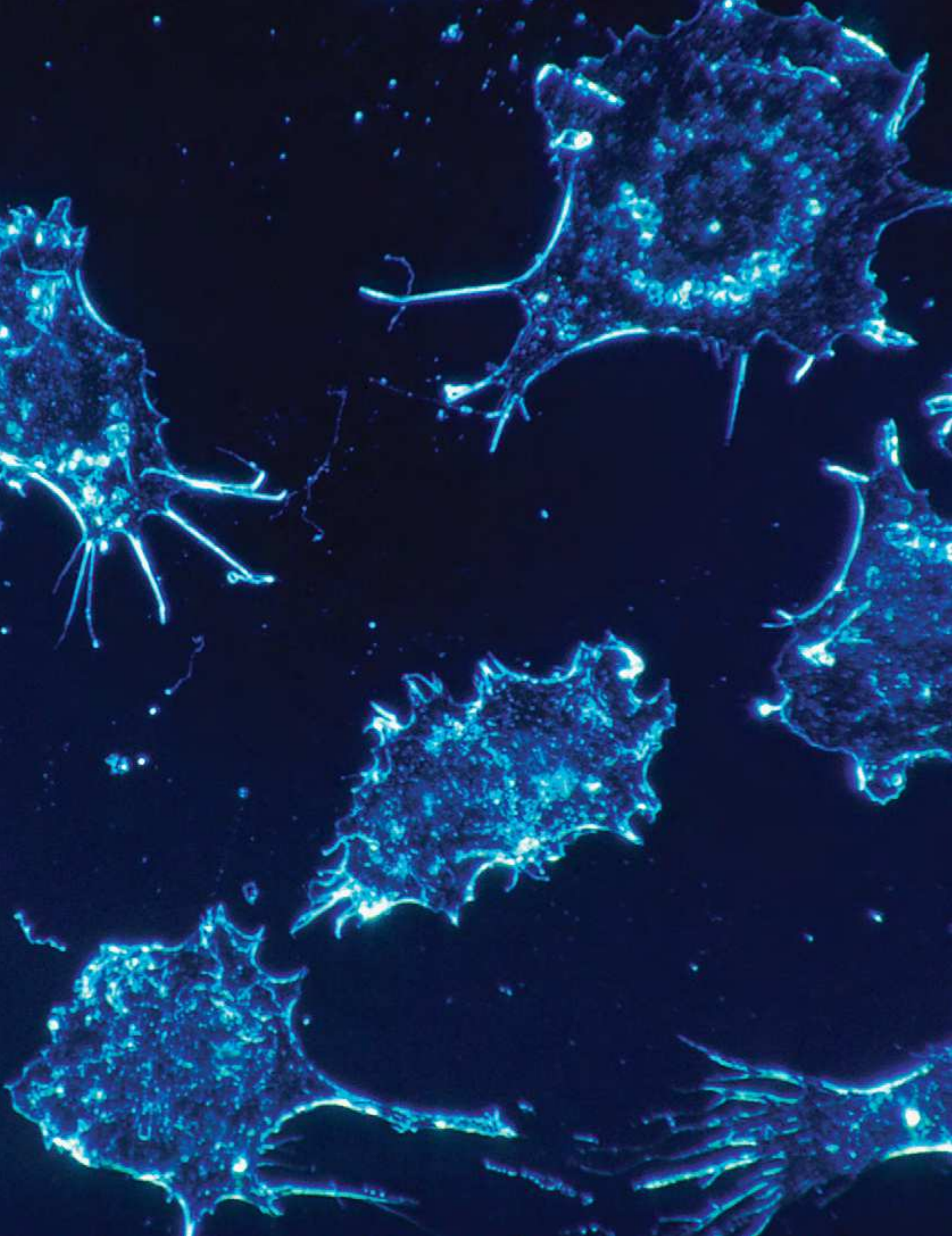
Over the past several years, the Panel has noted the growing body of research on increased cancer risks associated with various environmental contaminants. Additionally, in previous meeting series addressing other topics, issues concerning possible associations between environmental influences and risk for specific cancers have been raised. Further, public and governmental awareness of environmental influences on health has grown substantially. For these reasons, the Panel concluded that an exploration of the current understanding and emerging science regarding environmental cancer risk would be both informative and timely.

Four meetings were convened between September 2008 and January 2009. Each meeting, held on the dates and at the locations indicated below, focused principally on one aspect of environmental contaminants with known or suspected links to increased cancer risk:

September 16, 2008	Industrial and Occupational Exposures	East Brunswick, NJ
October 21, 2008	Agricultural Exposures	Indianapolis, IN
December 4, 2008	Indoor/Outdoor Air Pollution and Water Contamination	Charleston, SC
January 27, 2009	Nuclear Fallout, Electromagnetic Fields, and Radiation Exposure	Phoenix, AZ

The Panel received testimony from 45 experts from academia, government, industry, and the environmental and cancer advocacy communities, as well as from the public.

This report begins with an overview of the estimated cancer burden due to environmental exposures, biologic mechanisms that may be responsible for the effects of exposure to environmental contaminants, environmental cancer research and hazard assessment issues, and the current regulatory environment. Though not intended to be a complete evaluation of all sources and types of environmental contaminants, subsequent chapters describe the major sources of these contaminants and the known or suspected influence of selected substances on cancer risk. The Panel's conclusions, based on the testimony received and additional information gathered prior to and after the meetings, are followed by recommendations for assessing and mitigating cancer risk due to environmental factors. Appendices include a roster of meeting participants and other supplemental information.



PART 1

Overview

Despite modest overall decreases in cancer incidence and mortality, cancer continues to devastate—and in far too many cases end—the lives of Americans. In 2009, nearly 1.5 million new cases of cancer are expected to be diagnosed in the United States, and an estimated 562,000 Americans will die from this disease.[1] Approximately 41 percent of people in the U.S. will be diagnosed with cancer at some point in their lives, and about 21 percent of Americans will die from cancer.[2]

Apart from the incalculable suffering and personal loss cancer causes patients and their families, cancer also exacts a heavy economic toll on the nation. The National Institutes of Health (NIH) estimates that in 2009, cancer cost the nation $243.4 billion—$99 billion for direct medical costs, $19.6 billion for indirect morbidity costs (cost of lost productivity due to illness), and $124.8 billion for indirect mortality costs (cost of lost productivity due to premature death).[3]

The paragraphs below briefly describe our current understanding of environmentally induced cancer, biologic mechanisms by which environmental contaminants may increase cancer risk, environmental cancer research investments and needs, and key issues regarding the regulation of environmental pollutants.

Estimated Influence of Environmental Factors on Cancer in the United States

Though many important insights have yet to be achieved, we now understand better than ever before how human cancers develop, grow, and spread. Single-gene inherited cancer syndromes are believed to account for less than 5 percent of malignancies in the United States.[4] An unknown percentage of cancers develop due to normal endogenous (internal) processes. For example, cellular detoxification processes can produce oxygen radicals that damage DNA. Aging cells tend to make more errors in DNA replication than younger cells, and some DNA copying errors are inevitable due to the sheer volume of replication that occurs every day.

Other cancers develop as a result of exogenous (outside of the body) factors, some of which are controllable. It is not known exactly what percentage of all cancers either are initiated or promoted by an environmental trigger. Some exposures to an environmental

hazard occur as a single acute episode, but most often, individual or multiple harmful exposures take place over a period of weeks, months, years, or a lifetime. However, susceptibility to cancers resulting from environmental exposures may be inherited if a parent is exposed to a carcinogen that causes germ cell genetic changes, which subsequently are passed on to a child.[5]

...genes and environment interact in ways that are so complex that it's really not worth arguing in my mind about how much plays what role because... we cannot change our ancestors. So a rational place to begin a program of cancer prevention [is]... with the environment, and lifestyle is wound up in the environment.

SANDRA STEINGRABER
ITHACA COLLEGE

The widely quoted estimates of avoidable cancer deaths due to environmental factors developed by Doll and Peto in 1981[6] (and estimated in similar later studies using the same methodology[7,8]) are woefully out of date, given our current understanding of cancer initiation as a complex multifactorial, multistage process.[9] Subsequent to the 1981 publication, Sir Richard Doll recognized methodologic problems underlying the estimated fractions of the total cancer burden attributable to discrete, yet often complex factors (e.g., diet). Estimates of "attributable fractions" of the cancer burden due to occupation (approximately 4 percent), pollution (2 percent), industrial products (<1 percent), and medicines and medical procedures (1 percent) are now believed to underestimate significantly the true toll of cancer related to these exposures. Doll and Peto relied primarily on epidemiologic studies of workers in large industries and failed to include minorities, deaths among persons aged 65 and older, exposures in smaller workplaces, and the effects of indirect contact with carcinogens.

The greatest shortcoming of the Doll and Peto estimates, however, is that calculation of attributable fractions does not fully account for the fact that environmental contaminants interact with each other and that all avoidable causes of cancer are not known. Since the Doll and Peto estimates were published, environmental exposures have become more diverse and numerous. Perhaps most importantly, the impact of various exposures, whether individual, simultaneous, sequential, or cumulative over a lifetime, may not be simply additive. Instead, combinations of exposures may have synergistic effects that intensify or otherwise alter their impact compared with the effect of each contaminant alone.[10,11] In addition, we now recognize that critical periods of time exist across the life span (e.g., prenatal and early life, puberty) when individuals are particularly susceptible to damage from environmental contaminants. Moreover, a person's genetic make-up can significantly affect his or her susceptibility to the harmful effects of an environmental agent, and it also is becoming clear that some exposures can have effects across multiple generations.

Known or Suspected Mechanisms by Which Environmental Factors May Increase Cancer Risk

Exposure to environmental contaminants can result in harm to health because they may alter or interfere with a variety of biologic processes:

Hormone Production and Function

Many substances affect the production and function of hormones, which are crucial to normal growth and development, and to the maintenance of numerous biologic processes. For example, some synthetic chemicals and natural compounds act as weak estrogens in the human body. Among other effects, these substances appear to be contributing to earlier puberty and, therefore, to a longer period of estrogen exposure in women. Longer lifetime estrogen exposure is linked to higher risk of hormone-dependent cancers.[12] Male hormone

function also can be affected by these compounds. Known as endocrine-disrupting chemicals (EDCs), these substances typically are not listed as carcinogens by regulatory agencies, but the body of evidence linking EDCs to breast and other cancers is growing.[13–15]

Inflammation

The importance of inflammation as a contributor to or cause of numerous diseases (e.g., cardiovascular, certain digestive system diseases) is becoming increasingly understood. For example, it has long been known that the inflammation of lung tissue, caused by inhaling asbestos fibers, tobacco smoke, or fine particles in the air from diesel engine exhaust and industrial sources, is a major factor in lung and other respiratory tract cancers.[16]

DNA Damage

Some environmental exposures, particularly radiation, can damage DNA. Errors commonly occur when DNA is copied during cell division, but the cell has built-in mechanisms for identifying such errors and repairing them. If the damage is irreparable, the cell typically self-destructs. However, exposure to environmental carcinogens can result in more frequent DNA replication errors and can damage the cell's ability to identify and repair faulty DNA. This damaged DNA can result in gene mutations that permit or promote cancer development and can, in some cases, be passed on to subsequent generations.

Gene Suppression or Overexpression

Genes direct the initiation, moderation, or cessation of biologic processes, including cell growth and normal cell death. Numerous external influences, including environmental contaminants, can interfere with these processes by altering DNA structure without changing the underlying DNA sequences. Alterations such as these, referred to as epigenetic changes, can have significant effects on gene behavior.[17] Epigenetic changes may suppress gene expression (function) or cause gene overexpression. For instance, gene products that suppress tumor growth may not be produced, allowing individual tumor cells in the body to grow out of control, leading to cancer.

...low levels of exposure at a specific point in the development of an organism... could have really, really significant changes in ways that the classical idea about genetics would not predict.

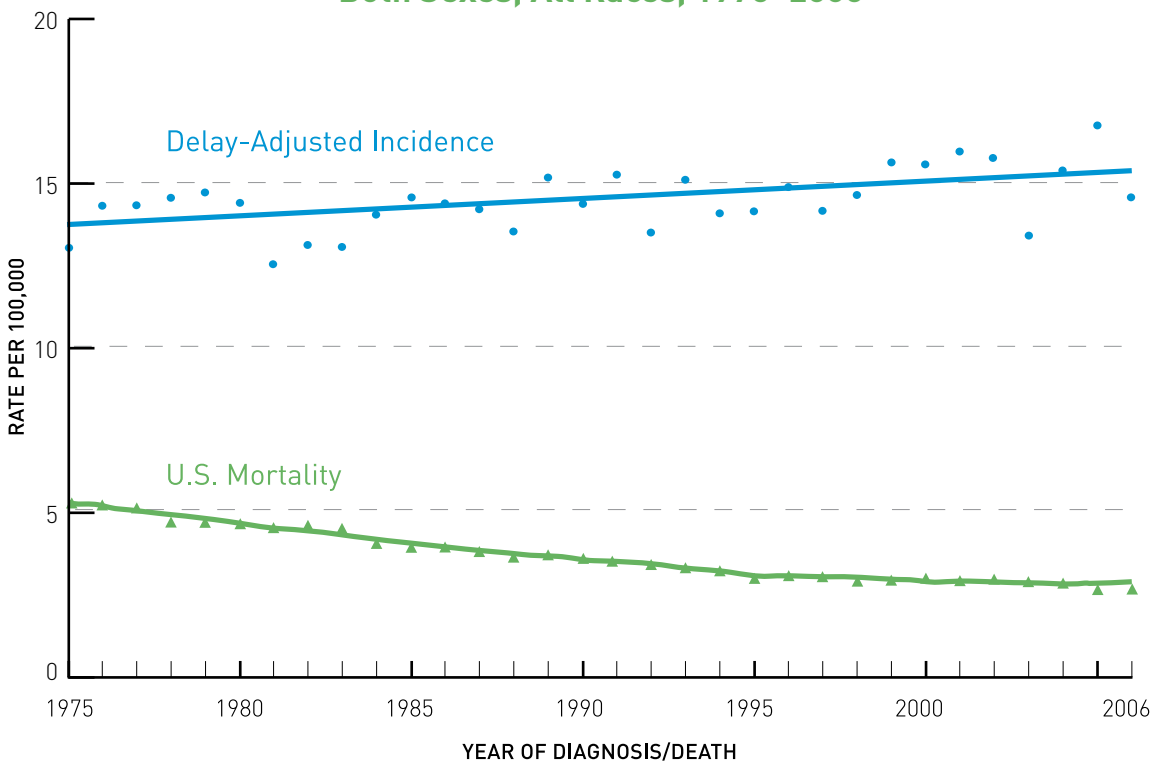
WILLIAM CHAMEIDES
DUKE UNIVERSITY

In addition, epigenetic inheritance[18] can occur, in which the behavior of genes in offspring is affected by the life experience (including exposure to environmental contaminants) of the parents. For example, from 1938 to 1971, thousands of pregnant women were prescribed diethylstilbestrol (DES), a drug intended to prevent miscarriage.[19] Some daughters born to these women (referred to as DES Daughters) have reproductive system malformations and have been predisposed to a rare type of vaginal and cervical cancer.[20] In some cases, epigenetic changes also may be passed on to future generations;[18] limited data[21,22] suggest that DES Granddaughters may have an increased risk for ovarian cancer.

Environmental contaminants can damage immune system and other types of cells so that they cannot function normally to maintain and protect the body. Cells interact continually with those around them, receiving and sending biochemical and bioelectric signals that maintain normal biologic functions and equilibrium.[23] If these signaling processes are altered or interrupted, the intracellular and/or intercellular (micro) environments may change such that tumor cells are able to proliferate. These problems may result from epigenetic changes.

Figure 1

SEER Delay-Adjusted Incidence and U.S. Mortality All Childhood Cancers, Under 20 Years of Age Both Sexes, All Races, 1975–2006



Source: SEER 9 areas and U.S. Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention. Rates are age-adjusted to the 2000 U.S. Std Population (19 age groups—Census P25-1103).

Regression lines are calculated using the Joinpoint Regression Program Version 3.3.1, April 2008, National Cancer Institute.

Delay-adjusted incidence is an algorithm used to estimate incidence if it were unaffected by reporting delays.

The Special Vulnerabilities of Children

Infants, children, and adolescents comprise 40 percent of the world's population.[24] In crucial respects (e.g., ability to control their environment, ability to care for and defend themselves), they are the most vulnerable group. Mortality from childhood cancers has dropped dramatically since 1975 due to vastly improved treatments that have resulted from high levels of participation by children in cancer treatment clinical trials. Yet over the same period (1975–2006), cancer incidence in U.S. children under 20 years of age has increased (Figure 1).

...epidemiology in the context of environmental epidemiology and occupational epidemiology, but particularly environmental epidemiology, is a very blunt tool. It's an area where we need a fine scalpel but we have just this jack hammer.

LYNN KATZ CHERRY
INDIANA TOXIC ACTION

The causes of this increase are not known, but as a meeting presenter emphasized, the changes have been too rapid to be of genetic origin. Nor can these increases be explained by the advent of better diagnostic techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). Increased incidence due to better diagnosis might be expected to cause a one-time spike in rates, but not the steady increases that have occurred in these cancers over a 30-year span. The extent to which environmental exposures are responsible for this trend remains to be determined.

Children are exposed to toxic and carcinogenic chemicals and radiation through the air they breathe, the food and water they consume, medications they are given, and the environment in which they live, including their homes, schools, day care centers, and even the motor vehicles in which they ride.[25] Pound for pound, children take in more food, water, air, and other environmental substances than adults. Children also can be exposed to toxins *in utero* via placental transfer and/or after birth via breast milk. Tests of umbilical cord blood[26] found traces of nearly 300 pollutants in newborns' bodies, such as chemicals used in fast-food packaging, flame retardants present in household dust, and pesticides.

An analysis by the National Academy of Sciences[27] found that children are particularly vulnerable to environmental contaminants for several reasons. Due to their smaller size, children's exposures to toxics are disproportionately large compared with adults. Because their metabolic pathways are immature (particularly during fetal development and in the first months after birth), they are slower to metabolize, detoxify, and excrete many environmental chemicals. As a result, toxins remain active in their bodies for a longer period of time than would be the case in adults. In addition, children have lower levels of some chemical-binding proteins, allowing more of a toxic agent to reach various organs, and their blood-brain barrier is more porous than that of adults, allowing greater chemical exposures to the developing brain. Children's bodies also are less able to repair damage due to toxic exposures, and the complex processes that take place during the rapid growth and development of children's nervous, respiratory, immune, reproductive, and other organ systems are easily disrupted.

Children have many more years of life ahead of them than do adults—more time in which to be exposed to environmental toxics and time to develop diseases (including cancer) with long latency periods initiated by early exposures. At this time, little is known about interactions among multiple exposures over time, but many exposures to environmental contaminants are cumulative and some may have intergenerational effects.

Environmental Cancer Research

Research on environmental causes of cancer has been limited by low priority and inadequate funding. As a result, the cadre of environmental oncologists is relatively small, and the consequences of cumulative lifetime exposure to known carcinogens and the interaction of specific environmental contaminants remain largely unstudied. There is a lack of emphasis on environmental research as a route to primary cancer prevention, particularly compared with research emphases on genetic and molecular mechanisms in cancer. At the National Cancer Institute (NCI), the Fiscal Year (FY) 2008 budget for occupational and environmental carcinogenesis and environmental epidemiology (intramural and extramural combined) comprised no more than 14 percent of NCI's nearly $4.83 billion budget.[28]

Unfortunately, while budgets have waxed and waned on the federal level, a consistent finding, I would say, is that occupational and environmental exposures have been under addressed.

ELIZABETH FONTHAM
LOUISIANA STATE UNIVERSITY

At the National Institute for Environmental Health Sciences (NIEHS), funding for cancer-related environmental research has remained flat since FY 1999 at approximately 28 percent of total appropriations, excluding funding related to Superfund sites. Superfund is the Federal government program to identify and clean up the nation's worst uncontrolled hazardous waste sites.[29] NIEHS receives funding specifically to conduct research on health effects of hazardous substances that aids in Superfund assessment and clean-up decisions.[30]

Studying these complex [gene-environment interactions] takes large multicenter studies that are costly and they need to be a national priority. We need to better study these relationships so that we can come up with better prevention efforts.

JOHN VENA
UNIVERSITY OF GEORGIA

NIEHS and NCI recently published a Request for Applications for the Breast Cancer and the Environment Research Program to support parallel ongoing investigations and new laboratory and epidemiologic studies of environmental influences during windows of susceptibility on breast cancer risk.[31]

Table 1

The 12 Principles of Green Chemistry

- Prevent waste that requires treatment or clean-up.
- Design chemicals and products to be fully effective but have little or no toxicity.
- Develop less hazardous ways to synthesize chemicals.
- Use renewable raw materials.
- Use catalysts to make chemicals instead of reagents that create more waste.
- Avoid chemical derivatives.
- Reduce wasted atoms.
- Avoid using solvents whenever possible or use innocuous solvents.
- Increase energy efficiency by running chemical reactions at ambient temperatures.
- Design chemicals to break down after use.
- Monitor for by-products in real time.
- Minimize the potential for chemical accidents.

Sources: U.S. Environmental Protection Agency. Twelve principles of green chemistry [Internet]. [cited 2010 Mar 12] Available from: http://www.epa.gov/greenchemistry/pubs/principles.html. Adapted from: Anastas P, Warner J. Green chemistry: theory and practice. New York: Oxford University Press; 1998.

Some additional funding for environmental carcinogenesis research is available outside of the Federal government. For example, in FY 2007–2008, American Cancer Society funding for environmental carcinogenesis totaled nearly $3.8 million.[32]

To address the many gaps in knowledge about the relationship between various environmental contaminants and human cancer, it has been suggested that academic centers for environmental oncology research and policy be established.[33] These cross-disciplinary centers would focus more attention and resources on primary cancer prevention, bringing basic (including genomic, proteomic, metabolomic, and other biomarker research) and epidemiologic sciences to bear to identify underlying causes of cancer incidence and progression as they relate to environmental stimuli. These centers also could develop better measurement tools and interventions to improve cancer prevention and develop policy recommendations based on research findings. Moreover, greater priority and improved funding for environmental cancer research could be expected to attract young researchers to this field.

Green Chemistry

Speakers emphasized the need for "green chemistry" research to identify alternative ways of obtaining desired social good without contaminating the environment, including accelerating initiatives to develop environmentally safe substitutes for harmful chemicals and manufacturing processes. The principles of green chemistry were defined more than a decade ago (see Table 1).

Due to growing public concern about the bioaccumulation of environmental chemicals (also reflected in retailers' new interest in environmentally safer products), some companies are devoting more resources to developing non-toxic alternatives to existing products.[34,35] However, many chemists lack training in understanding environmental

hazards and how to develop safer alternatives; they also face industry barriers to change.[35]

Research support for green chemistry is limited. At the Federal level, the Environmental Protection Agency (EPA) sponsors some green chemistry research through grants and fellowships, the Small Business Innovation Research program, and sustainable technologies research at its National Center for Environmental Research. EPA also has a program of awards to recognize companies and individuals for innovative green chemistry technologies. The National Science Foundation (NSF) supports a Science and Technology Center for Environmentally Responsible Solvents and Processes, based at the University of North Carolina-Chapel Hill.[36] Its mission is to support multidisciplinary fundamental research to identify and enable sustainable processes and products using carbon dioxide-related technology. In addition to research, the Center supports educational and information exchange initiatives. Some NSF green research is conducted jointly with EPA.[37]

Green chemistry initiatives are gaining momentum at the state level. For example, Michigan enacted the Michigan Green Chemistry Directive[38] in 2006 to support research and development for non-toxic chemicals and encourage the use of chemical products and technologies that reduce or eliminate hazardous substances during their design, manufacture, and use. Among other activities, the initiative also supports expanded education and training in green chemistry for chemists and chemical engineers in the state, including through industry partnerships.

A 2008 report[39] by the California Environmental Protection Agency (Cal/EPA) outlines a plan to give consumers, manufacturers, and retailers new ways to assess the dangers of common chemicals that people use every day. Manufacturers and suppliers would be required to disclose all of the chemicals in products sold in the state; the data would be published in an online database. A companion database would contain all known information on chemical hazards, enabling consumers to determine whether to expose themselves or their families to specific products. This proposed initiative is similar to the Household Products Database maintained by the National Library of Medicine at NIH.[40] Other recommendations in the Cal/EPA report call for developing educational programs to encourage green chemistry innovation and requiring manufacturers to find ways to make things more safely and with little or no waste that requires environmental clean-up.

...a simple way of thinking about moving to a healthy and sustainable world is that it requires green energy and green chemistry and green products.

MICHAEL LERNER
COMMONWEAL

Environmental Exposure Measurement, Methodologic, Assessment, and Classification Issues Affecting Research and Regulation

Efforts to identify and control environmental exposures that raise cancer risk, including both single agents and combinations of exposures, have been complicated and compromised by the use of different measures, standards, assessment processes, and classification schemes across agencies in the U.S. and among nations; a lack of effective measurement methods and tools; delay in adopting newer technologies; inadequate computational models; and weak, flawed, or uncorroborated studies.

Reference Dose

Standards (exposure limits) are established based on the estimated effect of a toxic agent on a person with specified characteristics. This benchmark dosage is known as the reference dose. The traditional approach to determining the reference dose is based on the assumption that "the dose makes the poison."[41] To find the reference dose, several different dosages of a substance are tested on laboratory animals. Starting at the highest dose, the toxicologist continues to lower doses until effects are no longer detectable (i.e., the dose at which experimental animals no longer differ from controls). This dose, called the "no observed adverse effect level" (NOAEL), is considered the highest dose that poses an acceptable risk. The NOAEL is then adjusted for a series of safety factors to determine the final reference dose. Once the NOAEL is established for a substance, testing at lower doses is seldom conducted, and very low-dose effects are unlikely to be detected.

A key underpinning of realistic reference dose establishment is appropriate characterization of the population to which the reference dose applies. For example, reference doses for radiation exposures have long been based on their assessed impact on a "Reference Man"[42]—a hypothetical male, 5'7" tall, weighing 157 pounds, who is "Western European or North American in habitat and custom." This standard human was created by the International Commission on Radiological Protection (ICRP) in 1975. Such an individual is representative of only a very small percentage of the current and future populations of the United States. Reference Man certainly is of questionable relevance to women (who are now known to face a risk approximately 50 percent higher than Reference Man from the same radiation dose[43,44]), to people who are not "Western European or North American in habitat and custom," and those who are substantially smaller or larger than Reference Man. In particular, this standard does not address growing concern about radiation exposures experienced *in utero* and by infants and children. Because of their smaller body mass, thinner bones, and rapid physical development, the effect of radiation exposures that may not harm

adults may be amplified several-fold to a level that increases cancer risk in children. EPA maintains that it moved away from using Reference Man as a basis for estimating radiation doses around 1990, but neither EPA nor the Nuclear Regulatory Commission has yet established new parameters more reflective of the population.[45]

Diversity in U.S. Toxicant Standards

The U.S. does not use most of the international measures, standards, or classification structures for environmental toxins that have broad acceptance in most other countries. Instead, U.S. agencies have developed their own metrics and systems for quantifying environmental exposures, with standards that often are less stringent than international equivalents. With a global scientific community, multinational employers, and a worldwide marketplace, these differences increase the difficulty of comparing research findings and conducting international commerce.

In addition, more than one U.S. agency may be responsible for measuring and setting exposure limits for the same environmental toxics and may do so using differing metrics. For example, both EPA and the U.S. Geological Survey (USGS) measure contaminants in drinking water; EPA determines Maximum Contaminant Levels, or MCLs, while USGS assigns Health-Based Screening Levels (HBSLs).[46]

Professional groups also may develop metrics and standards. In some instances, these privately developed standards are based on data more current than that used by government agencies. Public and private organizations may elect to adopt the privately generated standards rather than those developed by government. Occupational Exposure Limits (OELs) that apply to U.S. workers exemplify this situation. Several organizations are involved in protecting worker health, each setting a different type of OEL with a distinct method and purpose. The primary organizations involved in OEL-setting are the American Conference of Governmental Industrial Hygienists (ACGIH), the Occupational Safety and Health Administration (OSHA), and the National Institute for Occupational Safety and Health (NIOSH). ACGIH is a non-governmental organization of industrial hygiene professionals[47] that sets Threshold Limit Values (TLVs), which are levels that will produce no adverse health effect in nearly all workers with repeated daily exposure. ACGIH also establishes Biological Exposure Indices (BEIs) that set maximum levels of chemical concentrations in biological tissues and fluids. TLVs and BEIs are health guidelines based on ACGIH committee review of recent scientific literature. TLVs and BEIs do not consider economic or technical feasibility issues associated with meeting the standards and do not have the force of law.[48]

...OSHA standards are feasibility standards. They are not public health standards.

JEANNE MAGER STELLMAN
SUNY-DOWNSTATE MEDICAL CENTER

Both NIOSH and OSHA were established in 1970 by the Occupational Safety and Health (OSH) Act (P.L. 91-596). They have a shared mission to "assure safe and healthful working conditions for working men and women."[49,50] NIOSH, part of the U.S. Department of Health and Human Services (DHHS), is a research agency charged to generate new knowledge in occupational health and safety. NIOSH develops Recommended Exposure Limits (RELs) that do not have the force of law, but are considered by OSHA as it establishes Permissible Exposure Limits (PELs) for toxic substances.[49] OSHA, part of the U.S. Department of Labor, is a regulatory agency with the power to set standards and conduct workplace inspections.[50] OSHA PELs are informed by health sciences, but compliance must be economically and technologically feasible.[51] When OSHA was established, it

adopted the ACGIH TLVs from 1968 as PELs. Less than two dozen of these PELs have been updated since that time.[52] NIOSH RELs were last updated in 2005.

We need research methods development. We need it in epidemiology as well as in the laboratory, and that needs to be funded...

ELIZABETH FONTHAM
LOUISIANA STATE UNIVERSITY

In addition to granting OSHA authority to establish PELs, the OSH Act provided a mechanism for unions to petition OSHA to promulgate rulemaking on harmful worker exposures.[50] In 1973, the Oil, Chemical, and Atomic Workers Union, in conjunction with the Public Citizen Health Research Group, petitioned OSHA for an emergency temporary standard on certain well established carcinogens.[53] In response, OSHA developed the 13 Carcinogens Standard that did not lower exposure limits, but added requirements for increased worker safety controls in workplaces where the 13 chemicals are used.[54]

Despite the stricter nature of TLVs and their lack of legal authority, they have become the accepted standard of the industrial hygiene industry. Many large corporations, all branches of the U.S. military, and many other nations use the most recent ACGIH TLVs as OEL benchmarks.[55]

Research Methodology and Data Collection Issues

In addition to measurement and standard-setting issues, environmental and occupational cancer research and assessment have suffered from methodologic and data collection weaknesses. For example, an important weakness of occupational cancer research to date has been the failure to adequately include women's exposures in traditional and unpaid labor settings or their growing participation in the paid workforce.[56] In addition, information on occupational history and work and home environments is not collected routinely as part of the medical history by primary care and most other medical professionals.[57] These data have the potential to improve diagnosis and treatment, and would capture crucial information researchers need to study the impact of environmental exposures over time. Difficulties in obtaining health department records or other data also have been barriers to population-based state or regional studies of exposures.[58]

In an effort to expand the robustness and accessibility of environmental health data, EPA launched the National Environmental Public Health Tracking Network[59] in 2009. The network is intended to build on CDC's existing state-based tracking system to create a system of integrated health, exposure, and hazard data and other information from a variety of national, state, and city sources. Data are being collected on a variety of health conditions including cancer, and the database will include information on home environments, outdoor air, and water. It will be possible to generate maps, charts, and tables on data subsets of interest to governments, researchers, and the public.

In 1996, NIOSH convened a group of experts from academia, business, labor, and government to identify the gaps in occupational cancer research methods.[60] The group's recommendations for strengthening research methods, which became part of NIOSH's National Occupational Research Agenda, focused on four broad areas: identification of occupational carcinogens, design of epidemiologic studies, risk assessment, and primary and secondary prevention (see Appendix B).

The prospective National Children's Study (NCS)[61] is intended to address many of the weaknesses of environmental cancer research to date. Though it was authorized under the Children's Health Act of 2000,[62]

recruitment for the study did not begin until January 2009. Administered by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the NCS will follow more than 100,000 children, representative of all babies born in the U.S., from conception to age 21 years. During that time, environmental exposures will be assessed through multiple evaluations of the external environment and through measurements of biomarkers at predetermined intervals throughout pregnancy and childhood. A genetic evaluation of each child will provide information on individual susceptibilities. To increase the power of the study to detect environmental causes of childhood cancer, NICHD will collaborate with the International Childhood Cancer Cohort Consortium.[63] The Consortium is comprised of researchers conducting 11 infant/child cohort studies on four continents. The studies together represent approximately 700,000 children.

Toxicity Testing Methods

Current toxicity testing relies heavily on animal studies. One speaker at the Panel's meetings stated that a shortcoming of most animal toxicity testing is that chemicals are administered to experimental animals in their adolescence; they later are sacrificed at a point in life corresponding to a human age of 60–65 years. This approach fails to capture the impacts of early exposures and misses the late effects of such exposures.[64] Lifetime toxicity studies provide an alternative approach to better answer questions about early exposures and latent effects. Chemicals are administered to animals *in utero* or shortly after birth, and the animals are followed over their entire natural life span. Some lifetime toxicity studies[65] are being done and are demonstrating that early exposures are significantly more likely to cause cancer than similar exposures in adult life. These studies have strong potential for improving understanding and prevention of childhood cancer and may provide insight into adult cancers related to early exposures.

We need ways to carry out surveillance to watch for surprises and probably as we look to the future and think about new cohorts we need to think about how to do them efficiently; for example, using administrative databases.

JONATHAN SAMET
UNIVERSITY OF SOUTHERN CALIFORNIA

Our science looks at a substance-by-substance exposure and doesn't take into account the multitude of exposures we experience in daily life. If we did, it might change our risk paradigm. The potential risks associated with extremely low-level exposure may be underestimated or missed entirely.

HEATHER LOGAN
CANADIAN CANCER SOCIETY

However, a majority of scientists in the fields of risk assessment and toxicology acknowledge that long-term, high-dose exposure regimens typically used for animal models yield results that may not be applicable to typical human exposures.[66] The need to find better and faster ways of characterizing the possible toxicity of chemicals and other potentially harmful substances is widely recognized. In addition, the cost and ethical considerations of animal testing increasingly are being questioned.

Some believe that eliminating certain animal tests with negligible predictive value beyond the battery of tests already required by regulatory agencies could help reduce the use of animals without compromising knowledge about the toxicity of specific substances.[67]

A 2007 National Research Council report[68] called for collaborative efforts across the toxicology community to rely less on animal studies and more on *in vitro* tests using human cells and cellular components, and for improvements in dose-response research to better predict toxicity at exposures that humans may encounter. In 2008, NIH and EPA signed a 5-year Memorandum of Understanding to leverage the experimental toxicology expertise of the National Toxicology Program at NIEHS, high-throughput technologies at the NIH Chemical Genomics Center, and the computational toxicology capabilities at EPA's National Center for Computational Toxicology.[69] This nascent collaboration, called Tox21,[70] has the capacity to shift the toxicity testing paradigm away from reliance on animal studies and toward automated, simultaneous, multi-agent screening. These new approaches will have to be validated, however—a process that could take many years. In addition to the new technologies themselves, it also will be necessary to invest in research to develop approaches to interpreting the large volume of data that will emerge from the new testing methods.[71]

We are not creating a sustainable society in this country if we continue to bring chemicals to market that are almost untested, disseminate them widely in consumer products, and then wait decades to take action only after people have become sick. It's just not wise.

PHILIP LANDRIGAN
MOUNT SINAI SCHOOL OF MEDICINE

In Europe, activities similar to Tox21 are underway.[67] The European Commission (EC) announced a new program to make chemical exposure studies more predictive while using fewer animals. Critics of the EC's conservative approach to chemical management believe that compliance with its requirement for retrospective testing of chemicals being marketed in the European Union (EU) member states will require 20 times more animals and cost 6 times as much as previously estimated.[72] The new program will fund researchers with expertise in areas not widely used in traditional toxicology who will develop methods for reliably generating other types of human cells from stem cells, develop cellular models that simulate human organs, employ systems biology approaches, and apply computational modeling to new testing technologies.[67] The European consortium of cosmetics, toiletry, and perfumery industries is matching EC funds for the program. This support is motivated in part by the requirement in the 2003 amendment to the 1976 cosmetics directive to phase out all animal testing of cosmetic ingredients by 2013.[67]

Assessment and Classification of Environmental Carcinogens

As new research evidence accumulates on specific potentially carcinogenic or other harmful substances and exposure conditions, the data are evaluated through formal assessment processes and the agent or exposure setting is classified as to its danger to human health. These classifications often provide the impetus for regulatory decisions.

Organizations That Support Environmental Exposure Assessment

In addition to sponsoring or conducting research on environmental exposures, some Federal agencies also develop recommendations and guidelines on which regulation and policy may be based. NCI, NIEHS, and NIOSH, for example, evaluate risk levels (e.g., tobacco smoke, radiation effects, air and water quality, worker exposures to specific chemicals) and offer recommendations for protecting human

health. However, these agencies cannot develop or enforce regulations. Studies of environmental exposures and related guidelines also come from academic and other independent research funded by foundations, advocacy organizations, and other non-governmental entities.

Similarly, several international agencies study and provide guidance for policy development on environmental cancer issues. The World Health Organization (WHO) reviews existing evidence and takes positions or develops guidelines on a wide range of health issues, including environmentally induced cancer. The International Atomic Energy Agency (IAEA)[73] assesses radiation safety issues and provides expertise on radiation medicine and technologies, including patient protection from excess radiation. Among other activities, ICRP[74] develops reference dose data and recommendations for protection against excess exposure to ionizing radiation. WHO, IAEA, and ICRP are not regulatory bodies, but their assessments and guidance are used by regulators and the scientific community worldwide.

Like IAEA and ICRP, the International Agency for Research on Cancer (IARC),[75] an agency of WHO, is not a regulatory body. The agency coordinates and conducts research on the causes of human cancer and the mechanisms of carcinogenesis, and develops strategies for cancer prevention and control. IARC's monographs on carcinogenesis, considered the "gold standard" in evaluating evidence on cancer causation, are used by countries around the world. To guide its assessment and classification of potential carcinogens, IARC defined criteria (summarized in Table 2) for confirming or refuting whether exposure to a specific chemical, radiation source, or other agent causes cancer.[76]

Table 2

IARC Criteria for Assessing Cancer Causation Due to Environmental Exposures

- The link or association between the exposure and cancer is strong.
- The risk of cancer increases with more exposure to the agent.
- Multiple studies by different investigators with different groups of people yield the same finding.
- The exposure to the agent came before the cancer.
- There is a plausible biological explanation for how the agent would cause the cancer.
- The link is specific, and the agent causes a specific type of cancer.
- The link is consistent with what is known from other studies.

Sources: International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans—preamble. Lyon, France: IARC; 2006, and Emanuel EJ. Will your cell phone kill you? The New Republic. 2008 April 9.

Classification of Potential Carcinogens

Several U.S., European, and international systems exist for classifying the carcinogenic potential of specific environmental and workplace exposures. Table 3 arrays the classification schemes adopted by selected agencies. Though other classification schema exist, the table illustrates the diversity in how potential carcinogens are evaluated and classified. The terminology used by these various agencies in some cases is nearly identical, but the evidence required to assign a chemical or other agent to a particular category may differ substantially (see Appendix C for detailed definitions and evidence requirements). Thus, a toxic may be judged clearly carcinogenic to humans under one classification system, while another may classify the same substance a probable or likely carcinogen. Or, a chemical may be assigned to similarly named categories under two different systems (e.g., probably carcinogenic/likely carcinogenic), but the levels of evidence required for that classification may differ under each system.

Table 3

Selected Carcinogen Classification Systems*

EUROPE	INTERNATIONAL		UNITED STATES		
EU	**GHS****	**IARC**	**ACGIH**	**EPA**	**NTP**
Category 1: Substances known to be carcinogenic to man	**Category 1, Subcategory 1A**: Known Human Carcinogen	**Group 1**: Carcinogenic to Humans	**A1**: Confirmed Human Carcinogen	Carcinogenic to Humans	Known to Be Human Carcinogen
Category 2: Substances which should be regarded as if they are carcinogenic to man	**Category 1, Subcategory 1B**: Presumed Human Carcinogen	**Group 2A**: Probably Carcinogenic to Humans	**A2**: Suspected Human Carcinogen	Likely to Be Carcinogenic to Humans	Reasonably Anticipated to Be Carcinogenic
Category 3: Substances which cause concern for man owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment	**Category 2**: Suspected Carcinogen	**Group 2B**: Possibly Carcinogenic to Humans	**A3**: Animal Carcinogen	Suggestive Evidence of Carcinogenic Potential	
		Group 3: Not Classifiable as to Carcinogenicity to Humans	**A4**: Not Classified as a Human Carcinogen	Inadequate Information to Assess Carcinogenic Potential	
		Group 4: Probably Not Carcinogenic to Humans	**A5**: Not Suspected as a Human Carcinogen	Not Likely to Be Carcinogenic to Humans	

* Carcinogen categories are not equivalent across systems. See Appendix C for definitions and evidence requirements.

** Under development.

EU–European Union; GHS–Globally Harmonized System; IARC–International Agency for Research on Cancer; ACGIH–American College of Governmental Industrial Hygienists; EPA–Environmental Protection Agency; NTP–National Toxicology Program

Sources:

U.S. Department of Health and Human Services. Listing criteria. [Internet] National Toxicology Program [cited 2009 July 1] Available from: http://ntp.niehs.nih.gov/?objectid=47B37760-F1F6-975E-7C15022B9C93B5A6.

International Agency for Research on Cancer. Complete list of agents evaluated and their classification. [Internet; cited 2009 August 30] Available from: http://monographs.iarc.fr/ENG/Classification/index.php.

Duffus JH, Nordberg M, Templeton DM. IUPAC glossary of terms used in toxicology, second edition, annex III: classification of carcinogenicity. Pure and Applied Chemistry. 2007;79(7):1153-1344.

These differences may lead to different regulatory policies that may affect worker and public safety as well as international commerce.

Considerable differences also exist in the number of agents that have been classified using each system, though in all cases the number is small compared to the tens of thousands of chemicals and other potentially harmful substances in use. For example, the U.S. National Toxicology Program's (NTP) most recent Report on Carcinogens[77] lists 58 agents as known human carcinogens and classifies another 188 agents as "reasonably anticipated to be human carcinogens." As of April 2009, IARC had evaluated nearly 950 agents; of these, 108 were classified as carcinogenic to humans, 63 were identified as probably carcinogenic to humans, and 248 were deemed possibly carcinogenic to humans. However, 515 agents could not be classified as to their carcinogenicity due to lack of evidence or insufficient high-quality evidence.[78]

An initiative is underway to address the safety, health, and commercial problems created by multiple chemical classification systems. Though substantially less robust than some existing classifications (particularly IARC and ACGIH), a Globally Harmonized System (GHS)[79] is being developed under the leadership of the United Nations to standardize chemical classification, assessment processes, and labeling worldwide. The goal is to provide uniform information and protection to those who would be exposed to a given chemical and to facilitate trade. Companies would only have to submit product information for classification once for all authorities that implement GHS. Under GHS, the burden of proving chemical safety will be shifted to industry. Nations around the world are in various stages of considering or implementing GHS. In the U.S., EPA, the Consumer Product Safety Commission (CPSC), OSHA, and the Department of Transportation have formed an interagency working group to coordinate U.S. government participation in GHS activities. The State Department and other agencies also will be involved as appropriate. It is likely to take at least a few years before a substantial number of countries adopt GHS.

Comprehensive Assessment of Occupational and Environmental Exposures

The preceding sections have discussed assessment in the context of evaluating evidence for the carcinogenicity of specific agents or exposure settings. But exposure assessment also is needed more broadly to evaluate cancer risk associated with workplace or environmental exposures in the aggregate. In the U.S., most available exposure assessments are badly outdated. A comprehensive assessment of the extent of all workplace exposures, for example, has not been conducted since the flawed Doll and Peto estimates published in 1981.[6] Although OSHA's mission is to ensure that workplace environments are safe, it does not conduct a comprehensive national review of carcinogens in the workplace.

The newest EPA National Air Toxics Assessment (NATA) is based on 2002 data.[80] The next NATA is scheduled to be released in late 2009 or early 2010, but it will be based on 2005 data. Moreover, EPA emphasizes that NATA's purpose is not to characterize risks at a level sufficient to support regulation. It is designed to help EPA and others identify pollutants and source categories of greatest potential concern, and to set priorities for collecting additional information to improve future assessments.

Environmental exposures can change markedly over a 5- to 10-year period due to changes in agricultural practices, local industrial growth (or shrinkage), shifting population densities, and other factors. Up-to-date exposure assessments are crucial to set exposure limits and implement corresponding regulatory amendments to protect the health of workers and the public.

Regulation of Environmental Contaminants

The number and prevalence of known or suspected carcinogens is growing. Many environmental contaminants are manufactured synthetic chemicals; waste and by-products of industrial processes; chemical fertilizers, pesticides, and other chemicals used in farming and for landscaping; chemicals used in other commercial activities; combustion by-products of petroleum-powered engines; water disinfection/chlorination by-products; and both man-made and natural sources of radiation.

Right now, the numbers for how many workers are exposed to most of the known carcinogens are 20 to 30 years old so we don't really know what the contemporary workforce is experiencing in terms of exposure.

PAUL SCHULTE
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

In the United States, about 42 billion pounds of chemicals are produced or imported daily. Many of these chemicals are used in massive quantities exceeding one million tons per year.[81] Exposure limits have been set for some of these substances, but the vast majority are unregulated. Of equal concern, according to numerous speakers at the Panel's meetings, many of the current U.S. standards and related regulations for chemical and other exposures were set in the 1950s, and few are stringently enforced.

Reactionary versus Precautionary Approaches to Regulation

Even where reference doses and exposure limits have been established, a number of environmental health scientists and advocates believe that some exposure levels deemed safe by regulators are in fact too high. They maintain that exposures far below the reference dose are causing harm and in some cases, inducing cancer development. Moreover, they believe that some agents cause harm at very low doses that is not manifested at higher doses and that regulatory prudence is indicated until potential effects such as these are better understood.

However, the prevailing regulatory approach in the United States is reactionary in that it:

- Requires incontrovertible evidence of harm before preventive action is taken.
- Places the burden on the public to show that a given chemical is harmful.
- Does not consider potential health and environmental impacts when designing new technologies.
- Discourages public participation in decision making about the control of hazards and the introduction of new technologies, chemicals, or other exposures.[82]

This reactionary approach typically engenders secondary prevention measures (e.g., screening, other methods for early detection of disease) once a health hazard has become evident, rather than action to remove the hazard from the environment (primary prevention).

An alternative approach to regulation that supports primary cancer and other disease prevention is precautionary.[83] In 1998, a conference of international environmental scientists, scholars, activists, treaty negotiators, and others convened to discuss implementation of the Precautionary Principle[84] asserted in a consensus statement that "when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically."[85] The core tenets of the Precautionary Principle are:

- Taking preventive action in the face of uncertainty.
- Shifting the burden of proof to proponents of an activity.
- Exploring a wide range of alternatives to possibly harmful actions.
- Including public participation in decision making.

According to one speaker, precaution should be a key component of a sound approach to managing and communicating risk and uncertainty about risk, but should be applied selectively.[86] Specifically, when there is no evidence of risk, precaution is not warranted and no action is needed. If confidence exists that there is a hazard, prevention is called for, not precaution. However, when credible evidence exists that there may be a hazard, a precautionary approach should be adopted and alternatives should be sought to remove the potential hazard and still achieve the same social benefit. Such an approach acknowledges the uncertainty of identifying cancer risks in complex, poorly understood environmental systems. The determination of when sufficient evidence exists for preventive action often depends on context and the consequences of inaction or acting in error.

One author cautions that operationalizing the precautionary principle using decision models rather than intuitions or inclinations can be challenging and has the potential to have unintended consequences.[87] If decision criteria are not carefully selected, it might be decided to stop the use of a chemical or technology that actually would not have adverse effects, or conversely, allow the use of agents that will have negative effects on people or the environment. In either case, the monetary, health, and social costs and benefits to consumers and producers may be incorrectly distributed.

...when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause-and-effect relationships are not yet fully established scientifically... we don't need to wait until every single scientific question has been answered before we take action.

HEATHER LOGAN
CANADIAN CANCER SOCIETY

Those who support a precautionary approach to the regulation of environmental agents emphasize that while at a specific point in time average individual risk from exposure to one or more carcinogens may be low, health problems due to these exposures may develop over time. When populations exposed to the same carcinogen(s) develop related health problems, the result may be both higher health care costs at the individual level and potentially significant public health issues and societal costs.

...OSHA has not moved fast enough to control exposure to known human carcinogens. Instead of the precautionary paradigm of decision-making in the face of uncertainty, we have a refusal to act in the face of certainty.

FRANK MIRER
HUNTER COLLEGE

Participants at the Panel's meetings suggested that precautionary approaches may encourage innovation because once a chemical or other agent is identified as potentially hazardous, efforts to identify safer alternatives are likely to follow. This dynamic has recently been demonstrated. Consumers have become increasingly

anxious about the estrogenic effects of an organic compound, bisphenol A (BPA) that is used to harden plastics (e.g., baby and water bottles) and line the inside of food and beverage cans, including infant formula cans. BPA, which is detectable at biologically active levels[88] in the urine of an estimated 93 percent of Americans,[89,90] can leach into food when the plastic containers are heated in a microwave oven or washed in a dishwasher. Over the past decade, more than 130 studies have linked BPA to breast cancer, obesity, and other disorders.[91] In 2007, a group of 38 independent NIH-funded investigators concluded there was strong cause for concern that exposure could result in cancer and early puberty.[88] A 2008 study found that adults with higher urinary BPA levels had elevated rates of heart disease, diabetes, and liver abnormalities.[92] Studies also suggest that BPA may interfere with cancer treatments.[93,94]

...we have companies that are formulating products in the United States that are different from those in Europe because there is no regulation [in the United States] requiring the more stringent standards.

JEANNE RIZZO
BREAST CANCER FUND

Although the Food and Drug Administration (FDA) ruled in 2008 that BPA is safe even for infants (Letter from Stephen R. Mason, Acting Assistant Commissioner for Legislation, Food, and Drug Administration, to Rep. John D. Dingell, Chairman, House Committee on Energy and Commerce, 2008 Feb 25), Canada banned its use in baby bottles and infant formula cans the same year. More than 20 states (e.g., MN, CT, CA) and a number of municipalities in the U.S. (e.g., Chicago; Suffolk County, NY) are following suit with proposed or enacted BPA bans. In the face of consumer protests, many large retailers have pulled BPA-containing products from their shelves and manufacturers have moved rapidly to replace BPA with other chemicals that can harden plastics. While this case shows that industry can and will respond to strong consumer concerns, it should be noted that the safety of the substitute chemical(s) is yet unknown. Due to public concern about BPA and scientific criticism of its 2008 ruling, FDA conducted another review of the scientific evidence regarding BPA health effects. In January 2010, the agency acknowledged that there is cause for concern about BPA's effects, but concluded that there was insufficient scientific evidence to support a product ban or even a requirement to label BPA-containing products.[95]

In June 2007, the EC shifted to a markedly more precautionary approach to chemical regulation. The EC establishes health and safety policies that apply to the 27 EU member states. In addition to known carcinogens, the EC lists chemicals "of concern"—having a chemical on this list sends a signal to industry that a safer alternative should be sought. The Registration, Evaluation, Authorisation, and Restriction of Chemical Substances (REACH)[96] initiative is a major reform of the EC chemicals policy affecting all global supply chains that produce and use chemicals. REACH aims to improve protection of human health and the environment through better and earlier identification of intrinsic properties of chemical substances, while simultaneously encouraging the innovative capability and competitiveness of the EU chemicals industry. The initiative requires industry to take a greater role in managing risks from chemicals and to provide safety information on its products; these data will be registered in a central database available to consumers and professionals. REACH provisions are being phased in over an 11-year period.[97] U.S. chemical companies that wish to do business in EC member states must comply with REACH. The U.S. chemical industry has vigorously opposed suggestions that U.S. chemical management policy should use REACH as a model.

Key Issues in U.S. Regulation of Environmental Contaminants

In general, adequate infrastructure exists at the Federal level to perform necessary regulatory functions related to the manufacture, use, disposal, and exposure limits of known or suspected environmental carcinogens. However, key agencies are not fulfilling their responsibilities to protect public health. U.S. regulation of environmental contaminants is rendered ineffective by five major problems: (1) inadequate funding and insufficient staffing, (2) fragmented and overlapping authorities coupled with uneven and decentralized enforcement, (3) excessive regulatory complexity, (4) weak laws and regulations, and (5) undue industry influence. Too often, these factors, either singly or in combination, result in agency dysfunction and a lack of will to identify and remove hazards.

Inadequate Funding and Insufficient Staffing; Decentralized and Uneven Enforcement

Inadequate regulatory program funding and understaffing are partly to blame for many of the shortcomings in U.S. regulation of environmental and occupational hazards. For example, according to a former director of EPA's Office of Prevention, Pesticides, and Toxic Substances, staffing there has dropped from a one-time high of 600 employees to 320 in 2009.[98]

Staffing shortfalls such as these occur at the Federal level, but also lead to problems at the state level. In many instances, enforcement of Federal regulations is the responsibility of state agencies that lack the funding and staff to carry out this function effectively. This issue is described in a 2007 Government Accountability Office (GAO) study on EPA-state enforcement partnerships, which noted that overall funding to regions and participating states increased from 1997–2006, but that the increases did not keep pace either with inflation or the growth in enforcement responsibilities.[99]

In December 2006, the FDA Science Board formed a subcommittee composed of three of its members and other experts representing industry, academia, and other government agencies to assess whether science and technology at FDA can support current and future regulatory needs. The subcommittee concluded that science at the FDA is deficient and the agency is not prepared to meet regulatory responsibilities because of soaring demands coupled with flat funding. Between 1998 and 2007, FDA received responsibility for 123 new statutes,

I think we need national programs on a lot of things, and pesticide regulation is one of them, but EPA has chosen to give [regulation of] the administration of pesticides to the various states.

MARION MOSES
PESTICIDE EDUCATION CENTER

while gaining fewer than 700 employees and losing $300 million in funding to inflation. As a result, FDA suffers from an eroded scientific base with a weak organizational structure, insufficient workforce capacity and capability, and inadequate information technology infrastructure.[100]

EPA and OSHA have a terrible psychological relationship and often end up moving pollution from the workplace to the environment and back again. If we had these folks working together rather than apart, it would be good for the workers, good for the environment, and good for industry, who could use a little more predictability about what they're going to be asked to do.

ADAM FINKEL
UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY

Fragmented and Overlapping Authorities

Responsibility for regulating the manufacture, use, disposal, and exposure levels of known and suspected environmental contaminants is sometimes divided among numerous Federal agencies. Appendices D and E do not provide exhaustive inventories of Federal laws related to environmental hazards or the regulatory responsibilities of the agencies charged to implement them, respectively. However, they illustrate the fragmentation of authority that often results in regulatory gaps and lapses in enforcing existing regulations. In some cases, the regulatory responsibilities of agencies

...industry has a lot of data on these chemicals. They just don't have to give it to anybody.

RICHARD WILES
ENVIRONMENTAL WORKING GROUP

overlap and coordination among agencies is inconsistent. For example, some agencies, such as OSHA and CPSC, are focused more heavily on safety (e.g., preventing injury due to product or other mechanical failure or hazardous manufacturing processes) than on health issues (e.g., exposures that lead to disease) that are the principal focus of agencies like EPA and FDA. These differing missions and overlapping authorities may not be harmonized for the greatest benefit to the public's health and well-being.

Regulatory Complexity

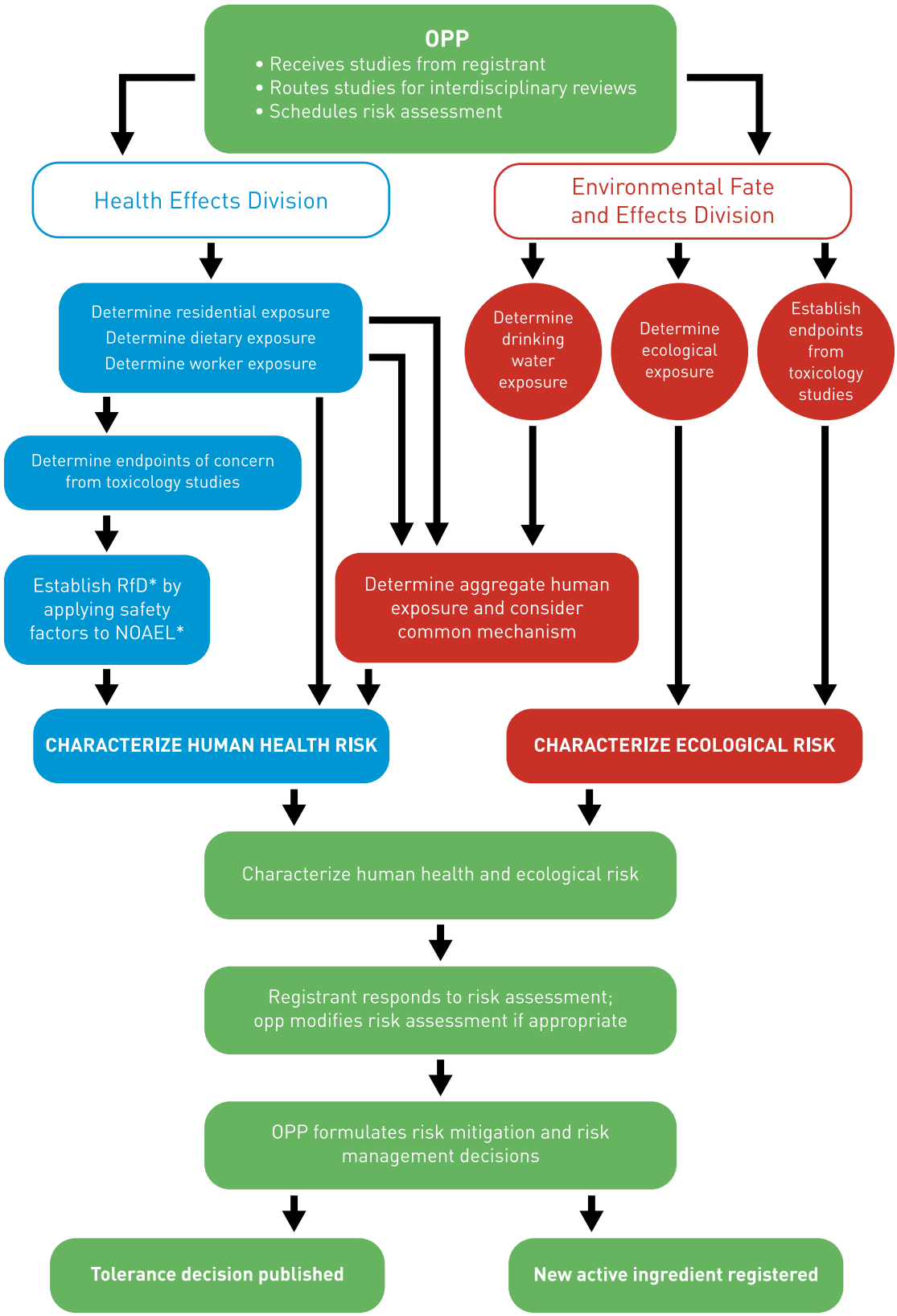
In some instances, the regulatory process is slowed by complex requirements dictated by the regulations themselves, affecting both industry documentation submissions and review processes at the regulatory agency. For example, Figure 2 illustrates the EPA registration (approval) process for a new pesticide or a previously registered pesticide having a new ingredient or proposed new use. Note that this process involves multiple EPA operational units with distinct roles in evaluating data submitted by the manufacturer, exposure assessment and limit-setting, and approval. Other processes are in place for active ingredients suspected of endocrine disruption, an entire different division for registration of biopesticides and antimicrobial products, and a separate division still to do pesticide reregistration for chemicals that were brought to market before 1984. Evaluation and standard setting for industrial chemicals are handled by yet other EPA divisions and offices.

Weak Laws and Regulations

The Toxic Substances Control Act of 1976 (TSCA)[101] may be the most egregious example of ineffective regulation of environmental contaminants. This legislation was intended to give EPA authority to control health risks from chemicals in commerce. TSCA grandfathered in approximately 62,000 chemicals; today, more than 80,000 chemicals are in use, and 1,000–2,000 new chemicals are created and introduced into the environment each year.[102] Yet TSCA does not include a true proof-of-safety provision.[103] At this time, neither industry nor government confirm the safety of existing or new chemicals prior to their sale and use. In fact, because companies are required by TSCA section 8e to report information about known health hazards caused by any of their products, to

EPA Office of Pesticide Policy (OPP) Registration Process

Figure 2



* RfD—reference dose; NOAEL—No Observed Adverse Effect Level

Source: U.S. Environmental Protection Agency

avoid litigation or the costly ban or restricted use of a product, chemical companies generally do not conduct toxicity tests. Under TSCA, EPA can only require testing if it can verify that the chemical poses a health risk to the public.[104,105] Since TSCA was passed, EPA has required testing of less than 1 percent of the chemicals in commerce and has issued regulations to control only five existing chemicals. Companies are required to provide health and safety data for new chemicals and to periodically renew approvals for the use of pesticides, but historically, chemical manufacturers have successfully claimed that much of the requested submissions are confidential, proprietary information. As a result, it is almost impossible for scientists and environmentalists to challenge the release of new chemicals.[106]

In 1989, EPA issued a ban on asbestos based on 45,000 pages of documentation on its risks. However, TSCA stipulates that chemicals should be restricted using the least burdensome regulations available. In 1991, the Fifth Circuit Court of Appeals nullified EPA's ban, ruling that EPA had failed to show that asbestos posed an unreasonable risk, as defined by TSCA, that was best addressed by banning it.[107] Because of TSCA's constraints and weakness, EPA also has been unable to substantially restrict or eliminate the use of other known carcinogens such as mercury and formaldehyde, and has not attempted to ban any chemical since the 1991 court ruling.

We need to think about chemical use as a cancer issue and concern ourselves with production and use of chemicals across our economy from fuel efficiency of vehicles and energy production to use of EDCs [endocrine-disrupting chemicals] in toys, wrinkle-free clothing, food processing, and computers, [and] protection of our water supplies from wastes. We need a systematic program that requires health assessment of synthetic chemicals, old and new, as a prerequisite for their use.

JULIA BRODY
SILENT SPRING INSTITUTE

By contrast, in 1976 the EU prohibited the use of approximately 1,100 chemicals in cosmetics.[108] Atrazine, a widely used herbicide believed to have endocrine-disrupting and possible carcinogenic properties, was banned by the EU in October 2003 because of its ubiquitous and unpreventable water contamination.[109] The same month, the EPA approved the continued use of atrazine in the U.S. Most recently, the EU banned dichloromethane, an ingredient commonly used in paint strippers that has been classified an EU Category 3 carcinogen (possibly carcinogenic to humans).[110]

Moreover, U.S. analyses of the small fraction of all chemicals and other substances in commerce were conducted on a chemical-by-chemical basis. It is not possible either to address the backlog of untested chemicals with this approach, or keep up with the introduction of new chemicals. Further, analyzing each chemical separately fails to address the potential hazards of being exposed to combinations of chemicals and other contaminants that may have synergistic deleterious effects.

In January 2009, GAO added TSCA to its list of government programs at "high risk" of failure, because the law does not provide the agency with enough authority to effectively

regulate chemicals.[111] Momentum is growing to reform TSCA, however, and the EPA Administrator has made chemicals assessment and management a top priority.[112] In February 2009, a Congressional hearing was convened to discuss TSCA reform; elements of such reform have been proposed.[104] A reform bill, initially called the Kid Safe Chemicals Act of 2008,[113] may be reintroduced in the 111th Congress and is expected to reflect the Administration's intention to overhaul regulation of chemicals in consumer products and the workplace, requiring more testing and providing greater authority to restrict toxic substances.[114] In addition, under the existing TSCA legislation, a number of chemicals, including lead, mercury, formaldehyde, and polychlorinated biphenyls (PCBs), recently have been identified for revised rulemaking to strengthen control of these substances. According to EPA, BPA, phthalates, and several other chemical groups also have been targeted for action to label, restrict, or ban them under the authority of TSCA section 6.[114]

Industry Influence on Environmental Contaminant Regulation

Like many other industries, the U.S. chemical, manufacturing, mining, oil, agriculture, transportation/shipping, and related industries are substantial political contributors and actively lobby legislators and policymakers on issues that affect their operations and revenue. For example, corporations aggressively block proposed chemical manufacturing, use, and disposal regulation, both through lobbying activities and in some cases, by manipulating knowledge about their products (e.g., industry-funded research).[115,116] Although the Doll and Peto assessment of attributable fractions of the national cancer burden related to specific causes has been largely abandoned by the scientific community, it remains the basis of many existing chemical regulations and policy. The chemicals industry in particular likewise continues to use the notion of attributable fractions to justify its claims that specific products pose little or no cancer risk. As a result of regulatory weaknesses and a powerful lobby, the chemicals industry operates virtually unfettered by regulation or accountability for harm its products may cause.

There's a knee-jerk reaction on the part of any business that any regulation is a bad idea, at least in public.

DAVID KRIEBEL
UNIVERSITY OF MASSACHUSETTS

State-level Regulatory Efforts

Some states have taken action to fill the regulatory void left by weak Federal regulation of environmental chemicals and other contaminants. California has long been a leader in this regard, but other states likewise are stepping up occupational and environmental protection efforts. For example, the Massachusetts Toxics Use Reduction Act,[117] enacted in 1989 and amended most recently in 2006, requires companies in the state that use large quantities of specific chemicals to evaluate, plan for, and implement (to the extent practical) pollution prevention opportunities. Companies are required to evaluate their efforts and update their toxics use reduction plans every 2 years.

...we know enough now to act in ways that we have not done, and that should be our focus on environmental and occupational cancer prevention in the coming years—act on what we know.

RICHARD CLAPP
BOSTON UNIVERSITY

In 2008, both Maine[118] and Washington passed legislation to reduce children's exposure to toxic chemicals. The Washington Children's Safe Products Act[119] focuses specifically on eliminating lead, cadmium, and hormone-disrupting phthalates in children's toys. Other states (e.g., OR, MN) also have enacted or proposed toy safety legislation.

Sources and Types of Environmental Contaminants

The line between occupational and environmental contaminants is fine and often difficult to demarcate. Many known or suspected carcinogens first identified through studies of industrial and agricultural occupational exposures have since found their way into soil, air, water, and numerous consumer products. Usually, higher doses to smaller populations are common in workplace exposures, while environmental exposures typically involve lower doses but larger populations (Figure 3). Most studies of environmental carcinogens have been conducted in the workplace because high dose effects are more readily identified and it often is easier to estimate exposure levels in a relatively consistent occupational setting. Findings there often provide clues to health problems observed in the community.

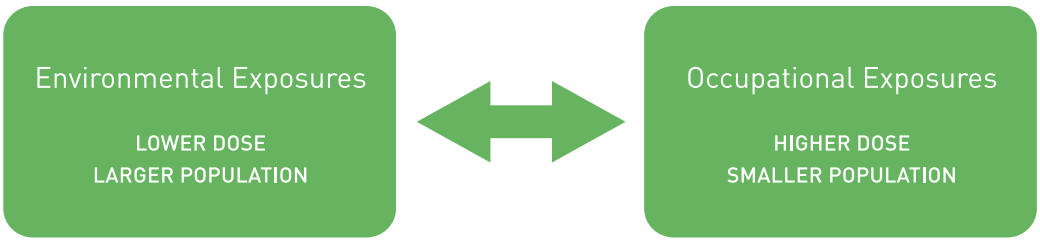


Figure 3

People from disadvantaged populations, however, are more likely to be employed in occupations with higher levels of exposure (e.g., mining, construction, manufacturing, certain service sector occupations) and to live in more highly contaminated communities.[120,121] For example, Louisiana and Mississippi are known as "Cancer Alley" because of the more than 100 chemical plants and oil refineries in the area and the high concentration of poor populations with limited health care access. The cancer rate in Louisiana in 2005 was approximately 17 percent higher than the national average.[122]

The reality of this unequal burden is not just a health issue, but an issue of environmental justice. Further, studies by the U.S. Centers for Disease Control and Prevention (CDC) show that while all Americans carry many foreign chemicals in their bodies, women have higher levels of many of these chemicals than do men.[123] Some of these chemicals are found in maternal blood, placental tissue, and breast milk samples from pregnant women and mothers who recently gave birth.[124–126] These findings indicate that chemical contaminants are being passed on to the next generation, both prenatally and during breastfeeding. Some chemicals indirectly increase cancer risk by contributing to immune and endocrine dysfunction that can influence the effect of carcinogens.

This section includes chapters that describe major sources of cancer-associated contaminants, including industry and manufacturing, agriculture, and exposures related to modern lifestyles. Additional chapters focus on potentially harmful exposures stemming from medical care, military activities, and natural sources. It is crucial to bear in mind that exposure to potential carcinogens most often occurs in mixtures that may have additive or synergistic effects.

Appendix F provides additional information on known and suspected environmental carcinogens. Appendix G provides basic information about electromagnetic energy that is relevant to discussions in Chapters 1 and 3 through 6; readers may wish to refer to this information in conjunction with the material in those chapters. In addition, a table listing units of measure across the electromagnetic spectrum is provided in Appendix H.

CHAPTER 1

Exposure to Contaminants From Industrial and Manufacturing Sources

Currently established or suspected carcinogens are far too many to enumerate in this report. As noted in Part I, the International Agency for Research on Cancer (IARC) has evaluated nearly 950 agents and classified more than 400 as known, probable, or possible carcinogens.[78] Similarly, the U.S. National Toxicology Program's (NTP) most recent Report on Carcinogens[77] lists 246 agents as known human carcinogens or substances "reasonably anticipated to be human carcinogens." Tens of thousands more chemicals and other substances are in use that never have been evaluated and whose carcinogenicity is unknown. A handful of chemical mixtures has been assessed, but virtually nothing is known about the toxicity of the myriad other possible combinations of various chemicals and other substances or differences in their carcinogenicity under various exposure scenarios.

A large percentage of these synthetic and natural compounds are used in or are by-products of manufacturing and other industrial processes. Many millions of workers are exposed on the job to toxic and potentially carcinogenic or endocrine-disrupting chemicals, metals, fibers, combustion by-products, and other substances. Their exposures tend to be at considerably higher levels than those typically experienced by the general population. Panel meeting speakers noted that the families of workers exposed to hazardous substances also tend to have higher exposure levels than the general public. Family exposures can become high enough to raise cancer risk, promote or cause other diseases, or alter immune system or endocrine function. These exposures most often occur when chemicals and other contaminants are brought into the home environment on workers' shoes and clothing.

Unfortunately, due to improper storage and disposal of chemicals and ineffective control of emissions into the air, soil, or water, many toxics that originate in manufacturing and industrial settings enter the environment and may affect people far from the source of the contamination. Of particular concern, many toxics from industrial and manufacturing sources accumulate in the tissues of living organisms.

In addition to spreading from their point of origin, some of these compounds become ubiquitous and are persistent in

We are not all exposed to a single agent, a single radiation or a single type of radiation, and we're not exposed at a single point in time. It's a cumulative effect...

WILLIAM SUK
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

the environment because they are used in huge quantities and break down extremely slowly, if at all. Other compounds are converted to other forms in reaction to or combination with other environmental elements, but the resulting compounds are highly toxic. In still other cases, toxic compounds enter the environment because they are integral components of or ingredients in manufactured consumer products. Examples of these types of manufacturing and industrial contaminants, their occupational and environmental impacts, and emerging contaminants of concern are described below.

Common Industrial and Manufacturing Contaminants That Are Persistent in the Environment

Numerous chemicals and other substances associated with industrial and manufacturing operations have become ubiquitous and persistent in the environment. The paragraphs below provide several examples discussed at the Panel's meetings.

Polyhalogenated Biphenyls

This large group of man-made organic chemicals includes numerous compounds such as polybrominated biphenyls (PBB) and polychlorinated biphenyls (PCB). The highest serum PBB levels are associated with significantly higher rates of breast cancer, non-Hodgkin lymphoma, and digestive system cancers (esophagus, stomach, liver, pancreas).[127] The many PCB compounds vary in their toxicity.[128] These chemicals are linked to liver and biliary cancers and are suspected carcinogens for breast cancer,[129] prostate cancer,[130] melanoma,[131] and non-Hodgkin lymphoma.[132] PCBs accumulate in adipose tissue. They also can induce fat cell differentiation and inflammatory responses, which may contribute to obesity.[133] In addition to increased cancer risk, EPA also indicates that PCBs are hormone disruptors with effects on the immune, reproductive, nervous, and endocrine systems.[134]

PCBs were banned in the United States in the late 1970s, but still are present in the bodies of people exposed to them and in the environment. Workers in electrical industries were exposed to PCBs, which were used as coolants and lubricants in transformers, capacitors, and other electrical equipment. PCBs also were used in oils for motors and hydraulic systems, adhesives and tapes, thermal insulation materials, oil-based paint, dyes, caulking, carbonless copy paper, and many other products.

These chemicals can still be released into the environment from poorly maintained hazardous waste sites containing PCBs, improper dumping of PCB wastes in landfills not designed to handle hazardous waste, and incinerating PCB-containing items.[128] PCBs persist in the environment because many of these compounds degrade very slowly and cycle between air, water, and soil. They also bioconcentrate significantly in the aquatic food chain and the above-ground parts of food crops and other plants.[128] As a result, humans continue to be exposed to PCBs through multiple routes.

In 2009, EPA recommended that owners of buildings, including schools, constructed or renovated between 1950 and 1978, test masonry and window caulking for high PCB levels.[135] The chemicals were mixed into caulking to make it rubbery when applied to interior and exterior building surfaces. As the caulking ages, however, it can disintegrate into PCB-containing particles and vapors that can fall to the ground or other surfaces and infiltrate building ventilation systems. In addition,

a recent study[136] found higher leukemia rates among children living in homes where PCBs were found in carpet dust compared to children without this exposure; leukemia rates rose with level of PCB exposure. The findings, however, require additional study to understand ethnic/racial differences among children with equivalent PCB exposure rates.

Asbestos

Asbestos is the generic name for a group of naturally occurring inorganic fibrous silicates that are used for a variety of industrial and other uses. It does not break down and has good insulating properties.

Inhalation of asbestos is the primary cause of mesothelioma, a rare cancer of the mesothelium, the membrane that covers and protects most of the body's internal organs.[137] Mesothelioma symptoms may not appear until 30 to 50 years after asbestos exposure. More than 70 percent of people with mesothelioma have a history of asbestos exposure at work. Asbestos is used in the manufacture of cement pipe, brake linings, and acoustical and thermal insulation. Other workers at risk of asbestos exposure include people working in the construction industries, shipyards, and asbestos mines and mills. However, in industrialized nations, nearly one in three people with mesothelioma have no history of workplace exposure to asbestos. There is some evidence that family members and others living with asbestos workers are at increased risk of developing mesothelioma and other asbestos-related diseases when asbestos dust is brought into the home on workers' clothing and hair.

This is where the real unacceptable part of this problem is—that the individual probabilities of cancer to workers are orders of magnitude greater than we accept in the general environment.

ADAM FINKEL
UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY

Asbestos exposure also can occur when other substances are contaminated with asbestos fibers. Perhaps the most striking example of asbestos contamination of other materials occurred at a mine near Libby, Montana, which was the source of more than 70 percent of all vermiculite (a lightweight, fire-resistant mineral that resembles mica) sold in the U.S. from 1919 to 1990. Because there also was an asbestos deposit at the mine, the vermiculite, which was made into an insulation product called Zonolite, was contaminated with asbestos.[138] The attics and walls of an estimated 30 million U.S. homes were insulated with Zonolite.[127] Homeowners are strongly cautioned not to disturb or try to remove this insulation as they are likely to be exposed to asbestos.

Asbestos is classified by IARC as a lung and laryngeal carcinogen, and some evidence suggests it may increase risk for non-Hodgkin lymphoma, chronic lymphocytic leukemia, and multiple myeloma.[78] One meeting speaker noted that the World Health Organization, the World Bank Group, international labor organizations, and numerous public health scientists and policymakers have urged a global ban on asbestos. Some countries (e.g., Brazil) have banned asbestos, but its use continues in many nations, including the United States.

...unfortunately, we have few regulations for the many known and suspected occupational carcinogens, and where we do have some permissible exposure levels or limits for substances that are reasonably anticipated to be carcinogens, those weren't based on cancer studies. They were based on looking at acute toxic effects. Consequently, the level that will be permitted is higher than would be allowed if it was based on research done to look at the carcinogenic effects.

PAUL SCHULTE
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

Chromium

Chromium exposure is a known cause of lung, nasal, and nasopharyngeal cancers. Hexavalent chromium directly damages cellular DNA, and studies[139,140] show a strong lung cancer dose-response relationship with human occupational exposures to hexavalent chromium. In addition, entire communities have been exposed to hexavalent chromium in soil and water contaminated following inappropriate disposal of the chemical by industrial users. Chromium is used in the leather tanning process, in the manufacture of dyes and pigments, and in wood preserving, chrome plating, and steel and other alloy production. Workers in all of these industries risk chromium exposure.

In July 1993, the Oil, Chemical, and Atomic Workers International Union and Public Citizen's Health Research Group petitioned the Occupational Safety and Health Administration (OSHA) for an emergency temporary standard to reduce occupational exposures to hexavalent chromium compounds.[141] While OSHA agreed that there was evidence of increased cancer risk from exposure at the existing permissible exposure limit (PEL) of 100 micrograms per cubic meter ($\mu g/m^3$), the agency did not agree that the evidence demonstrated the "grave danger" required to support an emergency temporary standard. OSHA did initiate a new review of its PEL for hexavalent chromium, but did not lower the exposure limit to 5 $\mu g/m^3$ until 2006—13 years later.

Perchloroethylene and Trichloroethylene

Perchloroethylene (PCE, also known as perc and tetrachloroethylene) is a solvent that has been a mainstay of the dry cleaning industry for decades. It is classified as "reasonably anticipated to be a carcinogen"

by the National Toxicology Program (NTP).[77] Approximately 28,000 dry cleaners in the U.S. use perc. Dry cleaning workers who inhale PCE are at risk for liver damage and neurological problems. Some large industrial and commercial dry cleaners emit more than 10 tons of PCE into the atmosphere each year. The public also has been exposed to PCE due to improper disposal that has contaminated soil and drinking water at hundreds of locations across the country.[142] High levels of PCE in drinking water are associated with elevated breast cancer risk.[143] Animals exposed to high levels of PCE developed kidney and liver tumors.[144]

Dry cleaning businesses reduced PCE emissions by more than half between 1996 and 2006 by replacing old machinery and improving efficiency. Some have begun using alternative cleaning methods that do not require PCE. The industry, however, has strongly resisted a ban on the chemical. EPA's most recent amendments (2008) to regulations on the use of PCE by dry cleaners require dry cleaners located in residential buildings (typically the smallest establishments) to phase out perc use by 2020. Larger freestanding and industrial/commercial dry cleaners are required to upgrade equipment to detect and reduce PCE emissions, but are not required to cease using the chemical.[145]

Trichloroethylene (TCE) is classified by IARC as probably carcinogenic to humans (Group 2A)[146] and as "reasonably anticipated to be carcinogenic to humans" by NTP.[77] A review of recent studies found evidence that TCE is strongly associated with kidney, liver, and biliary cancers, and is a suspected carcinogen for cervical cancer, Hodgkin and non-Hodgkin lymphomas, and leukemia.[147] Occupational exposures are greatest among workers involved in metal degreasing and the manufacture of adhesives, paint removers, varnishes, paints, lacquers, typewriter correction fluids, printing inks, and spot removers. TCE previously was used as a dry cleaning agent.

Because it often was disposed of improperly, many underground water sources have become contaminated with TCE, which has been found at more than 60 percent of Superfund sites nationwide. TCE now is the most frequently detected organic solvent in groundwater and is present in as much as 34 percent of the nation's drinking water supplies. Once in the groundwater, TCE may evaporate, infiltrating homes as a gas and creating inhalation and ingestion risks.[148]

Common Industrial and Manufacturing Chemicals or Processes with Hazardous By-Products or Metabolites

Some chemicals are harmless to human health, but when they are used in the manufacturing of other chemicals, used in other manufacturing processes, exposed to particular natural elements, or burned, they can form hazardous by-products or change into other forms of the chemical that are harmful (metabolites).

We really need to focus on how we can get our animal data and human data to be useful for risk assessment. We need dose exposure confirmation. We need disposition data. We need low-dose exposure information. We need information on the metabolites of these compounds, not just the parent compounds.

SUZANNE FENTON
U.S. ENVIRONMENTAL PROTECTION AGENCY

Particulate Matter from Industrial and Related Mobile Sources

Much of the particulate pollution generated by industry is produced by incomplete combustion of petrochemicals and other substances used in manufacturing and machining processes. Health risks related to particulate matter usually are related to the size of the particles; those small enough to be inhaled (smaller than 10 micrometers [μm] in aerodynamic diameter) are of greatest concern. Particles between 10 μm

and 2.5 μm are designated PM_{10}; those less than 2.5 μm are designated $PM_{2.5}$. The smaller particles, $PM_{2.5}$, can penetrate to gas exchange regions of the lung. Extended follow-up of the Harvard Six Cities Study, a cohort study that began in the mid-1970s, confirmed earlier findings that mortality from cardiovascular disease and lung cancer was positively associated with long-term exposure to $PM_{2.5}$ in ambient air, and that reduced $PM_{2.5}$ levels were associated with lower mortality from these causes.[149,150] A 2009 study[151] of changes in air quality and life expectancy between 1980 and 2000 in 51 U.S. cities found, after adjusting for variables (e.g., smoking, migration, education), that cleaner air accounted on average for 5 months of the 2.72 years of added life expectancy that occurred during that period.

...when you put your kids on a school bus to go to school, you're putting them in a microenvironment where the concentration of particulate matter is 10 or 100 times higher than the ambient concentration.

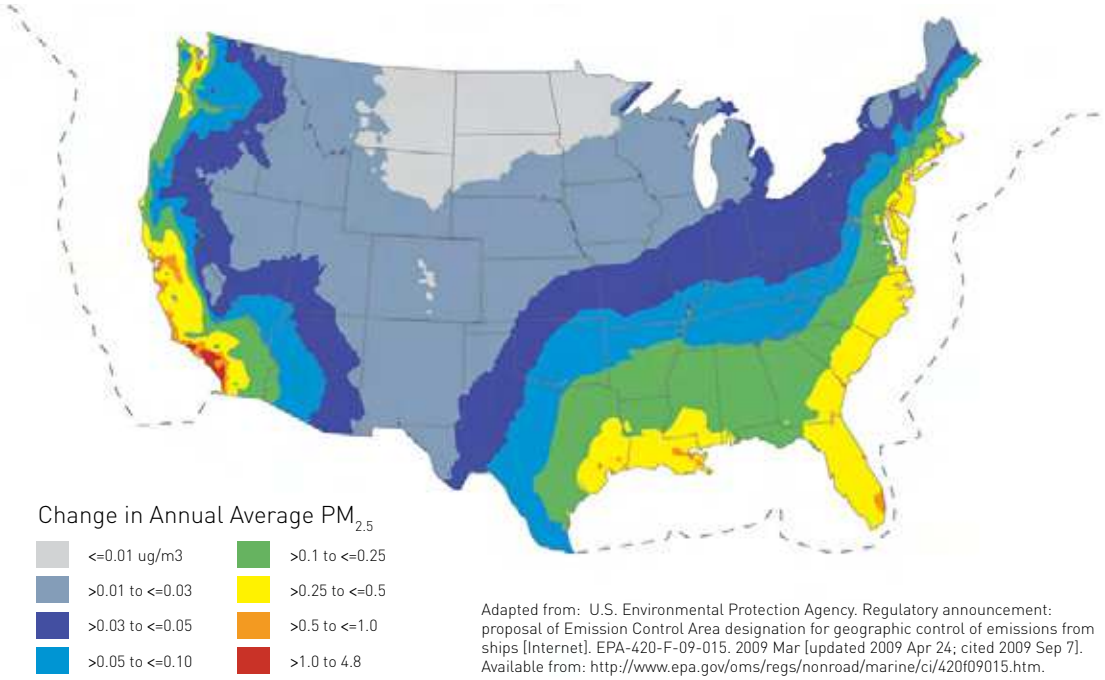
WILLIAM CHAMEIDES
DUKE UNIVERSITY

Children's exposure to particulate air pollution is of special concern because of their greater vulnerability to toxics of all kinds. In 2008, *USA Today* published a series of articles[152] based on its study that used EPA's model to track the path of industrial pollution and mapped the locations of nearly 128,000 schools to determine the levels of toxic chemicals near schools. Academic researchers who partnered with *USA Today* to conduct the study found that 20,000 schools—about one in six—are within a half-mile of a major industrial plant. Little is known, however, about the health and developmental effects of the multiple air pollutants these and other children are exposed to from industrial gaseous and particulate emissions. Exposure limits established by EPA are based only on assumptions about adult exposures, adjusted for safety and uncertainty factors. Further, establishing and quantifying the exact nature and level of exposure experienced by individual children is exceedingly difficult, as also is the case for adults. The *USA Today* study and computer modeling analysis of air toxics near schools prompted EPA to launch a Schools Air Toxic Initiative[153] to understand whether outdoor toxic air pollution poses health concerns for children. In collaboration with state and local air quality agencies, outdoor air monitoring is being implemented at 63 schools in 22 states. Air at each school will be monitored for 60 days; specific pollutants measured will vary based on the best available data on air toxics in the vicinity. It should be noted that some states have challenged the *USA Today* results. For example, Louisiana[154] and Pennsylvania[155] have published reports, based on their own testing, indicating that air quality near their schools meets health and safety standards.

Particulates from the incomplete combustion of diesel fuel are emitted by cars and trucks (including long-haul vehicles), boats, and rail cars, as well as industrial, construction, harbor, and mining operations. Diesel engine exhaust from school buses is of special concern because many children are exposed to it on a daily basis. However, diesel exhaust was not included in the 2002 National Air Toxics Assessment (NATA)[80] because EPA concluded that available health effects data were insufficient to develop a quantitative estimate of carcinogenic potency. Yet EPA believes that diesel exhaust is among the substances that may pose the greatest risks. Average lifetime cancer risk from exposure to diesel exhaust alone may exceed 1 in 100,000 and could be as high as 1 in 1,000.[156] Inhalation of particulate matter from diesel exhaust is classified by EPA as a likely human carcinogen,[156] and by IARC as a probable human carcinogen for lung cancer.[157] Diesel exhaust particles usually consist of an elemental carbon core surrounded by organic matter and other substances, including sulfuric acid, that adhere to it once airborne and are small enough to be inhaled into the alveolar regions of the lung.[77]

Area Proposed for ECA Designation and Potential Benefits of U.S. ECA Ambient $PM_{2.5}$ Reductions in 2020

Figure 4



Adapted from: U.S. Environmental Protection Agency. Regulatory announcement: proposal of Emission Control Area designation for geographic control of emissions from ships [Internet]. EPA-420-F-09-015. 2009 Mar [updated 2009 Apr 24; cited 2009 Sep 7]. Available from: http://www.epa.gov/oms/regs/nonroad/marine/ci/420f09015.htm.

A 2008 study[158] found that truckers who do short-haul pickups and deliveries from vehicles on loading docks, city streets, and highways have a higher risk of death and disease, including lung cancer, than other workers. Dockworkers also were found to have higher risks. The study authors believe these workers have more constant and concentrated exposure to newly released diesel exhaust particles, which have a greater potential to cause DNA mutations.

Concern also has been raised about air pollution in and surrounding U.S. coastal cities and ports due to diesel exhaust emissions from ocean-going ships, including container ships, tankers, cruise ships, and bulk carriers.[159] Approximately 87 million people live in these port and coastal areas. Moreover, emissions from the ships also can travel hundreds of miles inland, affecting many millions more. EPA estimated that in 2001, ocean-going ships emitted: more than 54,000 tons of fine particulate matter, equivalent to the pollution from 117 coal-fired power plants;[160] approximately 745,000 tons of smog-forming nitrogen oxides, comparable to the emissions from over 800 million new cars;[161] and an estimated 450,000 tons of sulphur dioxide, equal to more than 40 percent of the emission from the U.S. transportation sector.[160] A group of environmental and cancer advocacy organizations has urged the U.S. government to apply to the International Maritime Organization (IMO) for an Emission Control Area (ECA) where stricter environmental controls would be enforced.[159] In March 2009, the U.S. and Canada submitted a proposal to the IMO for an ECA;[162] Figure 4 shows the proposed ECA area and the estimated reductions in particulate concentrations that could be achieved by 2020.

In 1960, we said we're going to put a man on the moon in 10 years. In 10 years, we can get our hydrocarbon fuels out of our system. You say, 'Oh, come on. Is that possible?' I think it's possible. It just has to be a political priority.

JOHN VENA
UNIVERSITY OF GEORGIA

Mercury

Elemental mercury occurs naturally and also is released into the air through industrial pollution, contaminating food and water sources. It is a suspected carcinogen for brain and central nervous system (CNS) cancers. U.S. coal-fired power plants emit more than 48 tons of mercury into the air each year.[163] In 2008, a U.S. court of appeals ruled[164] that EPA violated provisions of the Clean Air Act when it promulgated the 2005 Clean Air Mercury Rule that exempted power plants from existing strict toxic control regulations intended to eliminate up to 90 percent of power plant mercury emissions by 2008. EPA was given 2 years to develop new emission standards for existing power plants. Proposed new power plants would be required to indicate how mercury emissions would be controlled. A recent report[165] by the General Accountability Office (GAO) found that it is technologically possible and affordable for coal-fired power plants to install state-of-the-art pollution control equipment that reduces mercury emissions by as much as 90 percent. Industry has long claimed that mercury controls would be too expensive, but the GAO report, based on a study of 25 boilers at 14 plants with advanced mercury control technology, found that the average cost of equipment installation ($3.6 million) translated into pennies per month on consumers' electric bills.

We are exposed to many pollutants, many at the same time or in sequences that [cause them to] interact with one another. And yet our policies and most of our research... for the most part [address] one pollutant, one exposure at a time.

WINIFRED HAMILTON
BAYLOR COLLEGE OF MEDICINE

In addition to workers at coal-fired power plants, those in factories that produce chlorine gas and caustic soda for use in some industrial processes may be exposed to mercury. Workers can be exposed to mercury in various forms when it is used to produce batteries, thermometers, and skin creams and ointments. Cement kilns are a major producer of mercury that contaminates both air and water in the U.S. These kilns also release hydrocarbons, particulate matter, sulfur dioxide, and sulfuric acid.

Unlike some pollutants, mercury emissions create toxic "hot spots" where environmental exposures can be especially severe.[166] This is believed to result from complex processes that move atmospherically released mercury through the environment; in addition, some sites (e.g., wetlands, forested areas) are particularly sensitive to mercury input.[167] Inappropriate disposal of batteries and other mercury-containing products add to mercury contamination of soil and water.

When exposed to microorganisms in water and soil, elemental mercury becomes methylmercury, a known neurotoxin that IARC classifies as a possible human carcinogen.[168] According to EPA statistics, more than 600,000 children born each year test positive for unhealthy levels of methylmercury,[169] exposures that may put them at risk for brain damage and future learning disabilities. A tragic exposure

to methylmercury in the 1960s in Japan proved that fetal exposures to mercury have devastating effects.[170] Pregnant women in a remote fishing village ate seafood contaminated by mercury discharged into Minamata Bay by a plastics factory. The mothers were unharmed, but their children suffered profound mental retardation and neurological effects.

Consumers, particularly pregnant and nursing women, women who may become pregnant, and young children, are cautioned to avoid eating swordfish, tilefish, king mackerel, and shark. Because methylmercury bioaccumulates in the marine food chain, these larger fish tend to have higher levels of methylmercury in their tissues than smaller fish.[171] Methylmercury accumulates in body tissues, and while it is removed from the body naturally, it may take over a year for levels to drop significantly in people who regularly eat fish containing high levels of mercury.

Common Industrial and Manufacturing Contaminants in Consumer Products

The manufacturing of myriad consumer products requires the use of chemicals. Some of these chemicals remain in or on the product as residues, while others are integral components of the products themselves. The paragraphs below provide key examples of such product contaminants.

Formaldehyde

Formaldehyde is an IARC Group 1 human carcinogen for cancers of the nasal cavity and nasopharynx.[172] IARC also concluded that there is strong but not sufficient evidence for a causal association between leukemia and occupational formaldehyde exposure. Formaldehyde is used as a disinfectant and preservative and in the production of urea, phenol, and melamine resins used to make molded products such as appliances, electric controls, and telephones. It also is used in a wide variety of building and home decoration products (e.g., plywood, particle board, surface coatings, foam insulation, carpet and draperies, furniture, permanent-press fabrics) and in toiletries. Formaldehyde is a component of auto exhaust, tobacco smoke, and other combustion processes.

An estimated two million workers are exposed to formaldehyde.[173] Workers in factories that produce formaldehyde have among the highest exposure risks. Embalmers, pathologists, and those employed in industries that manufacture the products listed above also are exposed to formaldehyde. New NCI study data[174] on worker exposure to formaldehyde in factories show a significant risk of death from Hodgkin lymphoma, multiple myeloma, and myeloid leukemia. Though a cause and effect relationship could not be established, death rates from blood and lymphatic cancers increased with level of formaldehyde exposure. These data are expected to help EPA complete a new assessment on formaldehyde exposure risk that has been delayed for almost 5 years, but could lead to stronger regulations on formaldehyde emissions from natural gas turbines, plywood manufacturing facilities, and other sources.[175]

...there is a very fine line between occupational carcinogens and environmental carcinogens... Historically, identification of carcinogens arose from relatively high exposures that occurred in the workplace and many of those human carcinogens that were identified have certainly found their way into soil, air, water, and commercially available products.

ELIZABETH FONTHAM
LOUISIANA STATE UNIVERSITY

Formaldehyde exists in all homes to some degree because of the diverse materials in which it is used.[176] Individuals can be heavily exposed to formaldehyde in homes with newly installed plywood, particle board, and carpeting. Consumers are advised to

vacate or ventilate well any indoor spaces with new formaldehyde-containing products, and to try to select products with low formaldehyde emissions. The health effects of formaldehyde exposure gained national media attention when it was reported that Gulf Coast families who occupied new trailers provided by the Federal Emergency Management Agency (FEMA) as temporary housing following Hurricane Katrina were developing respiratory and other illnesses. EPA considers 0.1 parts per million to be an elevated level that can cause illness. Testing conducted by the Sierra Club found formaldehyde concentrations as high as 0.34 parts per million in the FEMA trailers.[177]

Endocrine Disrupting Chemicals (EDCs)

EDCs are natural or synthetic chemicals that can interfere with normal animal and human hormonal systems. These chemicals have been developed and are used for a wide variety of industrial purposes. Recognition that these chemicals alter hormone action, and the possible implications of their effects, has developed slowly over the past several decades.[178] EDCs were first recognized by Congress as a public health concern when the Food Quality Protection Act[179] and amendments to the Safe Drinking Water Act[180] were passed. These laws mandated that EPA develop a screening program to identify EDCs to which humans may be exposed. However, after more than 10 years, EPA has yet to finalize a profile of tests to identify potential EDCs in the environment.

...I hope that especially with hormonally dependent cancers we really start to look at endocrine disrupters in the environment as important chemicals that may contribute to both the rising incidence, as well as the mortality from these cancers. I hope we can get past this concept of low-dose effects because they're not really low doses if you're an endocrinologist.

TYRONE HAYES
UNIVERSITY OF CALIFORNIA, BERKELEY

The endocrinology community has expressed concern that recent research findings may not be reflected in the final EPA screening program.[178] For example, it now is clear that EDCs affect hormone systems other than through thyroid and steroid receptor mechanisms, and that EDCs, which have been found in amniotic fluid,[181] may have *in utero* and multigenerational effects. Further, current EDC policy relies on toxicologic studies that examine high-dose effects, when many EDC effects may occur at low doses, even when high-dose effects are not apparent. In fact, higher doses of a hormone or hormone-mimicking chemical can depress a measurable low-dose effect by overwhelming or down-regulating the endocrine system's ability to respond. This pattern of effect has long been recognized by endocrinologists.[178] Thus, an effect seen at low exposure levels would not be observed at high exposure levels[178,41] in a typical high-dose oriented assay.

The knowledge base on EDCs is growing, but many questions remain. Some *in vitro* studies[182,183] have shown that EDCs can cause proliferation of human breast cells in culture. Animal studies[184] show that EDCs can cause mammary cancer, other tumors, and serious reproductive effects. However, most human studies of breast and other cancers due to EDC exposure have been inconclusive. Nonetheless, because of the long latency period of many cancers, the available evidence argues for a precautionary approach to these diverse chemicals, which include persistent organochlorides such as DDT/DDE, polychlorinated biphenyls, pesticides, polycyclic aromatic hydrocarbons, tobacco smoke, bisphenol A, some metals, phthalates, parabens, and growth promoters used in food production.[13] At this time, the majority of suspected EDCs are not classified by either IARC or NTP as carcinogens, and they are not regulated by any U.S. Federal agency.

Of the many known and suspected EDCs, bisphenol A (BPA) has received perhaps the most public attention in recent years (see

also Part I, p. 18). BPA is used in numerous products, including baby bottles and food and beverage can liners. It disrupts the endocrine system because it acts as a weak estrogen. Extensive research has linked BPA to breast cancer, obesity, diabetes, and other serious medical problems.[88,92] The Center for the Evaluation of Risks to Human Reproduction concluded in 2008 that there is "...some concern for effects on the brain, behavior, and prostate gland in fetuses, infants, and children at current human exposures to bisphenol A."[185] Yet in 2008, the FDA ruled that BPA is safe even for infants (letter from Stephen R. Mason, FDA, to Rep. John D. Dingell, Chair, Chairman, House Committee on Energy and Commerce, 2008 February 25), based on selected studies, some of which were industry-sponsored, and what is alleged to have been undue influence by industry lobbyists.[186] FDA's safety assessment was rejected by a March 2009 consortium of international experts from academia, government, and industry as incomplete and unreliable because it failed to consider all of the scientific work relating to BPA.[187] In January 2010, FDA completed a re-evaluation of scientific evidence on BPA, but concluded that neither a ban on the chemical or labeling of BPA-containing products was warranted.[95] In early 2009, NIEHS released a Request for Proposals for research on BPA effects on human health. The research will be supported for 2 years with $5 million of American Recovery and Reinvestment Act stimulus funds.[188]

...it seems to me that the indication of harm is our trigger for action but how much harm and how much weight of evidence do you want before you make a decision I think is the interesting question, and surely the answer is different depending on how many people are exposed.

SANDRA STEINGRABER
ITHACA COLLEGE

Like BPA, phthalates disrupt normal hormone function by mimicking estrogen. This group of chemicals is used to make plastics soft and pliable. They are found in a wide array of consumer products, including plastic bottles, IV tubing, toys (including soft teething toys for babies), cosmetics, hair conditioners, and fragrances. Phthalates inhibit normal binding to estrogen receptors

and suppress male androgens. In girls, phthalates may cause early puberty and higher breast cancer risk later in life.[189] Male fetuses in the first trimester of pregnancy appear to be particularly vulnerable to damage by phthalates, which may cause undescended testicles, hypospadias, and possibly higher testicular cancer risk. In humans, phthalates have been linked to problems with sperm count and sperm quality, and like other EDCs, phthalates are a suspected breast carcinogen.

... [breast cancer] incidence has stabilized in the U.S., but it's stabilized at one of the highest rates in the world, and as women move from lower risk regions of the world to the U.S., their incidence goes up and continues to rise over a couple of generations. So we know that that's not genes and there's something about industrial society that's playing an important role.

JULIA BRODY
SILENT SPRING INSTITUTE

Emerging Industrial and Manufacturing Contaminants

In the ongoing quest for more effective and efficient ways of making industrial and consumer products, improving processes, and achieving other desired outcomes, new chemicals and other substances are being created continually. In addition, existing substances are being put to new uses. Unanticipated environmental hazards may emerge from this push for progress.

Nanotechnology

Nanomaterials are an important example of an emerging environmental hazard born of new technology. Engineered nanomaterials (ENMs) are structures and systems as small as atoms and molecules that are enabling significant breakthroughs in material design and development for industry, consumer products, and medicine.[190] ENMs now are used in hundreds of consumer products, including cosmetics, sunscreens, other personal care products, stain-resistant clothing, food storage containers, computers, and other electronics. Anticipated applications may provide new ways to clean up pollution, increase fuel cell efficiency, and provide drug delivery systems for cancer and other diseases. According to NIEHS, global demand for nanomaterials and nano-enabled devices is expected to exceed $1 trillion by 2015.[191]

However, nanomaterials can be extremely toxic, and despite their promise, concern is growing about their potential health and environmental risks. Most ENMs are engineered at dimensions of 1 to 100 nanometers (nm), or 1 to 100 billionth of a meter. The width of a human hair is 80,000 nm.[190] Because of their structure and small size, they can be inhaled, ingested, and absorbed through the skin, entering the blood stream, penetrating cells throughout the body (including the brain), and perhaps interfering with DNA processes.[190] In August 2009, seven young Chinese women suffered permanent lung damage and two of them died after working for months without adequate protection in a paint factory using nanoparticles.[192] Once inhaled, nanoparticles that penetrate pulmonary epithelial cells or aggregate around red blood cell membranes cannot be removed.[193]

ENMs that have been shed from industrial processes, personal care products, and other sources also can build up in the environment and interfere with ecologic systems. For example, some research suggests that titanium dioxide nanoparticles from sunscreens may be toxic to algae and water fleas that are a vital part of marine ecosystems.[194,195]

ENM safety research and regulation is lagging behind their creation, and according to one report,[196] few have been adequately tested. NIEHS is funding research[191] on the health and safety effects of nanomaterials and also has, in collaboration with national and international partners, established an online searchable Nanoparticle Information

Library (NIL). The goal of the NIL is to help occupational health professionals, industrial users, worker groups, and researchers organize and share information on nanomaterials, including their health and safety-associated properties.[197] In September 2009, EPA announced new risk management actions on a number of chemicals and other substances,[114] including two carbon nanotubes (P-08-177 and P-08-328). The new regulations will require protective measures to limit exposure or otherwise mitigate potential health risks presented by the carbon nanotube chemical structures.

Ethanol Production and Combustion

Ethanol fuel production is increasing in the U.S.,[198] in part due to its potential (in concert with other alternative fuel strategies) to reduce U.S. dependence on foreign oil. Though it can be produced from plant matter such as switchgrass and cellulose, ethanol fuel is made primarily from corn.[199] Another factor encouraging ethanol fuel use is the ability to produce and refine the renewable raw material domestically. Ethanol production expansion also has been driven by favorable revisions to renewable fuels standards and tax credits.[200] However, its primary benefit is its purported ability to reduce air pollution.[201] Because it contains 35 percent oxygen, ethanol already is used as a fuel additive to help gasoline burn more completely, thereby reducing levels of carbon monoxide and carcinogenic benzene and butadiene pollution typically resulting from gasoline combustion. As a fuel additive, ethanol is blended at 10 percent with gasoline, a mixture referred to as E10.

...we don't think enough about engineering and about what drives industry and what drives how they make things and how we can interact with that kind of process engineering mentality to have a meeting of the minds where toxicity, effluent, and limitation of exposure are as important as the profit and aren't counted in the profit.

JEANNE MAGER STELLMAN
SUNY-DOWNSTATE MEDICAL CENTER

Though available data are limited, a review[200] of evidence regarding the environmental effects of fuel blends with 15 percent (E15) or greater ethanol content indicate that their combustion increases levels of formaldehyde and acetaldehyde, which EPA classifies as probable human carcinogens.[202] Moreover, production and combustion of E15 or higher ethanol-gasoline blends have been found to contribute to increased levels of other air pollutants including nitrogen oxides, volatile organic compounds, ozone, and particulate matter.[200] As the review author notes, increased ethanol fuel use may simply substitute one set of air pollutants for another.

CHAPTER 2

Exposure to Contaminants From Agricultural Sources

The entire U.S. population is exposed on a daily basis to numerous agricultural chemicals. Many of these chemicals are known or suspected of having either carcinogenic or endocrine-disrupting properties. The following sections describe the agricultural workforce, the population group most heavily exposed to these chemicals, and hazards associated with specific agricultural chemicals and veterinary pharmaceuticals.

The Agricultural Workforce

In 2007, approximately 1.75 million full-time workers were employed in agricultural production.[203] Unlike nearly all other industries in the U.S., families typically share in agricultural work; half of all farm-based children under age 20 perform farm work and an additional 307,000 children and adolescents are hired to work on farms.

In addition, between three and five million individuals and their families work as migrant or seasonal workers.[204] Due to working and housing conditions, including lack of child care that forces parents to take their children with them into the fields, these workers and their families often have disproportionate exposures to pesticides and other agricultural chemicals.[205] Many migrant workers are not provided with protective clothing or equipment. Further, migrants often have limited access to health care and may experience poor communication with health care providers due to language differences. Undocumented workers are likely to avoid seeking health care even if they become ill. These factors, combined with the mobility of the migrant population, have made it difficult to assess the magnitude of health problems migrants suffer as a result of their exposure to agricultural chemicals.

As with industrial chemicals and other environmental exposures, children are at higher risk for cancer and other adverse health effects from pesticide exposures. Risks for childhood cancers are linked with parental pesticide exposure prior to conception, *in utero* exposures, and direct exposures throughout childhood.[206] Chemical exposure levels of agricultural

Migrant workers and contract workers...are difficult to identify; it's certainly hard to track them, but they have the potential and often the reality of higher exposures and less monitoring.

ELIZABETH FONTHAM
LOUISIANA STATE UNIVERSITY

families (and in some cases, other rural residents) tend to be higher than the general population. As is the case with workplace chemicals and other agents, these substances often are introduced into the home on shoes and clothing, and when work clothes are washed with other family laundry. Pesticide levels in carpet dust in the homes of agricultural workers and non-farming families can be 10- to 200-fold higher than levels in the air inside the same home,[207,208] increasing exposure risk to children who are likely to crawl and play directly on the carpet. Leukemia rates are consistently elevated among children who grow up on farms, among children whose parents used pesticides in the home or garden, and among children of pesticide applicators.[209–211] Because these chemicals often are applied as mixtures, it has been difficult to clearly distinguish cancer risks associated with individual agents.

The ongoing NIH-sponsored Agricultural Health Study[212] (AHS) involves more than 89,000 participants, including private and commercial pesticide applicators and their spouses. The goals of the study are to investigate the effects of environmental, occupational, dietary, and genetic factors on the health of the agricultural population.[212] Among other findings, the AHS has found that although overall cancer rates among farmers and pesticide applicators are not higher than other men and women in the study states (IA and NC), there are increased risks for specific cancers. Farmers and pesticide applicators have significantly higher prostate cancer risk, and female spouses have a significantly higher incidence of melanoma. Female pesticide applicators have significantly higher incidence of ovarian cancer.[213]

Exposure to Chemicals Used in Agriculture

The chemicals most commonly used in agricultural settings are pesticides (including insecticides, herbicides, and fungicides), and fertilizers. Agricultural chemicals can be carried far from their application sites by wind and through soil and groundwater contamination. Some of these chemicals

break down very slowly and are persistent in the environment, even in non-agricultural areas. In addition, residues of agricultural chemicals are found in fruits, vegetables, grains, and beverages that are made from contaminated plants and water. Meats and dairy products also can be contaminated by the water and feed provided to livestock.

Pesticides (Insecticides, Herbicides, and Fungicides)

Nearly 1,400 pesticides have been registered (i.e., approved) by the Environmental Protection Agency (EPA) for agricultural and non-agricultural use.[214] Exposure to these chemicals has been linked to brain/central nervous system (CNS), breast, colon, lung, ovarian (female spouses), pancreatic, kidney, testicular, and stomach cancers, as well as Hodgkin and non-Hodgkin lymphoma, multiple myeloma, and soft tissue sarcoma.[147] Pesticide-exposed farmers, pesticide applicators, crop duster pilots, and manufacturers also have been found to have elevated rates of prostate cancer, melanoma, other skin cancers, and cancer of the lip.[215]

Approximately 40 chemicals classified by the International Agency for Research on Cancer (IARC) as known, probable, or possible human carcinogens, are used in EPA-registered pesticides now on the market.[216–219] Some of these chemicals are used in several different pesticides; for example, chromium trioxide, an IARC Class 1 carcinogen (carcinogenic to humans), is used in 14 different pesticide products from five different companies. Thus, the total number of registered pesticide products containing known or suspected carcinogens is far greater than 40, but few have been severely restricted in the United States. Among those that have been banned, or had their use restricted, are DDT, ethylene oxide, dimethlhydrazine, hexachlorobenzene, and some chlorophenoxy herbicides.[215]

An average of 18 new pesticides are introduced every year.[220] EPA standards for registration are primarily risk-benefit based. A pesticide will be registered for use if EPA determines that it does not pose "unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."[221]

I believe it is time for a new human experiment. The old experiment…is that we have sprayed pesticides which are inherent poisons…throughout our shared environment. They are now in amniotic fluid. They're in our blood. They're in our urine. They're in our exhaled breath. They are in mothers' milk….What is the burden of cancer that we can attribute to this use of poisons in our agricultural system?…We won't really know the answer until we do the other experiment, which is to take the poisons out of our food chain, embrace a different kind of agriculture, and see what happens.

SANDRA STEINGRABER
ITHACA COLLEGE

In the aggregate, registered pesticides contain nearly 900 active ingredients, many of which are toxic. Many of the inert ingredients in pesticides also are toxic, but are not required to be tested for causing chronic diseases such as cancer. For example, xylene is used as the inert ingredient in almost 900 pesticides[222] and has been associated with increased risk of brain tumors, rectal cancer, and leukemia.[223]

Pesticides, when applied to fields, don't always stay where they're intended to stay.

PEGGY REYNOLDS
NORTHERN CALIFORNIA CANCER CENTER

A key concern regarding pesticide use is whether, and to what extent, food products are contaminated with these chemicals. To estimate pesticide contamination of foods purchased by consumers, the Department of Agriculture's Pesticide Data Program (PDP)[224] samples more than 80 types of fruits, vegetables, nuts, meat, grains, dairy products, and other foods to identify and quantify residues from insecticides, herbicides, fungicides, and growth

regulators. The foods, including processed and imported products, are collected from 10 states representing all regions of the country; the samples are collected as close to the point of consumption as possible. In its most recent report, PDP analyzed 11,683 samples, conducting an average of 105 tests on each sample (more than 1.22 million analyses in total). Only 23.1 percent of samples had zero pesticide residues detected, 29.5 percent had one residue, and the remainder had two or more.[224] The majority of residues detected were at levels far below EPA tolerances (limits on pesticide residues on foods; referred to as maximum residue limits, or MRLs, in many other countries) but the data on which the tolerances are based are heavily criticized by environmental health professionals and advocates as being inadequate and unduly influenced by industry.

We use 80 million pounds [of atrazine] annually in the United States. It's the number-one pesticide contaminant of ground water, surface water, and drinking water. It's used in more than 80 countries but it's now outlawed in all of Europe or, as the company likes to say, has been denied regulatory approval. The main point here is that here's a compound that we use 80 million pounds of, and it's illegal in the home country of the company that makes it.

TYRONE HAYES
UNIVERSITY OF CALIFORNIA, BERKELEY

Atrazine

Atrazine is a broad leaf herbicide that has become ubiquitous in the population. Used primarily in corn production, approximately 80 million pounds of atrazine are applied annually in the U.S.—more than any other agricultural pesticide.[225] Atrazine is used to increase crop yields by preventing weeds from growing and stealing nutrients from the crop, but some evidence suggests that eliminating its use would have little impact on usable crop levels.[226]

Atrazine has been shown to affect mammary gland development in animal studies,[227] with some findings suggesting multigenerational effects.[228,229] The relatively few human studies of atrazine carcinogenicity have been inconclusive.[230] IARC has classified atrazine as a group 3 human carcinogen (not classifiable as to its carcinogenicity).[231] EPA has faced considerable criticism from the media and environmental groups on its oversight of atrazine and 2003 renewal of atrazine's classification as "not likely to cause cancer in humans." In October 2009, EPA announced a comprehensive reevaluation of atrazine's cancer and non-cancer effects based on the latest scientific data.[232] The evaluation is expected to be completed in September 2010; EPA will determine at that time whether the agency's regulatory position on atrazine should be revised and if new restrictions are needed to better protect health and the public.

DDT and Metabolites (e.g., DDE, DDD)

DDT was banned in the United States in 1973, but it remains important because it persists in the environment. It is found worldwide in the breast fat of humans and animals,[233] in human breast milk, and in placenta.[234] DDT is believed to be an endocrine disruptor. Girls exposed to elevated levels of DDT before puberty, when mammary cells are more susceptible to carcinogenic effects of

chemicals, hormones, and radiation, are five times more likely to develop breast cancer in middle age.[235] Because many American women exposed to high DDT doses in childhood have yet to reach middle age, the public health significance of DDT exposure may be larger than currently is apparent. A recent study indicated that males exposed to DDT were 1.7 times more likely to develop testicular germ cell tumors (TGCT) than men not exposed.[236] Since TGCTs likely are initiated very early in life, these findings raise the possibility that exposure during fetal development or through breastfeeding may increase TGCT risk.

In the most recent PDP sampling, DDE p,p' was the most frequently detected of the DDT metabolites. The chemical was found in 60 percent of heavy cream samples, 42 percent of kale greens, 28 percent of carrots, and at lesser percentages in many other foods sampled. In all cases, the residue levels detected were much lower than the FDA action levels, but the findings demonstrate the persistence of this carcinogen in the food supply and the environment.

...I'm a two-time breast cancer survivor [and] a scientist....I did everything healthy....this atrazine—it's everywhere...I wasn't being protected by the government and I resent that terribly....my children, my in-laws, my grandchildren are being exposed to this...and, you know, I want something done about it. I want something done about it now.

PEGGY FOLLY
BREAST CANCER SURVIVOR, INDIANA

Fertilizers

Nitrogen Fertilizers

By applying nitrogen fertilizers, burning fossil fuels, and replacing natural vegetation with nitrogen-fixing crops, humans have doubled the rate of nitrogen deposition onto land over the past 50 years.[237] Nitrogen fertilizers may increase cancer risk due to the breakdown of nitrogen by digestive enzymes. Most of the nitrogen in fertilizers is converted to nitrate that seeps into groundwater. Nitrate levels in groundwater under agricultural areas can be several- to 100-fold higher than levels under natural vegetation.[238] Rural populations in agricultural areas may have a much greater likelihood of elevated nitrate

exposures compared with those using public water supplies. Nitrate levels also can be high in streams and rivers due to runoff of nitrogen fertilizer from agricultural fields. Almost all public water supplies, however, have nitrate levels below the EPA Maximum Contaminant Level (MCL) of 10 mg/L.

Ingesting contaminated drinking water is the primary route of human exposure to nitrate from nitrogen fertilizers.[239] Nitrates in drinking water are important because the most likely known mechanism for human cancer related to nitrate is the body's formation of N-nitroso compounds (NOC), which have been shown to cause tumors at multiple organ sites in every animal species tested, including neurological system cancers following transplacental exposure.[240] Nitrite, the reduced form of nitrate, reacts in the acidic stomach to form nitrosating agents that then react with certain compounds from protein or other sources such as medications to form NOCs. NOC formation is inhibited by dietary antioxidants found in vegetables and fruits, which may account in part for the observed protective effect of fruits and vegetables against many cancers.[239]

Agricultural policy in this country has also encouraged the extensive use of fertilizers and that has resulted in the problems that we've seen with contamination of water supplies, which in addition to the concerns about human ingestion of nitrates, has large ecologic effects related to eutrophication [overgrowth of plant life and loss of oxygen in water].

MARY WARD
NATIONAL CANCER INSTITUTE

In humans, nitrosamines and NOCs are suspected brain and CNS carcinogens. In addition, a cohort study of older women in Iowa[241] found that those whose drinking water had higher long-term average nitrate levels had an increased risk of bladder and ovarian cancers. Other studies have had mixed results or shown no association with nitrate intake. Small numbers of epidemiologic studies of any one cancer site have been conducted; such research is needed to identify other potential nitrate-related cancer risks.[239] Limited mechanistic studies suggest that nitrate at levels below the MCL could be carcinogenic.[242] Further research into this question is warranted, particularly because nitrate levels continue to rise in groundwater as use of nitrogen fertilizers increases. With greater production of corn for fuel, nitrate levels in drinking water are likely to continue their upward trend.

Some research indicates that crop rotation and/or the use of cover crops (i.e., grass or legumes planted on a field between production seasons) can reduce or negate the need for nitrogen fertilizers without sacrificing crop yields.[243,244] Legume cover crops can fix (capture) nitrogen, which preserves it for the next growing season and prevents nitrogen in the soil from leaching into groundwater.

Phosphate Fertilizers

Phosphate fertilizers are often contaminated with cadmium and are responsible for significant cadmium soil and water contamination. Fertilized soils have been found to have two to six times the cadmium concentration of nearby unfertilized land.[245]

In the food supply, cadmium is most highly concentrated in grains and seafood. For decades, residents of Southern Louisiana have had pancreatic cancer rates markedly higher than the national average.[246] Research has demonstrated an association of rural residence, dietary factors (high consumption of rice, seafood, and pork), and cigarette smoking with higher pancreatic cancer risk, particularly among persons of Acadian (Cajun) ancestry.[247] Cadmium appears to be the common factor in all of these variables. Rice fields in the area are treated with cadmium-containing phosphate fertilizers, which is taken up into the rice, the predominant starch in Acadian diets. After the rice harvest, the fields are again flooded, and crawfish, a staple seafood in the local diet, are farmed in the previously fertilized fields. Urinary cadmium excretion levels in studied Louisiana pancreatic cancer patients have been found to be more than four-fold higher than control subjects.[247]

Industrially, cadmium is used in manufacturing processes such as electroplating, production of polyvinyl chloride (PVC) products, and nickel-cadmium batteries. An estimated half-million manufacturing workers are exposed to cadmium.[248]

Phosphate fertilizers also accelerate the leaching of arsenic from soils into groundwater.[249] The arsenic soil contamination is often the result of previous fertilization with arsenic-containing pesticides. Further, the addition of phosphates to soil has been found to increase arsenic accumulation in wheat.[250]

Veterinary Pharmaceuticals

Except for animals raised on organic farms, most livestock in feed lots and poultry farms are given antibiotics, growth hormones, and feed that may consist in part of animal tissue that itself may be contaminated by these drugs. When excreted, these medications become part of the toxic run-off from agricultural operations. The impact of this contamination on human cancer is unknown at this time, but there is speculation that the growth hormones may contribute to endocrine disruption in humans.

...agricultural exposures are very complex. We have talked a lot about pesticides but there are many other exposures that are agricultural as well and they are agricultural in an occupational setting but they expand into the general environment, and people are exposed through contaminated water. They are exposed through food, as well as the occupational exposures.

LAURA BEANE FREEMAN
NATIONAL CANCER INSTITUTE

CHAPTER 3

Environmental Exposures Related to Modern Lifestyles

Conveniences of modern life—automobile and airplane travel, dry cleaning, potable tap water, electricity, and cellular communications, to name a few—have made daily life easier for virtually all Americans. Many of these conveniences, however, have come at a considerable price to the environment. Some of the environmental effects of modern life are known or suspected of harming human health.

Air Pollution

In June 2009, the Environmental Protection Agency (EPA) released the results of its most recent National-Scale Air Toxics Assessment (NATA), which is conducted every 3 years to estimate concentrations of air pollutants across the country, population exposures, and the potential public health risk due to air toxics inhalation.[80] Using the most current available air emission inventory (2002) and census data, NATA characterized cancer and non-cancer effects from inhaling the 124 air toxics on which chronic exposure health data exist. Of the toxics assessed, 80 are carcinogens.

NATA estimated that the average increased cancer risk in 2002 due to inhalation of outdoor air toxics was 36 per million; that is, an additional 36 people per million (approximately 11,000 Americans based on current population estimates) could be expected to develop cancer as a result of breathing air toxics compared to those not exposed. The estimate assumes that individuals would be exposed at 2002 levels over the course of their lifetime.[251]

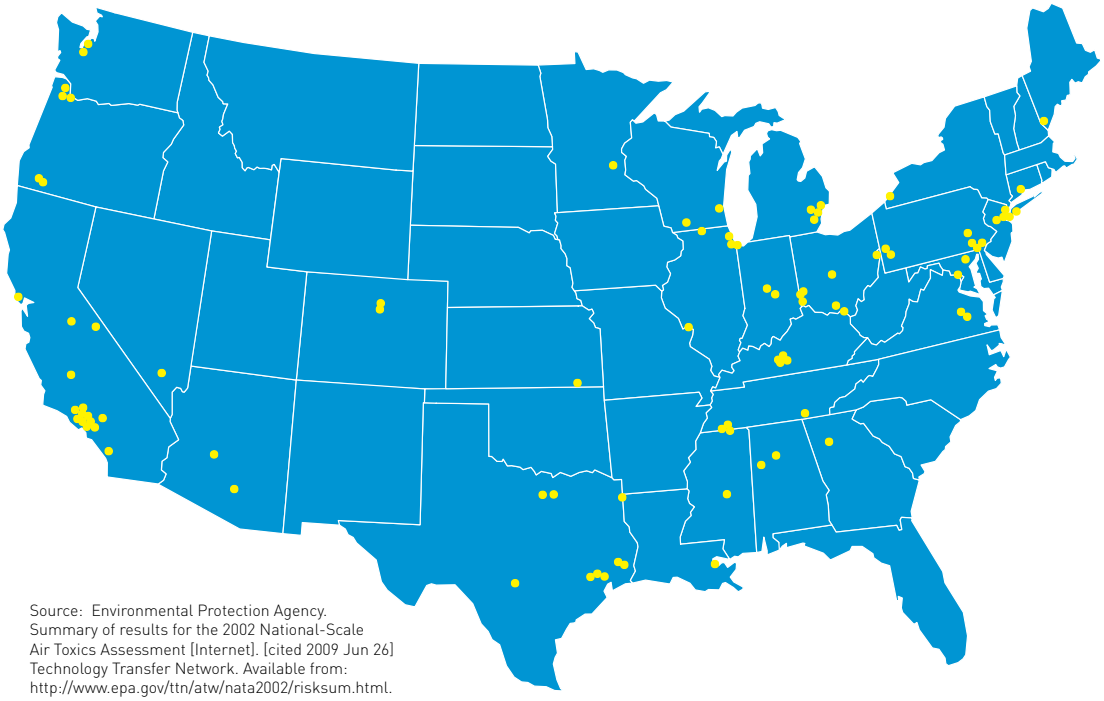
Figure 5 shows the distribution of the estimated 2 million Americans (<1 percent of the total U.S. population) with a cancer risk greater than 100 per million. Some of the areas shown are "hotspots" created by local industrial emissions. Examples of these emissions include tetrachloroethylene from dry cleaning operations and methylene chloride, a commonly used industrial solvent. NATA results indicate that local industry emissions account for about 25 percent of the average overall cancer risk due to air toxics.[251] EPA is preparing a NATA update using 2005 data that is expected to be released in late 2009 or early 2010.

Mobile Sources of Air Pollution

According to the 2002 NATA results, emissions from personal cars, power boats, off-road vehicles, and other on-road vehicles, excluding particulate matter from diesel exhaust, account for about 30 percent of the overall cancer risk from air pollutants. The majority of this risk is from benzene,

Figure 5

Census Tracts with 2002 NATA Estimated Cancer Risk Greater Than 100 Per Million



Source: Environmental Protection Agency. Summary of results for the 2002 National-Scale Air Toxics Assessment [Internet]. [cited 2009 Jun 26] Technology Transfer Network. Available from: http://www.epa.gov/ttn/atw/nata2002/risksum.html.

a known carcinogen. Smog, so common in many large urban areas, is composed of varied and changing mixtures of toxic gases (e.g., formaldehyde, benzene, sulfuric acid) and suspended particulates. Incomplete petroleum product combustion produces the particles most commonly found in smog.

U.S. regulation of air pollution is exceptionally fragmented and probably exceptionally costly for what it actually accomplishes.

WINIFRED HAMILTON
BAYLOR COLLEGE OF MEDICINE

Environmental Tobacco Smoke (ETS)

Tobacco smoke contains approximately 4,000 chemicals, including 69 known carcinogens.[252,253] Tobacco use (including the use of smokeless tobacco) is the number one cause of preventable death in the United States.[254] It is responsible for an estimated 87 percent of U.S. lung cancer deaths.[255] ETS, also referred to as secondhand smoke, passive smoking, and involuntary smoking, causes an estimated 3,400 annual lung cancer deaths among non-smokers in the U.S.[256] and evidence indicates that ETS exposure increases breast cancer risk.[257–259] In 2006, the U.S. Surgeon General stated that there is no safe level of exposure to environmental tobacco smoke.[260]

In 2006–2007, the President's Cancer Panel held hearings on tobacco use and cancer. The Panel's findings, conclusions, and related recommendations are contained in its August 2007 report.[261] Among other recommendations, the Panel strongly urged that the Food and Drug Administration (FDA) be empowered to regulate the contents, marketing, and sales of tobacco products. In June 2009, the Family Smoking Prevention and Tobacco Control Act[262] was signed into law.

Much progress has been made over the past decade in protecting workers from occupational exposure to tobacco smoke.

As of July 2009, 17,059 municipalities were covered by a smoke-free provision (in workplaces and/or restaurants and/or bars) that collectively cover almost 71 percent of the U.S. population.[263] A substantial number of workers, however, continue to be exposed to tobacco smoke on the job. Bar and restaurant workers continue to have among the highest exposure rates. All of the issues related to tobacco-related cancers in the workplace also apply to tobacco use and tobacco smoke exposures in the home and around children.

Drinking Water Contamination

Americans' drinking water comes from groundwater and rain that fills streams, reservoirs, rivers, lakes, and ultimately, the oceans. Chemicals improperly stored and disposed of by industry and individuals alike soak into the soil and eventually leach into groundwater. As clouds and rain, water absorbs chemicals in the air. As a result, the water we drink is steeped in varying mixtures of chemicals and other substances. Some of these contaminants are not harmful to human health in trace or extremely small amounts, while others can cause or contribute to numerous diseases, including cancer.

Assessing health hazards due to drinking water contamination is difficult, since it typically is challenging to estimate the levels and timing of exposures and the specific chemicals involved. It also can be difficult to define exposed populations clearly and select the most appropriate disease endpoints or intermediate biologic markers for study. Further, it often is not possible to identify the cause of observed health effects when there are multiple exposures or to link specific health effects with individual chemicals that occur in mixtures.

Public water filtration and treatment plants remove some contaminants, but current technologies cannot remove them all.

Water treatment systems vary significantly across the country since they are tailored (to the extent practicable) to treat the water contaminants that are found in each vicinity. Arsenic, microbes, nitrates, radium, uranium, selenium, antimony, sulfate, magnesium, calcium, iron, manganese, potassium, phosphorous, and other metals are among the substances commonly removed from drinking water supplies.[264] Because of concerns about water pollution, some people use home filtration systems to further treat water from public supplies or wells and/or use bottled water for drinking and cooking.

...in a country where I work hard and I vote, I feel like I have been involuntarily exposed to things that could have made me sick and I can't make informed decisions when that's the situation.

KATRINA COOKE
BREAST CANCER SURVIVOR, INDIANA

Water Supplies

Public Systems

Most Americans rely on public systems for the water they use for drinking, cooking, irrigating crops (including feed crops) and ornamental plants, and watering livestock. As Table 4 shows, the U.S. population is served by more than 52,000 community water systems. The quality of drinking water is regulated by the Safe Drinking Water Act (SDWA) of 1974, but enforcement takes place at the state level.[180] The legislation authorizes EPA to establish standards (Maximum Contaminant Levels, or MCLs) to protect tap water and requires that owners and operators of public water systems comply with these standards. Regulated chemicals in drinking water include 53 organic chemicals (e.g., atrazine, benzene), 16 inorganic chemicals (e.g., arsenic, nitrate), 7 disinfection by-products (e.g., trihalomethanes), 6 microorganisms (e.g., *cryptosporidium*), and 4 radionuclides (e.g., alpha particles from radon, radium).

Table 4

Community Water Systems in the United States

SYSTEM SIZE	NUMBER OF SYSTEMS	PERCENT OF SYSTEMS	POPULATION SERVED (IN MILLIONS)	PERCENT OF POPULATION
Very Large (>100,000)	398	1%	129	45%
Large (10,001–100,000)	3,702	7%	105	37%
Medium (3,301–10,000)	4,822	9%	29	10%
Small (501–3,300)	13,906	27%	20	7%
Very Small (<500)	29,282	56%	5	2%
Totals	**52,110**	**100%**	**286**	**100%**

Source: U.S. Environmental Protection Agency. Factoids: drinking water and groundwater statistics for 2007. EPA Office of Water. EPA 816-K-07-004; 2007.

However, an analysis[265] of more than two million drinking water test results acquired from 42 state water offices found 260 contaminants in tap water. Of these, 141 contaminants have no safety standards. Forty (40) of the unregulated contaminants were detected in tap water consumed by at least one million people.

EPA typically sets a level that they would call safe, which is as close to zero risk as they can get, and then they say, well, we can't do that because that costs money, so let's come up with another number that allows a certain amount of risk as a trade-off for cleaning up the water… I think our public policies need to be revisited because we're trading disease for costs probably unnecessarily.

RICHARD WILES
ENVIRONMENTAL WORKING GROUP

Private Wells

It should be noted that the population distribution shown in Table 4 does not account for the 10–15 percent of the U.S. population that uses wells or other private water supplies. Water from wells is not subject to SDWA standards, but usually is regulated by state programs. In 2009, the U.S. Geologic Survey (USGS) released a report on the quality of water from about 2,100 domestic wells throughout the United States;[46] samples were collected between 1991 and 2004. The analysis found that 23 percent of sampled domestic wells contained one or more contaminants at a concentration greater than EPA MCLs for public water supplies, or USGS Health-Based Screening Levels. Contaminants most often above benchmark levels were inorganic chemicals, with all but nitrate primarily from natural sources. Higher nitrate concentrations were more common in areas with intense agricultural land use, due primarily to fertilizers, livestock, and septic systems. Man-made organic compounds were detected in 60 percent of sampled wells, but concentrations seldom were above EPA MCLs. Contaminants usually co-occurred with other contaminants as mixtures, with the most common mixture consisting of nitrate, arsenic, radon, and uranium.

Bottled Water

Many bottled water users assume that it is cleaner than tap water. Bottled water is regulated by the FDA, and while standards for lead content are more stringent than Federal public water standards, other quality

standards are the same as Federal limits for public supplies. Bottlers, however, are not required to disclose either the content or the source of their water, as is the case for public supplies. Some bottled water is simply drawn from municipal supplies and receives no additional filtration or other treatment.

One study[266] has shown that the contaminant levels in bottled waters vary widely. Some of the 10 brands tested were found to be of no better quality, and in some cases were worse, than water available from municipal water systems. The testing found an average of eight contaminants in each brand. Half of the brands tested contained bacterial contamination. Two carcinogens were found in some of the samples at levels exceeding California and/or industry standards. Also detected were caffeine, the pharmaceutical acetaminophen, arsenic, radioactive isotopes, nitrates and ammonia from fertilizer residue, and industrial chemicals including solvents, degreasing agents, and propellants. Trace amounts of acetaldehyde, isobutane, and toluene also were found, but the investigators could not ascertain health effects at the low levels detected.

In addition to the contaminants indicated above, plastics such as BPA can leach from the bottle itself into the water it contains.

Wherever you chlorinate water, you have chlorination by-products... there is strong evidence that disinfection by-products are carcinogenic for bladder cancer.

KENNETH CANTOR
NATIONAL CANCER INSTITUTE

Water Disinfection By-Products (DBP)

Disinfection of public water supplies has dramatically reduced the incidence of waterborne illnesses and related mortality in the United States, with unquestionable public health benefit. However, chemical by-products are formed when disinfectants such as chlorine react with organic matter, and long-term exposure to these chemicals may increase cancer risk.

Hundreds of disinfection by-products have been identified; the most common of these are trihalomethanes (THMs, including chloroform, bromoform, and others) and haloacetic acid. Only a small percentage of identified DBPs have been tested for carcinogenicity. Some rodent studies have been positive for cancer, and some DBP components have shown mutagenic effects in *in vitro* testing, suggesting carcinogenicity.[267]

The Federal standard for disinfection by-products in public water supplies is 80 parts per billion of THM as an annual average.[268] THMs are measured because they generally reflect levels of other chemicals in DBP mixtures. If not controlled, DBPs in water systems can range up to several hundred parts per billion. In addition, a recent study[269] suggests that THM levels vary within a water system, with the highest levels found in water that stays in the system the

longest after disinfection. In this study, rectal (bromoform THM only) and bladder cancer risks were highest among those who consumed the greatest amount of water at points within the distribution system with the oldest post-disinfection tap water.

People are exposed to DBPs through consumption and through inhalation and absorption through the skin during bathing, showering, and swimming in chlorinated pools.[267] Relatively little research has been done on DBPs and cancer; the strongest data show increased bladder cancer risk with long-term (up to 40 years) exposure to DBPs, particularly among men.[270] In addition, several metabolic pathways and key genes have been identified that may increase bladder cancer risk among individuals with common variants in these genetic factors. Other very limited research suggests possible DBP associations with colon and rectal cancer, renal cell carcinoma, and glioma.[271,272] One speaker underscored the need for further research on DBPs and cancer, noting that exposure assessments should account for at least 35 years of exposure prior to a cancer diagnosis. DBPs represent a situation in which observed relative risks are modest, but because of the high numbers of people exposed, such risks may translate into potentially significant public health problems.

Metals such as beryllium, cadmium, and lead from industrial sources are found in U.S. water supplies, usually under 100 micrograms per liter (µg/L), but can increase or decrease due to water treatment. Little research has been conducted on possible cancer risks associated with these trace minerals in drinking water.

Landscaping Use of Agricultural Chemicals

Fertilizers, herbicides, and pesticides used for residential and other landscaping purposes (e.g., parks, golf courses), in some cases the same as those used on farms, represent a considerable component of water contamination because they seep into groundwater and run off into streams, rivers, and other drinking water supplies. About a quarter of the pesticides used annually in the U.S. are for landscaping purposes.[273]

Landscaping workers who apply these chemicals to lawns and other non-agricultural sites can sustain high levels of exposure, with cancer risks similar to those of farm workers. Homeowners can be exposed to fertilizers, herbicides, and insecticides when mowing residential lawns after chemicals have been recently applied and by handling and applying chemicals themselves. Children may be exposed when playing in areas where chemicals have been applied. In addition, individuals can be exposed to these chemicals by swimming in or eating seafood from contaminated bodies of water.

Electromagnetic Energy

Electromagnetic fields (EMF), also referred to as electromagnetic radiation (EMR), is the non-ionizing energy generated by the growing multitude of wired and wireless technologies that are so much a part of life in developed countries and, increasingly, worldwide. There are two types of EMF/EMR: radiofrequency radiation (RF) and extremely low frequency electromagnetic fields (ELF). RF is emitted by cellular and cordless telephones, cellular antennas and towers, radar, and broadcast transmission towers. ELF comes from electric power lines and from electrical and electronic appliances. Table 5 provides definitions and conversions for units of measure used to describe non-ionizing radiation.

Cellular Telephones and Other Wireless Devices

As Figure 6 illustrates, cellular (mobile) telephone use in the United States has grown rapidly since the mid-1980s, with especially large annual increases in

this decade. According to the Cellular Telecommunications and Internet Association, Americans spent a total of 2.2 trillion minutes on their mobile phones in 2008, up 100 billion minutes from the previous year.[274] Usage is expected to continue to rise, along with the use of other wireless devices and networks, as these become affordable for greater proportions of the population and more people give up their landlines in favor of wireless phones. Cell phone use also is becoming increasingly common among children, for many of whom electronic communications (e.g., text messaging, social networking, access to games and music) are considered a crucial link to friends and their overall social milieu. Similarly, many parents now provide cell phones to their children to help coordinate and facilitate family activities, and as a means of communication in the event of an emergency.

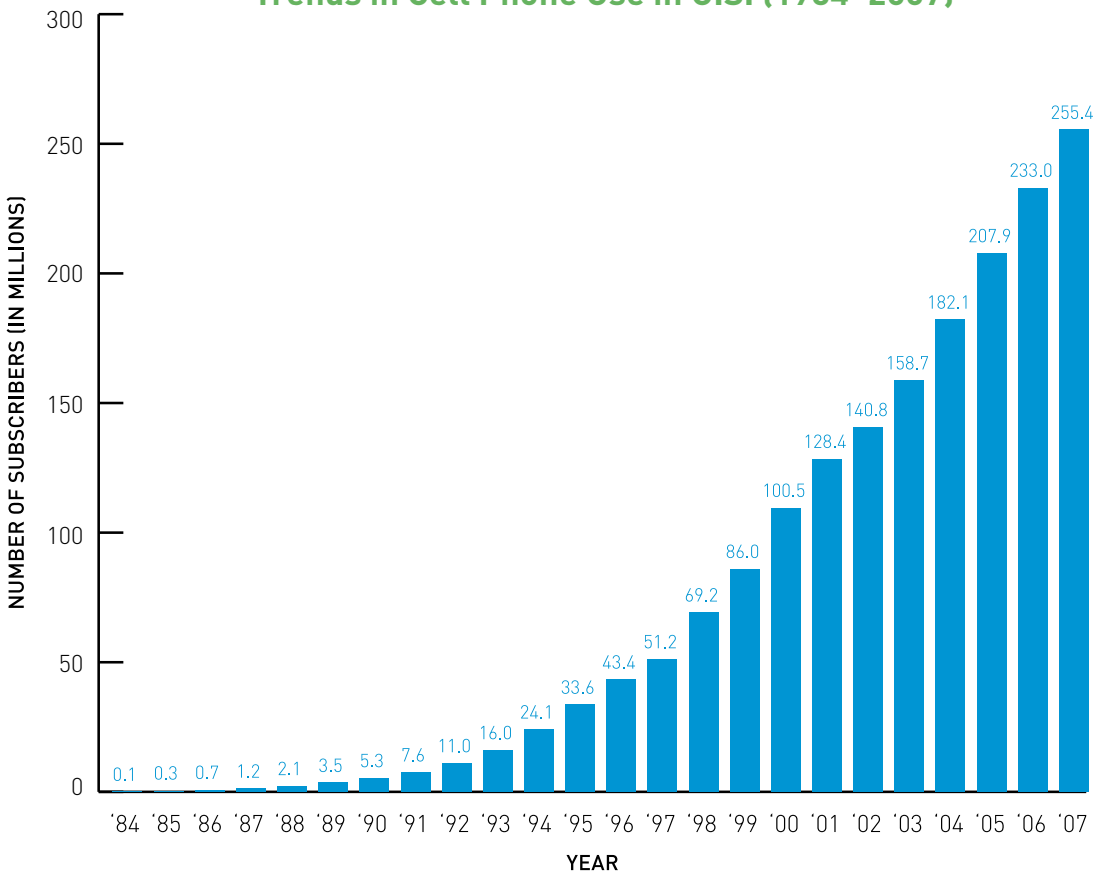
As the use of cell phones has increased, so has concern about their potential harmful health effects, particularly whether cell phone users are at greater risk for brain cancer. Cell phones and related devices become more sophisticated each year, and they are producing energy at increasingly higher radiofrequencies necessary for their expanded functions. The number of cell phone towers also is growing as cellular service providers strive to provide customers a maximally robust network. At the same time, patterns of cell phone use appear to be

...with over a million people using cell phones, even if the risk is of an increase in brain tumors that's relatively small, say 5 or 10 percent. Five or 10 percent of a million people is going to be a very, very large number.

MICHAEL LERNER
COMMONWEAL

Trends in Cell Phone Use in U.S. (1984–2007)

Figure 6



Source: Cellular Telecommunications and Internet Association [Internet]. [cited 2009 Jan 9] Available from: http://www.ctia.org.

changing, with a rising proportion of people using headsets or using the phone primarily to send and receive text messages. Using a cell phone in these ways dramatically reduces the time during which the phone is held against the head, and therefore, reduces individuals' cranial exposure to RF.

...the most urgent issue that we need to address... is whether children or adolescents using cell phones are at increased risk. Studies on ionizing radiation have shown that children are most sensitive among all members of populations in terms of carcinogenic exposure to ionizing radiation.

MARTHA LINET
NATIONAL CANCER INSTITUTE

Considerable disagreement exists within the scientific community regarding potential harm due to RF exposure from cellular phones and other wireless devices, and many of the available studies have been interpreted quite differently by researchers on both sides of the issue. As one speaker noted, data on the long-term use of newer equipment still are relatively sparse, and it may be several years before enough data accumulate to reach informed conclusions about the harm cell phones, cell phone towers, and other wireless devices/networks may cause.

Limited evidence suggests that risk of a brain tumor (specifically, glioma) on the same side of the head where the user typically holds the phone may be increased among long-term cell phone users,[275,276] but other studies[277,278] show no association. A 2009 meta-analysis[279] of 23 case-control studies involving almost 38,000 people found no connection between cell phone use and cancerous or benign tumors, but a subset analysis of the eight studies considered most rigorous methodologically showed that long-term cell phone users had a 10–30 percent increased risk of tumors compared with people who seldom or never used a cell phone. All but one of these eight studies were conducted by the same researcher in Sweden, which has raised questions[280] about whether specific characteristics of the Swedish population could have influenced the results. For example, a high proportion of Swedes live in rural areas, and more RF energy usually is needed to operate cell phones in rural areas; higher RF exposures in this population could be a factor in the stronger cell phone-tumor association.

Brain cancer incidence trends by age from 1973–2005 show that incidence rates have not increased apace with the explosive rise in cell phone use in the United States since 1992.[281] Studies also have assessed and failed to show an increased risk of cancer of the parotid gland, acoustic neuroma, meningioma, or uveal melanoma, even among longer-term (5–10 years) and heavier users.[282–285]

In addition, it was noted that findings from available case-control, questionnaire-based studies may be confounded by recall bias,[286] selection bias, or other questionnaire limitations. Cohort studies may avoid some of these methodologic limitations.[287] Epidemiologic study results have been limited regarding the relative importance of different RF sources. These studies also have been able to assess only short lag periods and have focused on a small number of cancer types.[288] Thus, while considerable research has been conducted on cancer

risk due to RF from cell phones, cell phone towers, and other wireless devices, the available data are neither consistent nor conclusive, and a mechanism of RF-related cancer has yet to be identified. Forthcoming results from the INTERPHONE combined studies[289] from 13 populations are expected to provide the most stable risk estimates yet on glioma, meningioma, acoustic neuroma, and parotid gland tumors. However, the methodology and partial industry funding of some of the INTERPHONE studies have been criticized.

Speakers emphasized that continued research is needed to resolve key questions, including:

- Are cancer risks increased among long-duration cell phone users of contemporary equipment?
- Do heavy users experience elevated cancer risks?
- Do children or adolescents using cell phones face increased cancer risk?

Until these questions are answered with some degree of confidence, cell phone users can reduce their exposure to radiofrequency energy by making fewer calls, reducing the length of calls, sending text messages instead of calling, using cell phones only when landline phones are unavailable, using a wired "hands-free" device so that the phone need not be held against the head, and refraining from keeping an active phone clipped to the belt or in a pocket.

In the face of uncertainty about RF energy and cell phone-related cancer risks, some researchers,[290] several countries (Germany, France, Austria, United Kingdom, Russia), and the European Environment Agency have taken a precautionary stance regarding cell phone use, particularly by children.[291] Unlike adults—even longer-term cell phone users—children have ahead of them a lifetime of RF and other radiation exposures and, therefore, special caution is prudent. At this time, no long-term epidemiologic studies of cancer risk related to cell phone use by children or adolescents are available. Large cohort studies of children's cell phone use and subsequent cancer risk are underway in Denmark and Norway, and a case-control study of cell phone use during childhood is ongoing in Denmark, Norway, Sweden, and Switzerland.[292]

Electric Power Lines and Other Sources of Extremely Low Frequency (ELF) Radiation

As with RF radiation, current and potential harm from ELF is sharply disputed within the scientific community. To an even greater degree than is the case with cell phones, determination of potential harm has to date been hampered by the great difficulty in isolating and quantifying multiple exposures,

separating the effect of such exposures from numerous potentially confounding variables, and clearly ascertaining a mechanism of injury. Some studies suggest an effect on cancer risk, while others do not.

The strongest suggestion of harm has been found in studies of people living near electric power lines, some of which found an increase in childhood leukemia rates among families living in close proximity to electric power lines compared with a control group. A 1996 review of epidemiologic studies by the National Academy of Sciences[293] concluded that the available data suggested that there were twice as many cases of leukemia among children who lived near power lines. However, many of these studies shared three weaknesses: (1) they measured the distance from the power line to the nearest part of the house—a proxy measure of the ELF inside the home, (2) the studies were not blinded, and (3) there was selection bias in choosing which children with leukemia were included in the study.[294] An NCI study[295] attempted to overcome these issues by measuring radiation levels inside the homes of all children with acute leukemia under age 15 in 9 states covered by Surveillance, Epidemiology, and End Results (SEER) cancer registries. Radiation levels were measured in a blinded manner and technicians measured radiation levels over a 24-hour period in the houses patients lived in for the 5 years prior to diagnosis. The study found no significant excess childhood leukemia risk associated with actual radiation exposures in the home.

...exposure assessment is the Achilles heel of environmental epidemiology.

PEGGY REYNOLDS
NORTHERN CALIFORNIA CANCER CENTER

Those who believe RF and ELF EMR are harmful maintain that U.S. and international organizations are denying a substantial threat to future population health and failing to protect the public. Mechanisms by which ELF EMR may be harmful have

been proposed, but are not supported by peer-reviewed research. For example, it has been suggested that these exposures can cause cells to produce stress proteins (i.e., indicating that the cell recognizes the energy as harmful).[290] The scant peer-reviewed literature on ELF EMR health effects highlights an important area in which research is needed to elucidate if, and how, ELF EMR raises risks for specific cancers in defined populations and at defined exposure levels.

Findings of a lack of association between ELF EMR from power lines or other sources and cancer are consistent among numerous international organizations, including WHO,[296,297] IARC,[298] the EU Scientific Committee on Emerging and Newly Identified Health Risks,[299] and the International Commission for Non-ionizing

Radiation Protection.[288] All emphasize the need for further research in this area. U.S. environmental organizations such as the National Institute of Environmental Health Sciences (NIEHS),[300] the Occupational Safety & Health Administration (OSHA),[301] and the American Industrial Hygiene Association[302] generally conclude that the link between ELF EMR and cancer is controversial or weak.

Ultraviolet Radiation (UV) from Sun Exposure and Tanning Devices

Exposure to UVA and UVB radiation from the sun, sun lamps, and tanning beds is the major cause of all three types of skin cancer—melanoma, squamous cell carcinoma, and basal cell carcinoma. The body of research demonstrating this causal link is extensive. IARC classifies ionizing radiation, solar, and UV radiation as Group 1 carcinogens (carcinogenic to humans).[303] In July 2009, IARC also classified UV-emitting tanning devices as a Group 1 carcinogen.[303]

In 2009, nearly 69,000 new cases of malignant melanoma will be diagnosed, and more than 8,600 people will die from this disease.[1] In addition, substantially more than one million Americans will be diagnosed with basal and squamous cell skin cancers. Though usually not life-threatening and easily cured in most cases, these lesions must be removed because they can be invasive and disfiguring.

Consistent sunscreen use can reduce or prevent the radiation damage that enables the transformation of normal skin cells to cancerous ones. Despite broad public knowledge about the risk of skin cancer from UV radiation exposure and how to avoid it (e.g., staying out of the sun when it is most intense, wearing protective clothing, using sunscreen, avoiding tanning beds and lamps), many people, particularly younger individuals, fail to protect themselves adequately from UV exposure.

At the same time, total protection from UV is also harmful, since a modest amount of UVB is required for the body to produce vitamin D in the skin. Research on the health effects of vitamin D suggests that this vitamin may be protective against numerous diseases, including some cancers, and that vitamin D deficiency may be associated with chronic diseases that are more prevalent in northern latitudes.[304,305] Vitamin D is produced rapidly and abundantly when skin is exposed to UVB in direct sunlight. The frequency and duration of sun exposure needed to produce adequate amounts of vitamin D varies depending on factors including latitude, altitude, air pollution levels, season, time of day, age, and skin type and sensitivity. Very few foods naturally contain vitamin D, and it is unclear to what extent the vitamin D in fortified foods (e.g., milk, orange juice, infant formula, some cereals and breads) or supplements is used by the body.

Radiation Exposure From Air Travel

Air travel has become relatively commonplace for some segments of the population in the U.S. and in many other nations. On the ground, cosmic radiation accounts for a small percentage of the natural background radiation to which all people are exposed (see Figure 7, Chapter 4, p. 65). At commercial aircraft altitudes, cosmic radiation can be 100 times greater than on the ground, but still is insignificant for occasional fliers.[306] According to Health Canada, the chance of a fatal cancer occurring would be approximately one percent following 30 years of flying, at 1,000 hours per year. Most people fly far less and, therefore, the chance of a fatal cancer from this exposure also would be greatly diminished. However, for those who fly frequently, such as aircrew and some business travelers, the annual exposure may be comparable with or exceed that of radiation workers in ground-based industries.[306]

CHAPTER 4

Exposure to Hazards from Medical Sources

In the past two decades, significant strides have been made in our ability to diagnose and treat human disease, including cancer. Many of these advances, particularly in diagnosis, have been made possible by improved imaging technologies and nuclear medicine examinations. Other treatment advances have been accomplished through new pharmaceutical interventions for numerous diseases. It is becoming increasingly clear, however, that some of these same drugs and technologies that have contributed so greatly to health status and longevity also carry risks. This chapter describes issues of significant concern regarding medical radiation and unintended exposure to pharmaceuticals.

Medical Radiation

Medical imaging and nuclear medicine tests have become invaluable tools for cancer and other disease screening, diagnosis, minimally invasive surgical procedures, treatment, and treatment monitoring. Speakers described trends in the use of these technologies, special considerations when imaging vulnerable populations, and training and safety issues related to imaging equipment and imaging technologists. Table 6 provides definitions of terms commonly used to describe medical radiation exposures.

Trends in Medical Imaging and Nuclear Medicine

Figure 7 indicates the contribution of various sources of radiation exposure to the total collective effective dose (see Table 6 for definitions of medical radiation dose terms) in the United States, as recently reassessed by the National Council on Radiation Protection and Measurements (NCRP).[307] NCRP is a non-profit body chartered by the U.S. Congress to make recommendations on protecting people from excess radiation exposure and on metrics for exposure assessment.

While ionizing radiation exposures from radon, occupational, and other sources have remained essentially stable over the past 30 years, Americans now are estimated to receive nearly half (48 percent) of their total radiation exposure from medical imaging and other medical sources, compared with only 15 percent in the early 1980s (Figure 8).[308]

As Figure 8 shows, computed tomography (CT) and nuclear medicine tests alone contributed 36 percent of the total radiation

Table 6

Terms Commonly Used to Describe Medical Radiation Exposure

Absorbed Dose: The physical quantity describing energy deposited per unit mass. Expressed in Grays (Gy).

Organ Dose: Energy absorbed by an organ being studied or directly in the primary radiation beam; a measure of risk associated with radiation to that organ. Usually expressed in Gy.

Effective Dose: A calculated (not measured) age- and sex-averaged value that is used as a robust measure to estimate detriment from cancer and hereditary effects due to various procedures involving ionizing radiation. Among the limitations in its use, however, is about a ±40 percent uncertainty for a "reference" patient (i.e., a hypothetical individual defined in terms of gender, ethnicity, height, and weight). Expressed in Sieverts (Sv).

Collective Effective Dose: The total estimated amount of radiation to all members of a population over a specified period of time. Expressed in Sv.

Sources:
Mettler FA Jr., et al. Effective doses in radiology and diagnostic nuclear medicine: a catalog. Radiology. 2008;248(1):254-63.

Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. N Engl J Med. 2007;357(22):51-8.

Martin CJ. Effective dose; how should it be applied to medical exposures? Br J Rad 2007;80(956):639-47.

exposure and 75 percent of the medical radiation exposure of the U.S. population.[308] In 1993, an estimated 18.3 million CT scans were performed in the U.S.; by 2007, that number had risen to nearly 69 million scans—an annual growth rate of approximately 10 percent[309] (Figure 9). Moreover, the increase in medical radiation has nearly doubled the total average effective radiation dose per individual in the United States to 6.2 millisieverts (mSv) per year.[310]

Medicine now is the largest controllable source of radiation exposure, but it remains essentially unregulated.

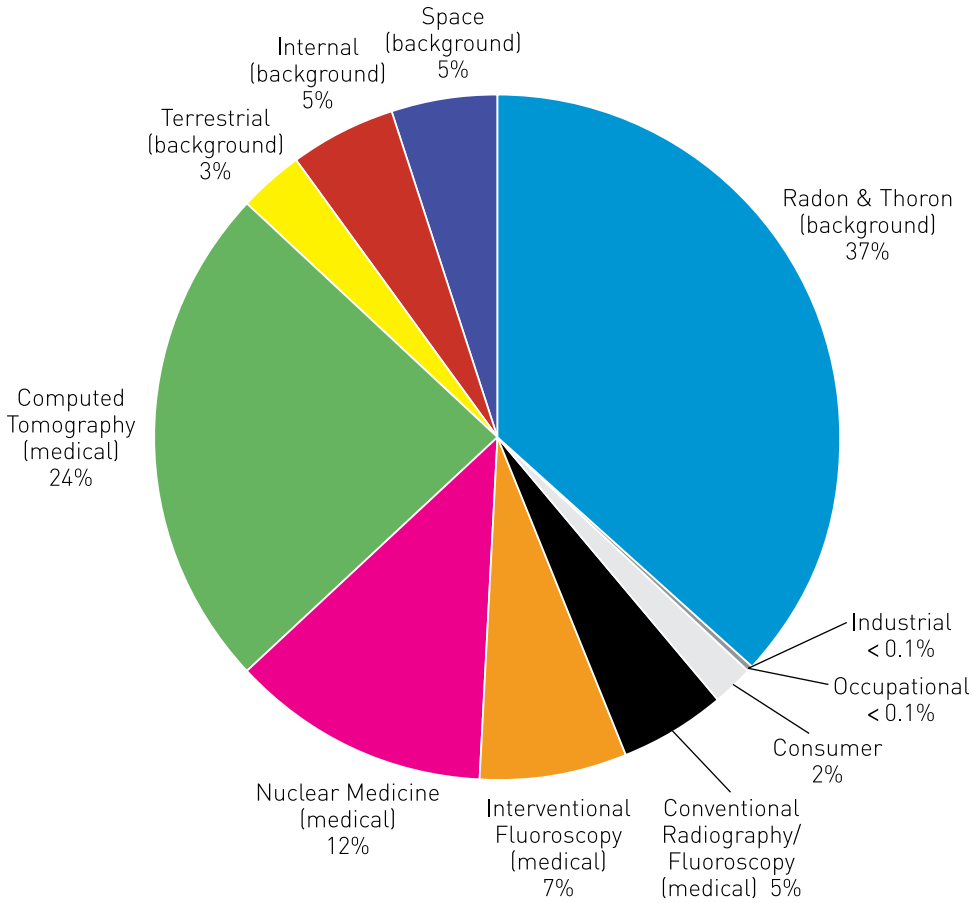
FRED METTLER, JR.
UNIVERSITY OF NEW MEXICO
NEW MEXICO VA HEALTHCARE SYSTEM

The NCRP estimates are considered somewhat controversial among medical imaging and related professionals,[311,312] who note that the per capita effective dose attributed to medical imaging assumes an equal exposure level among all individuals in the U.S. population. In fact, they emphasize, many people may not undergo any imaging studies in a given year or years, while other parts of the population (e.g., the elderly, cancer patients who receive scans to monitor treatment response, victims of auto accidents, persons in other emergency medical situations) receive a higher dose than the NCRP average. They caution that people may misinterpret the NCRP estimates and be unnecessarily fearful of receiving needed diagnostic and other imaging studies. The Panel, however, notes that the same may be said of estimated average exposures of numerous types (e.g., radon, electromagnetic fields) for which exposure levels vary across the country.

Without question, recent advances in medical imaging have saved many thousands of lives, virtually eliminated exploratory surgery (with its attendant infection and other risks), enabled the introduction of numerous minimally invasive surgical procedures, and been instrumental in earlier detection and more effective treatment of many diseases and other medical conditions. Despite these enormous benefits, however, medical radiation is not inconsequential. Table 7 lists

All Exposure Categories
Collective Effective Dose (percent), 2006

Figure 7

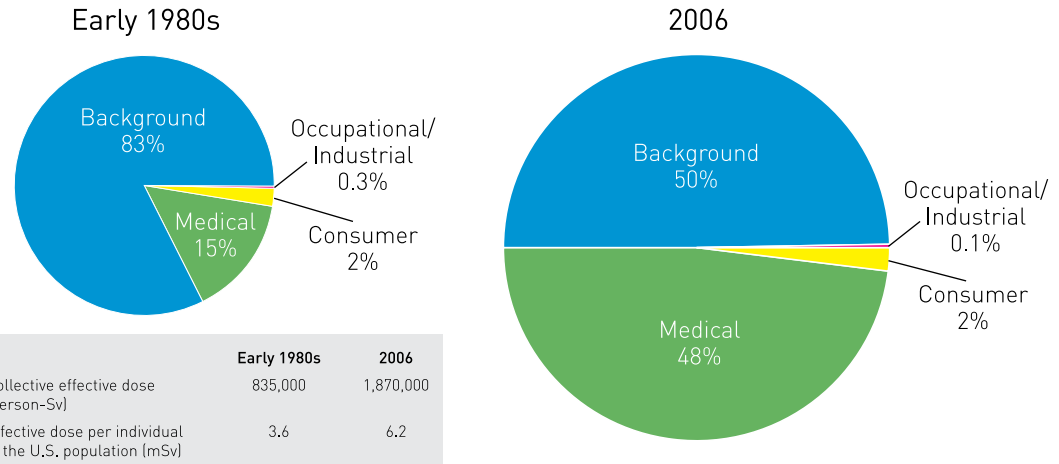


Total collective effective dose (1,870,000 person-sieverts [Sv]) and total effective dose per individual in the U.S. population (6.2 millisieverts [mSv]). Percent values rounded to the nearest 1%, except for those <1%.

Source: National Council on Radiation Protection and Measurement. Ionizing Radiation Exposure of the Population of the United States. Report No. 160, Figure 1-1. Bethesda, MD: NCRP; 2009.

NCRP Report No. 160, Ionizing Radiation Exposure of the Population of the United States

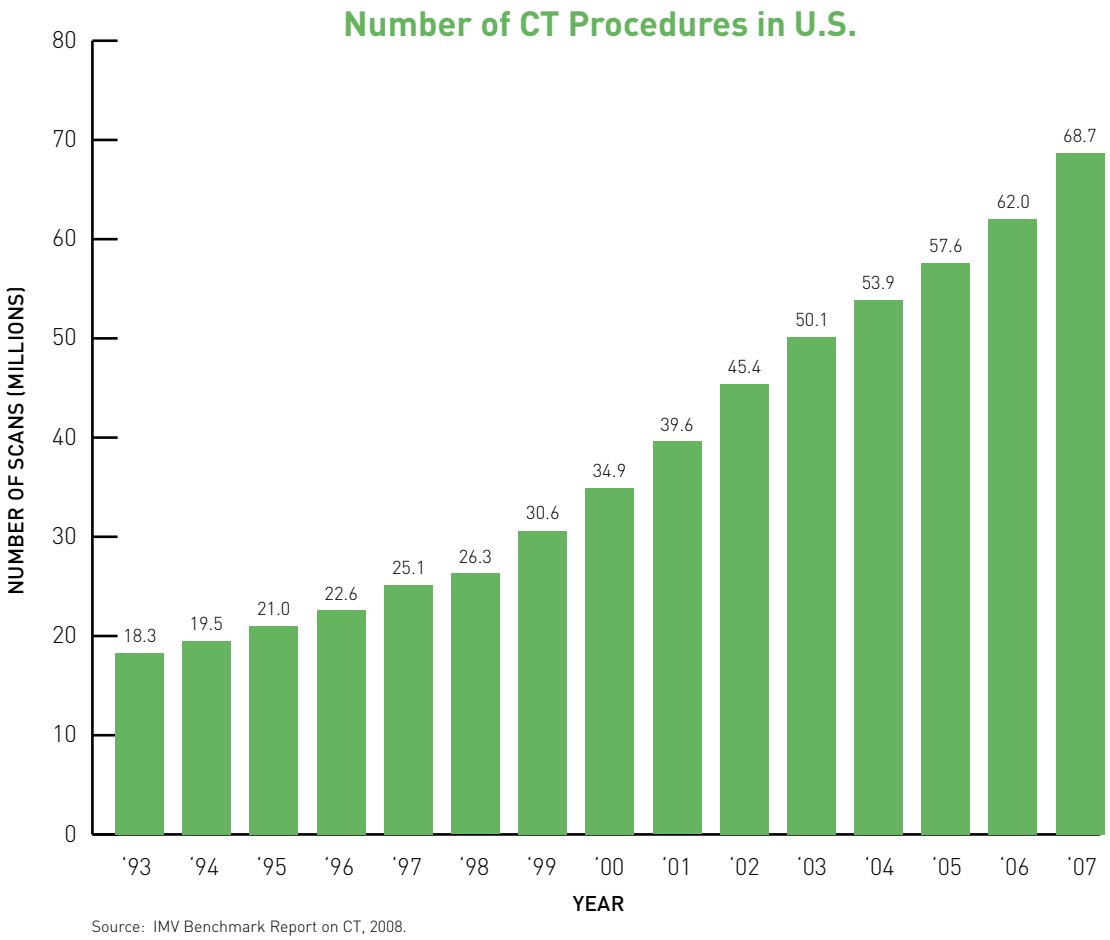
Figure 8



	Early 1980s	2006
Collective effective dose (person-Sv)	835,000	1,870,000
Effective dose per individual in the U.S. population (mSv)	3.6	6.2

Source: National Council on Radiation Protection and Measurements, Report No. 160, Figure 4-12; 2009 March 3.

Figure 9



Source: IMV Benchmark Report on CT, 2008.

sample radiation doses for common medical imaging and nuclear medicine procedures.

CT produces a larger radiation dose than other imaging tests that require radiation. As Table 7 shows, an average chest CT delivers an effective radiation dose (~7.0 mSv) equivalent to as much as 350 chest x-rays (posterior/anterior, 0.02 mSv). Moreover, many individuals who receive a CT scan will have more than one scan related to a single medical condition. According to one study,[313] 30 percent of patients who have CT scans have at least three scans, 7 percent of patients who have CT scans have at least five scans, and 4 percent of patients will receive at least nine scans. Trauma patients receive a mean of three scans in their initial evaluation.[314] Taking into account machine variability, usage variability, mean multiple scans, and other factors that can easily vary dose by a factor of two, the relevant organ dose range for CT is 5–100 mSv.[315]

As Figure 10 shows, survivors of the atomic bomb attack on Hiroshima who were 2,000–3,000 yards from ground zero received an effective dose in the same 5–100 mSv range.

Adult Effective Radiation Doses for Various Radiology, Interventional Radiology, Computed Tomography, and Nuclear Medicine Examinations

Table 7

SOURCE	AVERAGE EFFECTIVE DOSE (mSv)	VALUES REPORTED IN LITERATURE (mSv)
X-ray		
Chest X-ray (posterior/anterior)	0.02	0.05–0.24
Abdominal X-ray	0.07	0.04–1.1
Mammography	0.4	0.10–0.6
Cervical spine X-ray	0.2	0.07–0.3
Panoramic dental X-ray	0.01	0.007–0.09
Barium enema (includes fluoroscopy)	8.0	2.0–18.0
Computed Tomography (CT)		
Head CT	2.0	0.9–4.0
Chest CT	7.0	4.0–18.0
Abdominal CT	8.0	3.5–25.0
Pelvis CT	6.0	3.3–10.0
Three-phase liver CT	15.0	--
Coronary angiography CT	16.0	5.0–32.0
Virtual colonoscopy CT	10.0	4.0–13.2
PET CT	45.0	--
Interventional Radiography (IR)		
Coronary angiography (diagnostic) IR	7.0	2.0–15.8
Nuclear Medicine (NM)		
Brain NM with FDG	14.1	--
Cardiac stress-rest test with thallium 201 chloride	40.7	--
Renal NM	1.8–3.3 (depending on radiopharmaceutical used)	--
Bone	6.3	--
Tumor NM with ^{18}F-FDG	14.1	--

--: Data not available; PET: positron emission tomography scan; FDG: fluorodeoxyglucose; ^{18}F: fluorine 18

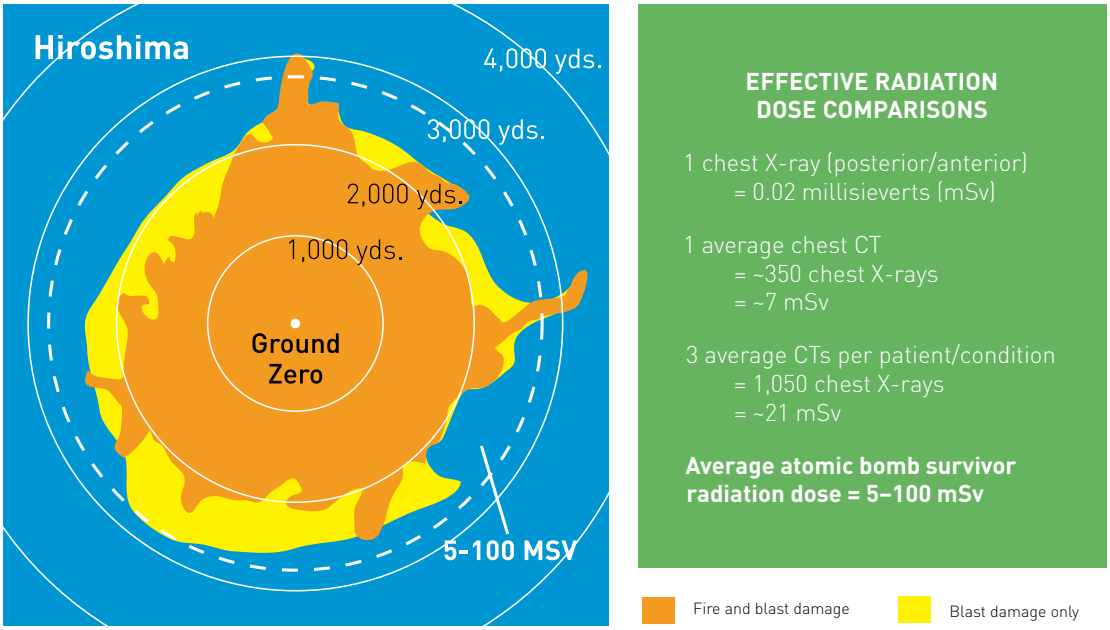
Sources:
Mettler FA Jr, Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic nuclear medicine: a catalog. Radiology. 2008; 248(1):254-63.

Mettler FA Jr, White Paper and Presentation, President's Cancer Panel Meeting, 2009 January 27.

Most estimates of radiation-related cancer risk are based on studies of atomic bomb survivors.[316] The Life Span Study (LSS),[317] a 40-year study of nearly 28,000 atomic bomb survivors exposed to this dose, showed a small but statistically significant radiation-associated increase in solid tumor risk. A recent large-scale study of 400,000 radiation workers in the nuclear industry[318] who were exposed to an average cumulative

Figure 10

Radiation Dose Sustained by Some Hiroshima Blast Survivors



Adapted from: Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, et al. Solid cancer incidence in atomic bomb survivors: 1958-1998. Radiation Research 2007;168:1-64.

effective dose of approximately 20 mSv reported a significant association between radiation dose and mortality from cancer. Risk of cancer among these workers, who received doses of 5–100 mSv, was quantitatively consistent with that reported for atomic bomb survivors. According to one speaker, such studies provide direct evidence that the radiation doses associated with CT scans are associated with increased cancer risk. It was further emphasized that while excess cancer risk due to medical radiation may be small at an individual level, this risk—multiplied by millions of examinations a year in an ever-growing population—is likely over time to result in a significant population risk with substantial societal costs.[319]

The predominant contributor to escalating CT dose is increased usage, not CT scanner type.[320] The trend toward the use of CT and other imaging utilizing ionizing radiation is expected to continue as new uses are found for the tests (e.g., virtual colonoscopy),[321] insurance reimbursement is secured for new applications of the technology, and the equipment becomes more readily available nationwide. For example, relatively new 64-slice CT scanners, which scan more quickly than earlier machines and provide more accurate data, are used extensively for cardiac angiography. According to a recent market research report, the number of 64-slice scanners in cardiology offices has more than doubled in the past 2 years.[322]

It also was suggested that when physicians have financial interests in imaging facilities, they may tend to refer patients for more scans than those who do not have such an incentive.[323] In addition, whole-body scans are being marketed heavily for early detection of disease or as "virtual physicals" to people who have no specific medical complaint. By one estimate,[324] a 45-year-old adult who plans to undergo annual full-body CT examinations up to age 75 (30 examinations) would increase his or her lifetime overall risk of dying from cancer by almost two percent (lifetime attributable risk of mortality). At the population level, if many people made the same decision to have annual full-body CT scans, the result could be a significant number of additional new cancer cases.

Many primary care physicians and other referring medical professionals are unaware of the magnitude of radiation exposure from various imaging or nuclear medicine procedures, or the potential cancer risk of increasing a patient's lifetime cumulative radiation dose. In a recent survey of radiologists and emergency room physicians, three-quarters of the group significantly underestimated the radiation dose from a CT scan; further, more than half of the radiologists and 91 percent of emergency room physicians surveyed did not believe that CT scans increased lifetime cancer risk.325 A speaker noted that many tests are ordered at least in part as protection against possible future litigation based on accusations that the physician withheld the most cutting-edge technology from the patient. Conversely, some imaging studies are performed because patients demand them. In other instances, scans are repeated needlessly because of poor communication within the health care system.[320]

Some believe that as many as one-third of all CT scans performed in the U.S. could be avoided.[326,327] Speakers emphasized that regardless of the patient's age or condition, the radiation-related cancer risk of a given test must be weighed against its benefit. To this end, in 2006 the American College of Radiology (ACR) convened a Blue Ribbon Panel on Radiation Dose in Medicine to make recommendations aimed at optimizing radiologic image quality and radiation dose and preventing inappropriate use of procedures involving ionizing radiation.[328] In addition to recommendations regarding physician education about radiation risk, one recommendation called for incorporating radiation dose information into the ACR Appropriateness Criteria,[329] a guide used by physicians to select imaging procedures for specific medical conditions. Responding to this recommendation, relative radiation level designations were added to the Appropriateness Criteria in 2007.

Cardiologists, general physicians, and surgeons have the modalities for colonoscopy and these things, but they don't have any idea about these consequences to the patient.

MAHADEVAPPA MAHESH
AMERICAN COLLEGE OF RADIOLOGY

Strategies for reducing radiation dose exist and studies have shown that dose reductions of up to 50 percent are possible without sacrificing image quality.[330–332] Education for radiologists, technologists, medical physicists, device manufacturers, and their training personnel about these strategies is being disseminated, though not yet uniformly, according to speakers. Successes, however, already are being documented. For example, a Michigan quality improvement program led by the Advanced Cardiovascular Imaging Consortium showed that in less than a year, the average radiation dose used at the 15 participating centers decreased by nearly half without diminishing the quality of the resultant images.[333]

Medical Radiation and Breast Cancer Risk

Substantial evidence exists that medical radiation is an important and controllable cause of breast cancer.[334,335] Therefore, minimizing radiation dose to breast tissue is critically important, particularly in girls and young women.[336] For example, a chest CT delivers an organ dose to the breast equal to about 15 sets of mammograms.[323] Organ doses to the breast have been estimated to be 20–60 milligrays (mGy) for a CT examination performed to detect pulmonary embolism, 50–80 mGy for a CT coronary angiography examination, and 10–20 mGy to just the lower part of the breast from an abdominal CT examination.[336–338] By comparison, the American College of Radiology[339] and the Mammography Quality Standards Act of 1992[340] regulations require that the mean glandular dose for a single mammogram be less than 3 mGy.

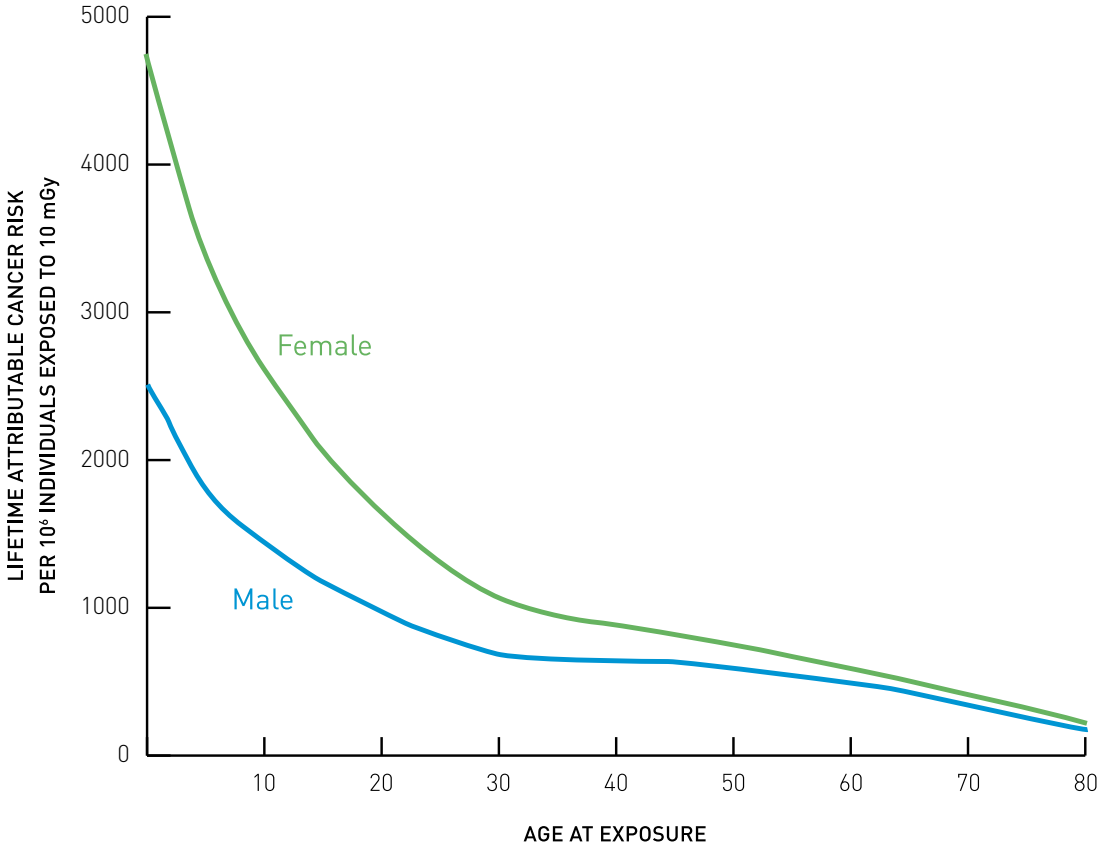
CT and Other Imaging in Children

Rapid growth in the use of CT and other sources of ionizing radiation for diagnostic and other imaging in children is of special concern. In 1989, approximately one-half million CT scans were performed on children. In 2007, CTs on children numbered in the range of 3.5–7 million (5–10 percent of all CTs); of these, 750,000–1.5 million were scans of children under 5 years of age.[315]

Children are inherently more sensitive to radiation than adults. They are three to five times more vulnerable[341] to the damaging effects of radiation because of their rapid development; they have a much higher number of dividing cells than do adults. In addition, unless the radiation dose is reduced to account for a child's smaller mass, organ doses for the same test can be much larger than for adults—as much as 50 percent of the dose may be unnecessary.[342] Dose

Estimated Radiation-Induced Lifetime Cancer Risk as a Function of Age at Exposure

Figure 11



Source: BEIR-VII, 2006.

estimates for many tests are made using adult-sized acrylic models ("phantoms") and computational models; models are needed for estimating dose using phantoms that more appropriately consider the size, shape, and composition of children's anatomies.[341]

Further, compared with adults, children have many more years of life ahead, time during which a radiation-induced tumor can grow, possibly potentiated by other environmental exposures. Most solid tumors take decades to develop to a point at which they can be detected or cause symptoms. As Figure 11 illustrates, the potential for radiation-induced lifetime cancer risk increases the younger the child is at the time the dose is received, even when the dose is the same. According to one estimate, a 1-year-old is 10–15 times more likely than a 50-year-old to develop a malignancy from the same dose of radiation.[343] Thus, avoiding unnecessary radiation risks in this sensitive population is crucial.[344] As many as one-third of CTs currently performed in children may be unnecessary.[345]

Pediatric CT usage is increasing very rapidly in children and generally speaking, children are more sensitive to radiation than adults...

DAVID BRENNER
COLUMBIA UNIVERSITY MEDICAL CENTER

The Image Gently℠ campaign[346] is a new initiative of the Alliance for Radiation Safety in Pediatric Imaging, which began as a committee of the Society for Pediatric Radiology in late 2006. The campaign was launched in January 2008. Its goal is to change medical practice by increasing awareness of the opportunities to lower radiation dose in the imaging of children. The campaign provides educational

...in many, many places it's clear that while doses could have been reduced by a factor of half from regular X-rays [to digital systems], they've actually gone up by a factor of 50 percent for the same study.

FRED METTLER, JR.
UNIVERSITY OF NEW MEXICO
NEW MEXICO VA HEALTHCARE SYSTEM

materials to community radiologists, pediatricians, radiologic technologists, medical physicists, and parents. Four ways to decrease radiation to children are emphasized:[347]

- Reduce or "child size" the amount of radiation used. Reduce dose as low as reasonably achievable (ALARA) to produce a quality image.
- Scan only when necessary.
- Scan only the indicated region.
- Scan once; multiphase scanning usually is not necessary in children.

As of May 2009, 29 organizations dedicated to reducing the radiation doses children receive from medical imaging examinations have endorsed the Image Gently campaign.[341] It is reasonable to anticipate that such broad support will speed information dissemination and practice change in imaging and nuclear medicine studies in children. In addition, the Society for Pediatric Radiology and the National Cancer Institute (NCI) collaborated to develop and circulate a pamphlet[348] for health care providers on pediatric CT and radiation risks.

Medical Radiation Technologists, Radiologists, and Health Professionals

Protecting radiation technologists and other medical staff from excessive radiation exposure has been a concern for many years, with dose limits and lifelong monitoring procedures established in most countries.[349] The dose limit recommended by the International Commission on Radiological Protection (ICRP) and adopted by all but a few countries is 20 mSv annually, or 100 mSv over 5 years.[350] Nearly 98 percent of those who work with ionizing radiation in any aspect of medical practice receive a radiation dose lower than the typical annual dose from all natural sources (e.g., radon,

cosmic radiation, radiation from soil and food)—about 3 mSv. Only one-half percent of medical workers reach or exceed this dose limit.[349] It should be noted, however, that the U.S. is one of the countries that does not adhere to the ICRP recommended dose limits. The Occupational Safety and Health Administration regulations stipulate a dose limit for whole body radiation of 50 mSv per year and, under certain conditions, up to 120 mSv per year.[351]

Since 1982, the U.S. has conducted a collaborative cohort study of more than 146,000 radiation technologists certified for two or more years from 1926–1982.[352] This cohort has been followed since 1983 to estimate the annual and cumulative radiation doses of each technologist, with the goal of assessing occupational radiation-related dose-response patterns. Although follow-up continues, to date, cancer risks elevated to a statistically significant level have been found only among technologists working before 1950. Historically, patient exposures have been of less concern since it was assumed that they would undergo examinations involving ionizing radiation only rarely and that any risk was offset by the expected diagnostic benefit of the test.

Radiation Equipment and Technologist Licensure and Regulation

Radiation exposure from the same test varies considerably depending on the age of the equipment and the skill and knowledge of the technician. Newer equipment assesses the shape of the individual being scanned and determines the minimum amount of radiation needed to produce an acceptable image. This approach typically lowers total radiation dose, and therefore cancer risk.[353] In addition, newer machines used for cardiac angiography shut off while the heart is in motion during heart beats, emitting radiation only between beats; this approach also reduces radiation dose substantially.[354]

Licensure of imaging and radiation therapy technologists varies from state to state depending on the type of test performed by the technologist. Some states have only partial regulation, and six states and the District of Columbia have no licensure or regulatory provisions of any kind (Figure 12). It is estimated that of approximately 50,000 radiologic technologists who perform CT scans, only about 23,000 are certified in CT.[341]

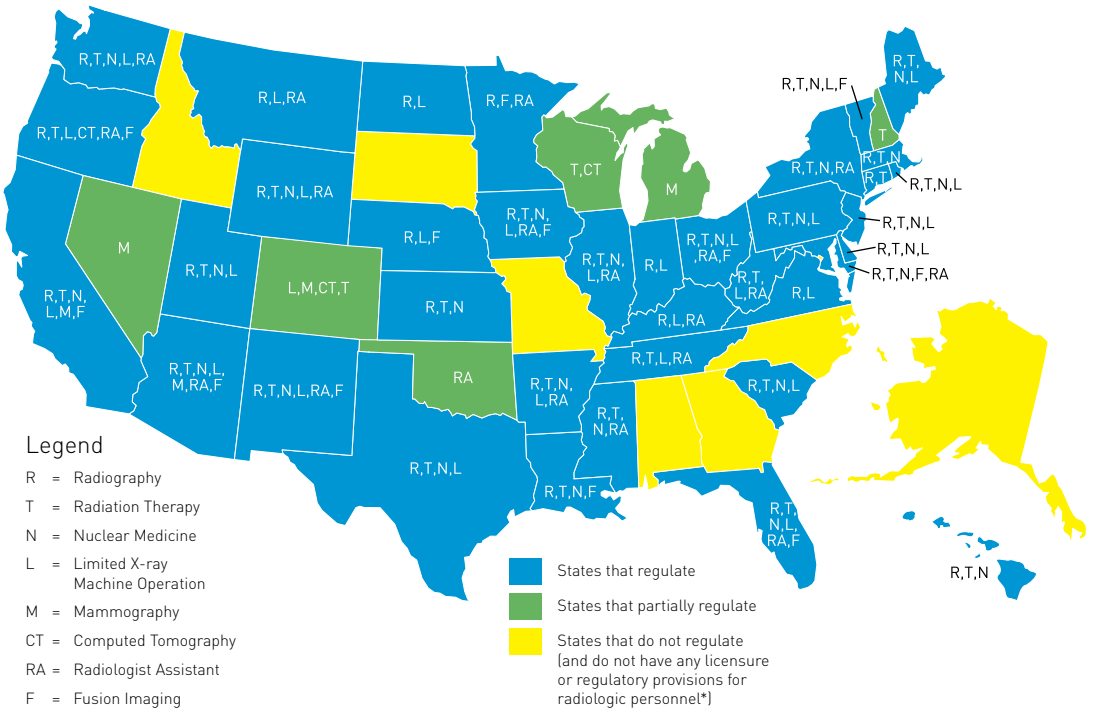
...a third of all CT scans practically could be replaced by other approaches or don't have to be performed at all. But it's going to be really hard to target this one-third because there are so many pressures on physicians to do CT scans.

DAVID BRENNER
COLUMBIA UNIVERSITY MEDICAL CENTER

The public is largely unaware of the radiation doses delivered by CT, positron emission testing, and other examinations that involve ionizing radiation, or of potential lifetime medical radiation doses and associated cancer risk. Speakers suggested that if patients were more aware of radiation exposure due to specific tests and the cancer risk that can accrue with cumulative medical radiation exposure, they might be more likely to raise this issue with their physicians. Doctors then may suggest alternatives that do not involve radiation (e.g., blood tests, magnetic resonance imaging, ultrasound) but still yield sufficient diagnostic information. A recently initiated international project would facilitate such doctor-patient discussions; efforts are underway to develop "smart cards" on which all radiation doses received by an individual are recorded.[349] This information, when shared by the patient, also could prevent unnecessary repeat scans and would overcome data gaps related to patient recall. Though not using readable card technology, a number of other medical centers in the U.S. record and/or provide patients with dose information for all procedures that require radiation exposure. The number of institutions adopting this practice appears to be growing; among them, the Clinical Center at the National

Figure 12

Does Your State Regulate Medical Imaging and Radiation Therapy Technologists?*



* List complete as of July 1, 2008. In addition to the listed states, the District of Columbia also does not license radiologic personnel.

Source: American Association of Radiologic Technologists

Institutes of Health began providing radiation dose information to patients in 2009.

Responding to rising concerns in the radiology community and among the public, the Food and Drug Administration (FDA) announced a new initiative[355] in February 2010 aimed at reducing unnecessary radiation exposure due to medical imaging. FDA intends to issue targeted requirements for CT and fluoroscopic device manufacturers for the addition of new safeguards on machines to prevent radiation overdose, and to increase training for machine operators. Devices may be required to capture and transmit dose information to a patient's electronic medical record and to national dose registries. Under the initiative, FDA will further encourage the development of dose registries to monitor patient dosages and establish reference doses where none currently exist. FDA also will collaborate with other organizations to develop a patient medical imaging history card that will be made available on the agency's Web site. The card will enable patients to track their medical imaging history, which they may share with their health care providers.

...not all CT scans are the same...in the same exam you can be getting ten times as much dose as somebody else...

DAVID BRENNER
COLUMBIA UNIVERSITY MEDICAL CENTER

Pharmaceuticals

Pharmaceuticals have become a significant water pollutant nationwide. Water filtration plants generally are unable to remove dissolved medications that enter water systems after being excreted or poured into household drains or toilets.

Excreted pharmaceuticals (or their metabolites) are a substantial pollution problem that may increase as the population

ages and a growing percentage of people are prescribed medications to treat acute and chronic health conditions. The National Health and Nutrition Examination Survey, a national sample of the U.S. civilian population, found that during the period 2001–2004, 46.7 percent of the surveyed population reported taking at least one prescription drug in the previous month; 20.2 percent reported taking three or more prescription drugs in the prior month.[356] Among the human medications found in water supplies are antidepressants, medications for high blood pressure and diabetes, anticonvulsants, steroid medications, oral contraceptives, hormone replacement therapy medications, codeine, non-prescription pain relievers, chemotherapy drugs, heart medications, and antibiotics.[357,358]

In addition, because unneeded or expired prescription drugs cannot by law be returned to the pharmacy, people have few options for disposing of them. Legislation[359] has been introduced in the 111th Congress that would amend the Controlled Substances Act[360] to facilitate the safe disposal of legally prescribed controlled substances by authorized facilities. If passed, it would help limit the disposal of these medications into the water supply and prevent their diversion into illegal sales.

The Federal government has not established limits on the amounts of pharmaceuticals in drinking water and does not require water testing to determine the amounts present.[361] Scant research has been done on the long-term or synergistic effects of multiple drug exposures of this kind. Since medications are intended to have specific effects at very low doses, environmental scientists and others are urging increased research to identify both human and environmental risks and greater attention by the U.S. Environmental Protection Agency to this issue. One *in vitro* study showed that exposure to a complex mixture of medications at environmental levels can inhibit human embryonic kidney cell growth.[362] The possible cancer-related effects of pharmaceuticals in drinking water are as yet unknown.

CHAPTER 5

Exposure to Contaminants and Other Hazards from Military Sources

The military is a major source of toxic occupational and environmental exposures that can increase cancer risk. Information is available about some military activities that have directly or indirectly exposed military and civilian personnel to carcinogens and contaminated soil and water in numerous locations in the United States and abroad. However, we may never know the full extent of environmental contamination from military sources. This chapter provides examples of chemical and radiation contamination related to military operations.

Chemical Contamination

As noted in Part I, Superfund sites are areas that have been designated as among the worst areas of toxic contamination in the United States. Nearly 900 Superfund sites are abandoned military facilities or facilities that produced materials and products for or otherwise supported military needs.[363] In some cases, Superfund sites and the areas surrounding them became heavily contaminated due to improper storage and disposal of substances such as solvents, machining oils, metalworking fluids, and metals. Many of these substances are known or suspected carcinogens. In some cases, these contaminants have spread far beyond their points of origin because they have been transported by wind currents or have leached into drinking water supplies. Perchlorate and the solvents trichloroethylene (TCE) and perchloroethylene (PCE/perc) are examples of this type of contamination.

Perchlorate

Perchlorate is a rocket fuel component and by-product of rocket and missile testing. It has spread from numerous manufacturing sites into drinking water systems; it also can accumulate in leafy food crops and fruit irrigated by perchlorate-contaminated water.[364] Now ubiquitous in the environment, perchlorate has been detected in the urine of people in all parts of the United States.[365] Perchlorate accumulates in the thyroid gland and can block iodide transfer into the thyroid, resulting in iodine deficiency. Adequate iodide is crucial for neurological development. A recent study found that all types of powdered baby formula (e.g., milk, soy) are contaminated with perchlorate.[365] If perchlorate also is in tap water used to mix the formula, babies may be doubly dosed with the chemical. Long-term exposure to perchlorate has been shown to induce thyroid cancer in rats and mice,

but no research to date has indicated that perchlorate causes human cancer.[366]

Trichloroethylene (TCE) and Perchloroethylene (PCE/perc)

For 30 years beginning in the late 1950s, soldiers and others living at or near Camp Lejeune, North Carolina, consumed drinking water from wells contaminated by TCE and another solvent, perchloroethylene (also called tetrachloroethylene), at concentrations more than 40 times the current U.S. Environmental Protection Agency (EPA) limit.[367] The chemicals came from an off-base dry cleaning company. The water also was contaminated with the highly toxic solvent benzene, which was used to clean military equipment and was dumped or buried near base wells for years.[368] As many as a half million people may have consumed the contaminated water.[367] In addition to the high incidence of cancers (including at least 53 cases of male breast cancer[369]) among those who drank, bathed in, and ate food prepared with the contaminated water, many children born at the base suffered birth defects and illnesses. Women exposed in their first trimester of pregnancy had unusually high miscarriage rates. After years of denying any relationship between health problems and Camp Lejeune's water supply, the U.S. government now has established a registry of people potentially contaminated, as well as a Web site and call center for those seeking information about their possible exposure or exposure-related health problems. In addition, an ongoing case-control study was launched in 2005 to identify childhood leukemia, non-Hodgkin lymphoma, and other serious health effects in children born at Camp Lejeune to mothers exposed to the contaminated water.[370]

... my family lived in base quarters in Camp Lejeune, [the] Marine Corps base in 1970 and 1971....In my case, I lost a [grand]child and I have no idea how long I am going to live... [my cancer] was Stage IV when it was diagnosed....The Marine Corps and Department of Defense did know about the contamination from 1957 until they closed the wells in 1985....my mission today is to let you know that there are thousands and thousands and thousands of us out there.

GLORIA FALL
CANCER SURVIVOR

In some cases, chemical contaminants from military sources are substances used or encountered in warfare that have profound effects on the lives of those exposed. The paragraphs below describe two such cases.

Agent Orange

Agent Orange is an herbicide initially developed to control broad-leafed weeds in agricultural settings. The chemical mimics a plant growth hormone, inducing rapid, uncontrolled growth; in large quantities, it causes catastrophic defoliation. It primarily was used during the Vietnam War to defoliate large areas in order to deprive the opposition forces of cover and food crops. Agent Orange also was used to clear areas around military base perimeters.[371] Between 1962 and 1971, more than 21 million gallons of Agent Orange were sprayed across Southeast Asia. Though unknown to the military at the time of its initial use, it was discovered that the herbicide also contained a dioxin, TCDD, which was a by-product of the manufacturing process.[372] TCDD is classified by the National Toxicology Program (NTP) as a human carcinogen.[77] Approximately 4.8 million Vietnamese people were exposed to Agent Orange, resulting in 400,000 deaths and disabilities and a half million children born with birth defects.

Because of its extensive use, all of the more than two million American service members who served in Vietnam are presumed to have been exposed to Agent Orange.[372] In 1991, Congress enacted the Agent Orange Act,[373] giving the Department of Veterans Affairs (VA) authority to declare certain conditions 'presumptive' of exposure to Agent Orange/Dioxin, thereby enabling Vietnam veterans to receive treatment and compensation for these conditions.[374] The cancers currently

recognized by the VA as associated with exposure to Agent Orange and other herbicides are chronic lymphocytic leukemia, Hodgkin lymphoma, multiple myeloma, non-Hodgkin lymphoma, prostate cancer, and some soft tissue sarcomas.[375]

Chromium

According to recent reports,[376,377] defense contractor employees assigned in 2003 to rebuild a water pumping facility in Iraq and National Guardsmen from several states responsible for their security were exposed via inhalation and skin contact to a chemical containing hexavalent chromium that was left at the site. The chemical originally was used to remove and prevent corrosion in the water pipes; it later may have been used by Baathists during the U.S. invasion in an attempt to destroy or sabotage the plant. While on site, many of the exposed individuals suffered skin sores, nose bleeds, nausea, stomach pain, and respiratory problems, including coughing up blood. Some still have residual respiratory and other ailments. As of September 2008, one soldier who served at the facility had died from lung cancer and another had been diagnosed with cancer of the sinus cavity. While chromium exposure has not been proven to be the cause of disease in these cases, both are consistent with evidence for chromium-induced cancers.

Radioactive Contamination

Hundreds of thousands of military personnel and civilians in the United States received significant radiation doses as a result of their participation in nuclear weapons testing and supporting occupations and industries, including nuclear fuel and weapons production, and uranium mining, milling, and ore transport. Hundreds of thousands more were irradiated at levels sufficient to cause cancer and other diseases. These populations include the families of military and civilian workers, and people—known as "downwinders"—living or working in communities surrounding or downstream from testing and related activities, and in relatively distant areas to which nuclear fallout or other radioactive material spread. As speakers at the Panel's meetings detailed and as summarized below, Federal responses to the plight of affected individuals have been unsatisfactory.

Radiation Exposures Due to Nuclear Weapons Testing

Exposure to ionizing radiation related to nuclear weapons testing is an underappreciated worldwide issue. Longstanding denial by many governments as to the type and magnitude of cancer and other radiation-related health risks from nuclear weapons testing exposures has kept many of those affected from receiving needed care. In recent years, some countries have begun to acknowledge radiation exposures resulting from their nuclear weapons testing programs. For example, the government of France has agreed to monetary settlements with persons exposed during its nuclear weapons tests in Algeria and French Polynesia.[378]

Most of those affected, both in the United States and elsewhere, lack knowledge about the extent of their exposure or potential health problems they may face. Similarly, most health care providers are not aware of cancer and other latent radiation effects and therefore are unlikely to adequately monitor patients for these health conditions.

An estimated 210,000 people, mostly service members, took part in atmospheric nuclear weapons tests between 1945 and 1962 in the U.S. and in the Pacific and Atlantic oceans. The Department of Veterans Affairs (VA) estimates that the average radiation dose received by these individuals was about 0.6 rem (6 mSv). In addition, an estimated 195,000 service members participated in the post-World War II occupation of Hiroshima and Nagasaki, Japan, or were prisoners of war in Japan; the estimated average radiation dose sustained by these individuals was < 0.1 rem (<1 mSv).[379,380] Since 1978, the Defense Threat Reduction Agency's Nuclear Test Personnel Review program has maintained a database of U.S. atmospheric nuclear test activity participants and individuals who served with the occupation forces or were prisoners of war in Japan.[381]

The testing was almost all done above ground....and the yield was equal to 7,200 Hiroshima bombs....That's like exploding 1.6 Hiroshima bombs per day for 12 years in the Marshall Islands. That's how much radiation there was.

NEAL PALAFOX
UNIVERSITY OF HAWAI'I

Nuclear Weapons Plants

The Hanford nuclear weapons facility (also called the Hanford Nuclear Reservation) in south-central Washington is one of dozens of nuclear weapons and weapons fuel production sites in the U.S.; others include facilities at Oak Ridge, Tennessee and Savannah River, Georgia. Many Hanford fuel production workers have developed cancers they maintain were caused by radiation

exposures they experienced during their employment. In addition, a recent study[382] of former Hanford construction workers found they were three times more likely to develop multiple myeloma, a relatively rare blood system cancer, than the general population. Higher incidence of multiple myeloma also has been documented at other DOE weapons production sites. The construction workers also were found to be 11 times more likely to develop mesothelioma, probably due to asbestos exposures at the site.

In its 2002 report,[383] the Panel described radiation exposures and health problems, including cancer, experienced by the Yakima Nation and other Northwest Native Americans who live in close proximity to the Hanford nuclear weapons production plant. In addition to numerous gaseous emissions of radioactive iodine (I-131) during its nearly 30 years of operation, the Hanford site, which covers nearly 600 square miles, discharged over 400 billion gallons of radioactive waste into the surrounding soil and the Columbia River.[384] The plant ceased operations in 1972, but it now is the largest nuclear waste storage site in the country.

Nuclear waste at Hanford has an estimated 195 million curies of radioactivity.[385] Nearly 5 tons of plutonium and over 53 million gallons of radioactive plutonium waste are stored in hundreds of underground tanks.[386] Many of the storage tanks have a capacity of one million gallons. DOE acknowledges that approximately 60 of the tanks have leaked, and others are suspected of leaking.[387] As of 2008, only seven of the leaking tanks had been emptied.[388] An estimated one million gallons of high-level nuclear and chemical waste have leaked into the soil, contaminating 200 square miles of land under the Hanford facility. This radioactive waste continues to leach into the groundwater that empties into the Columbia River, the principal site of salmon spawning in the region and main water source for agriculture and recreation in most of southern Washington and northern Oregon. The river also supplies drinking water for nearly a million people.

The Hanford cleanup program is perhaps one of the most complex, technically challenging, and costly hazard remediation projects ever attempted.[388] Its annual budget is greater than that of hundreds of other Superfund cleanups combined. The cleanup was initiated in 1989 with an expectation that the job would be completed in 30 years. In 2009, the job was less than half completed, and the current Department of Energy (DOE) budget allows for emptying only one storage tank per year.

Uranium Miners, Mill Workers, and Ore Transporters

Uranium mining and milling were essential underpinnings of the U.S. nuclear weapons program. Military and civilian personnel, including Native Americans, received substantial radiation doses in the course of their employment and are eligible for compensation for lung and renal cancers and certain other medical conditions (see below). Much of the uranium mined in the U.S. was located in or near Navajo tribal lands in New Mexico. The Navajo banned uranium mining and milling in 2005. More than 1,000 uranium mines and mill sites exist in the region, and most have not been sealed or cleaned up[389] since mining declined following the Cold War years; some are designated Superfund sites. Many of the miners and mill workers were Navajo who worked without respirators or other protection and still live with their families near the work sites, where they continually breathe uranium dust and drink uranium-contaminated water. Both the Navajo and Laguna tribes have experienced markedly higher than average rates of lung cancer, as well as kidney disease, birth defects, and other health problems.

...a whole group of kids exposed as children have been ignored completely. (referring to Hanford and Nevada Test Site)

TRISHA THOMPSON PRITIKIN
HANFORD DOWNWINDER

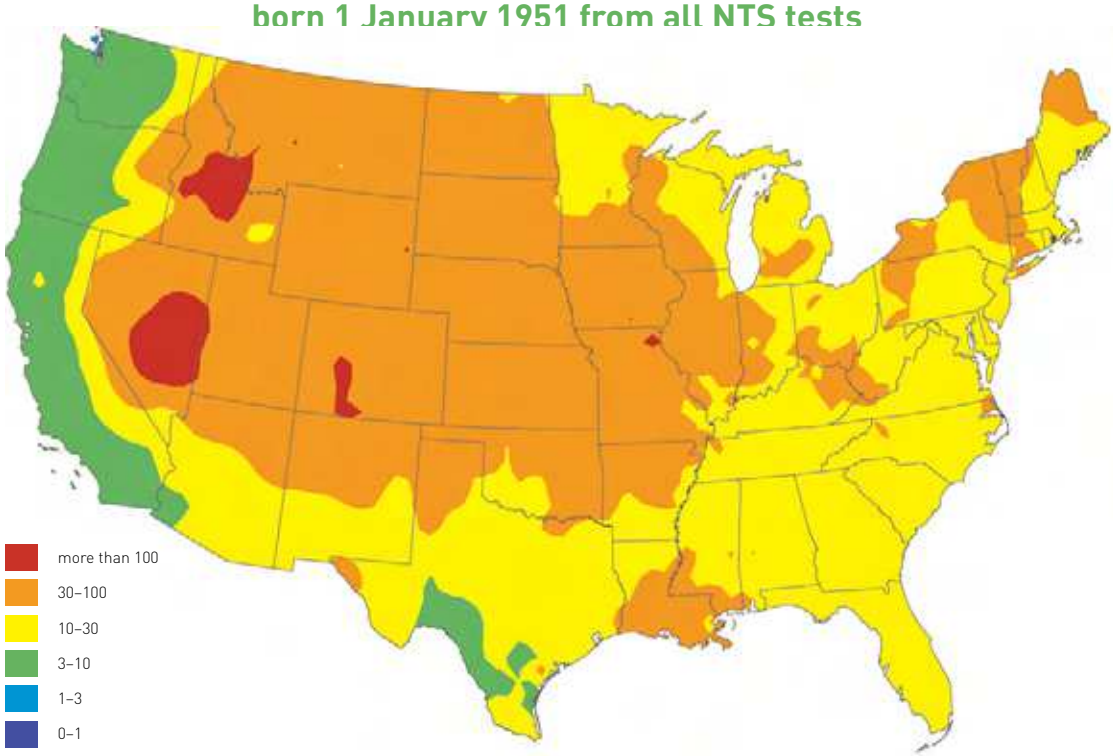
Of late, global warming and fluctuating oil prices have brought a renewed interest in nuclear power, which in turn has caused a resurgence of interest in uranium mining, primarily in New Mexico. Several companies have applied for mining licenses;[390,391] these actions are of great concern to the Navajo Nation.

Downwinders and Other Communities Near Nuclear Test Sites, Nuclear Power and Weapons Plants, and Uranium Mines and Mills

It may never be known how many hundreds of thousands—or millions—of people living near and downwind and/or downstream from nuclear weapons testing sites, nuclear power and weapons plants, uranium mines and mills, and nuclear waste storage sites have been exposed to significant radioactive contamination. This contamination occurred due to nuclear weapons tests, radioactive gaseous emissions, radioactive waste

Figure 13

Internal dose (mGy) to the thyroid of persons born 1 January 1951 from all NTS tests



Source: Centers for Disease Control and Prevention, National Cancer Institute. Report on the feasibility of a study of the health consequences to the American population from nuclear weapons tests conducted by the United States and other nations [Internet]. Atlanta (GA): CDC; 2005 May [cited 2010 April 1]. Volume 1, Chapter 3, Figure 3.13; p. 48. Available from: http://www.cdc.gov/nceh/radiation/fallout/default.htm.

discharges into streams and rivers, and massive dumping of radioactive sludge in landfills. Those affected were exposed to numerous biologically important radionuclides in inhaled airborne radioactive particles (fallout) and in contaminated soil, water, crops, and livestock.

A National Cancer Institute (NCI) study[392] acknowledged that nuclear fallout affected Americans nationwide, not just those living close to the Nevada Test Site (NTS), where from 1951–1962, nearly 100 above ground nuclear tests were conducted.[393] As a former Hanford-area resident testified before the Panel, studies of contamination have been limited primarily to exposures to I-131 in and around the NTS, the nuclear operations at Oak Ridge, Tennessee, and the Hanford nuclear weapons complex.[394] Figure 13 gives an indication of the general geographic distribution of I-131 dose across the United States. As noted above, nuclear waste stored at Hanford continues to leak radioactive waste into the Columbia River and vast tracts of land surrounding the Hanford complex.[387] Though perhaps less well documented, similar situations exist at numerous nuclear facilities across America.[395] People with multiple exposures (at different locations, to multiple radionuclides, or both) have no measurement tool or mechanism that enables them to combine estimated doses to determine their cumulative radiation exposure and resultant health risks.

In the Pacific, inhabitants of the Republic of the Marshall Islands (RMI) were exposed to 67 nuclear tests over the 12-year period 1946–1958.[396] Almost all of the testing was done above ground and affected all 33 islands. The total yield from these explosions was equal to 7,200 Hiroshima bombs, or the equivalent of 1.6 Hiroshima bombs per day for 12 years.[397] The largest hydrogen bomb test, known as Castle Bravo, had the force of 1,000 Hiroshima bombs. It vaporized the test island and parts of two others; fallout from the blast covered 7,000

square miles. A wind change caused the fallout cloud to drift over four other atolls inhabited by more than 600 people. These people received acute radiation doses estimated at 2,000 mSv.[398] Although they were evacuated from these islands for several years following the blast, they were returned there for a period of years while the islands still were contaminated before being rescued by Greenpeace, an environmental protection advocacy organization. As a result, prolonged radiation doses followed the acute exposures. Some of the affected islands remain uninhabitable. Other islands and atolls were affected to varying degrees.

In addition to the Marshallese, many workers from U.S.-associated Micronesia were brought to the Marshall Islands to clean up after the blast; their level of exposure is unknown. NCI's 2004 report[399] estimated that 530 excess cancers would be expected in the people living in the Marshall Islands during the testing period, and that due to the latency period of cancer, about half of these malignancies had yet to be detected. The increase in all cancers resulting from fallout exposure was estimated at 9 percent, but radiation-related cancer estimates varied considerably by cancer type and atoll of residence at the time of the blast. The population of the Rongelap and Ailinginae atolls received the highest radiation exposure. In that population, 98 percent of projected thyroid cancers and 76 percent of projected stomach cancers were estimated to be radiation-related. Since publication of the 2004 report, work has been underway to develop more refined estimates of radiation exposure among the Marshallese, using additional collected data and more contemporary environmental radiation measurements. Eight manuscripts have been prepared and submitted for peer review and publication before the end of 2009.[400] One speaker stated that health care standards for the Marshallese affected by the nuclear testing program are lower than those for peoples affected by ionizing radiation from the Nevada Test Site or Hanford nuclear weapons site, but emphasized strongly that they should be fully commensurate with U.S. standards for prevention, screening, diagnosis, and treatment. In addition, it was noted that there has been no consideration of the stress and related illness suffered by the Marshallese due to the irreparable disruption of their culture and loss of their homeland.

Federal Compensation and Related Programs for Persons Exposed to Radiation from Nuclear Sources

People exposed to radiation from nuclear sources, and the families of exposed individuals, have sought appropriate medical care and monetary compensation for health problems, disabilities, and premature death resulting from radiation exposures. Claimants, however, have encountered significant barriers to accessing benefits through Federal programs created to provide such health care and compensation. As detailed below, the principal barriers have been difficulties claimants face in documenting radiation exposures and proving that their injuries or disease resulted from those exposures.

...the medical system in the Marshall Islands and a lot of Micronesia can't handle this. We're talking about cancers and radiation oncology, and in all of the U.S.-associated Pacific there is one oncologist; that person is in Guam.

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UNIVERSITY OF HAWAI'I

The Radiation Exposure Compensation Act (RECA)

In 1990, the Federal government passed the Radiation Exposure Compensation Act (RECA),[401,402] to provide for compassionate payments to individuals who developed certain cancers and other serious diseases as a result of their exposure to radiation released during above-ground nuclear weapons tests, due to radiation exposure during employment in underground uranium mines, and as a result of living or working

We were lied to. We were children. We did not give voluntary consent to be exposed or be placed in harm's way...RECA does not cover many areas where there [was] a high level of fallout and it doesn't cover places like Hanford or Oak Ridge.

TRISHA THOMPSON PRITIKIN
HANFORD DOWNWINDER

in specified areas "downwind" of the NTS. Amendments to RECA[403] expanded the program to, among other provisions, include two additional claimant categories (uranium mill workers and ore transporters), add to the list of illnesses for which compensation could be claimed, lower the radiation exposure threshold for both underground and above ground miners, and add to the geographic areas acknowledged to have been downwind of the NTS above-ground tests. Amendments in 2002[404] clarified and amended certain eligibility criteria and claims adjudication procedures. Table 8 lists the cancers for which compensation is available under RECA. Lump-sum payments of up to $100,000 may be made to some claimants.[402] However, the claimant has always borne the burden of proof regarding exposure type and duration, and for reconstructing dose estimates, in some cases covering decades of an individual's life. This requirement is a major barrier for some, since data on exposures are extremely limited or nonexistent and individuals may not add doses resulting from multiple exposures to determine their cumulative exposure. No compensation program exists for people living and working outside of the RECA-eligible counties. In addition, because they are not U.S. citizens, civilians irradiated during nuclear weapons testing in the Marshall Islands or elsewhere in the Pacific Ocean are not eligible for RECA compensation.

Table 8

Cancers and Claimants Eligible for Compensation Under RECA

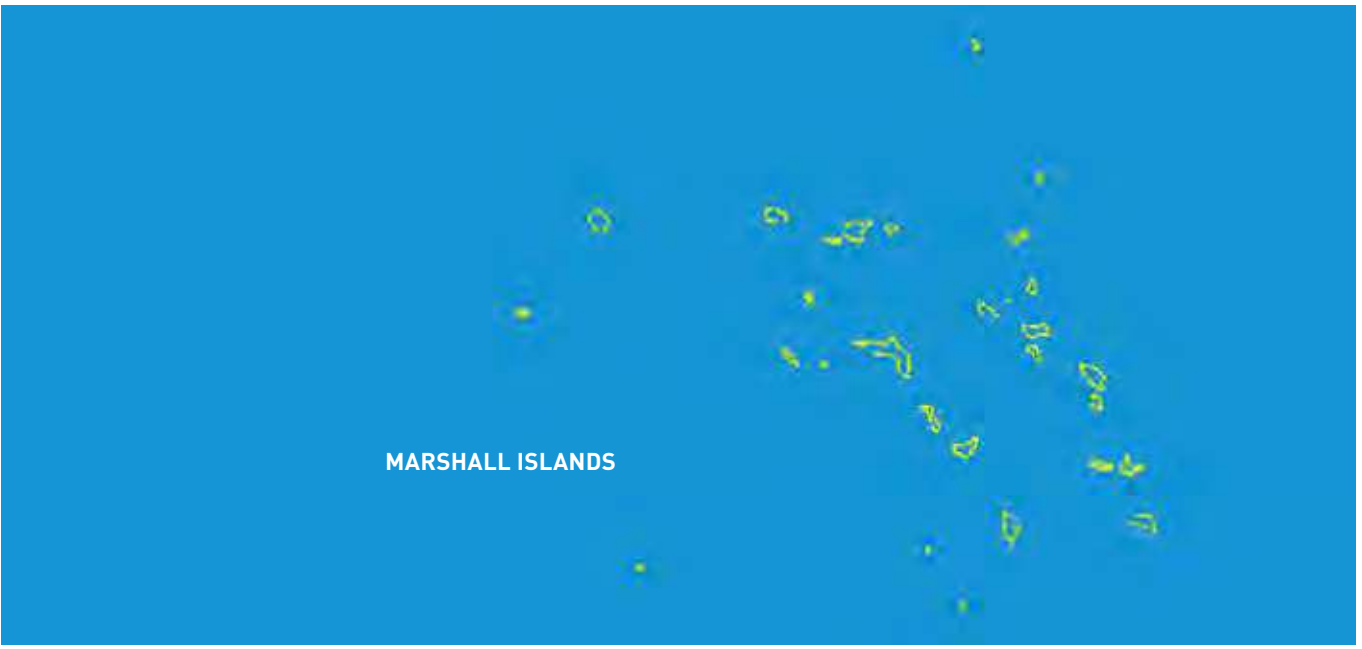
CANCER	ELIGIBLE WORKERS
Lung (primary)	UM, UMW, OT, DW, OS
Renal	UMW, OT
Bile ducts	DW, OS
Breast (male or female)	
Brain	
Colon	
Esophagus	
Gall bladder	
Leukemia (except CLL)	
Liver (except cirrhosis or hepatitis B-related)	
Lymphomas (except Hodgkin)	
Multiple myeloma	
Ovary	
Pancreas	
Pharynx	
Salivary gland	
Small intestine	
Stomach	
Thyroid	
Urinary bladder	

UM–uranium miners; UMW–uranium mill workers; OT–ore transporters; OS–onsite test participants; DW–downwinders; CLL–chronic lymphocytic leukemia

Source: U.S. Department of Justice. Radiation Exposure Compensation Program [Internet]. [cited 2009 Jun 6]. Available from: http://www.usdoj.gov/civil/torts/const/reca/about.htm.

Department of Energy Section 177 Health Care Program and Marshall Islands Special Medical Care Program

The 177 Health Program (177 HP) [405] was developed as part of the implementation of Section 177 of the 1986 Compact of Free Association (P.L. 99-239), in which the U.S. Government accepted responsibility for compensating citizens of the Marshall Islands and Micronesia for personal injury and property damage resulting from the nuclear testing program. The program was conducted under a Cooperative Agreement with DOE but has been significantly underfunded; annual funding beginning in 1986 was $4 million. Annual funding dropped to $2 million after about 4 years. Since 2006, funding has been level at approximately $984,000 per year.[406,407]



The Marshall Islands Special Medical Care Program[408] is a separate medical care program established to provide care for individuals directly or indirectly suffering radiation-related injury, illness, or other conditions as a result of the Castle Bravo nuclear bomb test. There has been disagreement, however, as to who should be covered under this program, with individuals from Micronesia and Guam maintaining that they too were affected by fallout from the blast. According to one speaker, authority governing the program has been unclear, and funding for the program has been grossly inadequate.

Funding issues are exacerbated by the limited health resources available in the Marshall Islands and elsewhere in the Pacific Islands to treat affected individuals who seek care through the Section 177 and Special Medical Care programs.

Marshall Islands Nuclear Claims Tribunal

In June 1983, a formal agreement was established between the U.S. Government and the RMI in which the U.S. recognized the contributions and sacrifices of the Marshallese with regard to the U.S. nuclear testing program. Under the Section 177 Agreement, a Nuclear Claims Tribunal was established with jurisdiction to "render final determination upon all claims past, present and future, of the Government, citizens and nationals of the Marshall Islands...in any way related to the Nuclear Testing Program."[409] The U.S. provided $150 million for compensation for damages caused by the testing program. In 2000, following the release of previously classified individual records and other documents describing effects of the testing program, the RMI submitted a Petition of Changed Circumstances, requesting additional compensation for injuries and damages.[410] As of June 2007, $45.75 million has been paid toward the $83 million in claims for personal injury awarded by the Tribunal. In 2007, the Tribunal awarded over $1 billion in property damage awards in a class action suit filed by residents of two of the most highly affected islands. This award has not been paid. Other medical and property damage claims continue to be filed.

Energy Employees Occupational Illness Compensation Program[411]

In July 2001, Congress passed the Energy Employees Occupational Illness Compensation Program Act in recognition

that workers in the nation's atomic weapons programs may be suffering from illnesses (including beryllium disease, silicosis, or radiation-induced cancer) due to exposure to radioactive and toxic substances. Individuals, or their eligible survivors, who worked as employees, contractors, or subcontractors at a DOE facility may be eligible for compensation under this program. Those whose claims are approved may receive a lump-sum payment of $150,000 and medical benefits for the covered illness. Uranium miners who received compensation under RECA are eligible for an additional $50,000 in compensation under this program.

Department of Veterans Affairs (VA) Programs for Veterans Exposed to Radiation[379]

Veterans who participated in nuclear tests by the U.S. or its allies, who served with the U.S. occupation forces in Hiroshima or Nagasaki, Japan (August 1945–July 1946), were exposed to radiation as prisoners of war in Japan, or worked at specified gaseous diffusion plants are eligible for compensation for the following 15 cancers: leukemia (except chronic lymphocytic leukemia); cancer of the thyroid, breast, pharynx, esophagus, stomach, small intestine, pancreas, bile ducts, gall bladder, salivary gland, and urinary tract (including renal); lymphomas (except Hodgkin); multiple myeloma; and primary liver cancer. In addition, veterans may file claims for diseases (not covered by the statute) from service-related radiation exposure under regulations that specify specific malignant and nonmalignant diseases, duration of exposure, and elapsed time between exposure and disease onset. The VA regulations identify all cancers as potentially radiogenic (i.e., caused by radiation exposure). Compensation rates depend on the degree of disability and are determined by a payment schedule that applies to all veterans; for deaths in 1993 and later, compensation to survivors is paid at a flat rate regardless of the deceased veteran's military rank.

Veterans' Advisory Board on Dose Reconstruction (VBDR)[412]

Radiation dose reconstructions have been performed since 1978 for military

personnel who participated in atmospheric nuclear weapons tests at the Trinity Site in New Mexico, the NTS, and in the Pacific, or who were stationed or prisoners of war in Japan after the atomic bombs were detonated. Following the recommendation of a 2003 National Academy of Sciences report[413] on the Dose Reconstruction Program, the Veterans' Benefits Act of 2003[414] provided for the establishment of an independent advisory board—the VBDR—to oversee the dose reconstruction and claims settlement programs.

Advisory Committee on Energy-Related Epidemiologic Research (ACERER)

Created in 1992, ACERER was charged to help the U.S. Department of Health and Human Services (HHS) ensure that its research into the potential health effects of nuclear production and testing was scientifically sound and that questions from downwinders about health risks were answered. ACERER was critical of a 2002 CDC study[415] on radiation-related disease that found little or no cancer risk. The study was revised in January 2007, but the cancer-related findings were essentially unchanged.[416] Based on the 2002 study, ACERER recommended that the government notify Americans known to have received high radiation doses. These recommendations were at odds with HHS policy at the time.[393] ACERER's commission was allowed to expire in February 2002, without notice either to members or stakeholders. According to one speaker, ACERER was the only avenue for community input on radiation-related disease due to government nuclear production and weapons testing.

Legislation Introduced Since the Panel's Meetings

The Charlie Wolf Nuclear Compensation Act (S.757/H.R.1828), introduced in Congress in April 2009, would make it easier for former Rocky Flats, Tennessee nuclear weapons plant workers to seek compensation for illnesses contracted due to exposure to radiation and toxins at the plant. The plant itself was closed in 1992; most of its buildings were removed by 2005 and worker records are no longer available or no longer exist.[417] Importantly, should this or a similar bill become law, it would for the first time shift the burden of proof from the workers and their families to the federal government.

The Atomic Veterans Relief Act (H.R.2573) was introduced in Congress in 2009; the bill would revise the eligibility criteria for presumption of service-connection of certain diseases and disabilities for veterans exposed to ionizing radiation during military service. The bill also would require the government to follow specific procedures for the mathematical calculation of the level of exposure sustained by the veteran.

Depleted Uranium

As the sections above detail, thousands of military and civilian workers were exposed to ionizing radiation during World War II and throughout the Cold War era in doses that are acknowledged to be cancer-causing. More recently, many participants in the Balkan conflict and in the wars in Afghanistan and Iraq have been exposed to depleted uranium (DU), a by-product of uranium enrichment. DU has some civilian applications, but in the military it is used to make DU "penetrator" ammunition and military armor.[418] Individuals in the vicinity of exploded DU penetrator ammunition or damaged military armor can be exposed to DU by ingesting food and water contaminated by DU particles or uranium from corroding DU penetrators, inhaling airborne DU particles, and if wounded, by shrapnel. Little is known about the DU exposure of munitions and military equipment manufacturing workers. *In vitro* and rodent studies suggest that chronic DU exposure may be linked to leukemia and have genetic, reproductive, and neurological effects.[419]

CHAPTER 6

Exposure to Environmental Hazards from Natural Sources

As the preceding chapters indicate, most environmental hazards with the potential to raise cancer risk are the product of human activity. Some environmental carcinogens, however, come from natural sources.

Radon

Radioactive radon is an inert (i.e., not chemically reactive), colorless, odorless gas, one in a chain of natural by-products of uranium decay.[420] Radon is produced from the decay of radium released from uranium ore, which is ubiquitous in soils and rock worldwide. As radon forms in the earth, it rises to the surface where it dissipates rapidly in the air. However, when radon enters residential and other tightly enclosed structures, its concentration can rise to levels that increase cancer risk, particularly when inhabitants of homes with higher radon levels are exposed over a period of years. Inhaled radioactive alpha particles produced by radon's two short-lived decay products can directly or indirectly damage DNA in lung cells.[421]

Miners who frequently work underground are exposed to high levels of radioactive radon, which is associated with elevated lung cancer risk; miners who smoke are at particularly high risk. People also can be exposed to waterborne radon; these exposures usually occur among workers such as water plant operators and fish hatchery attendants[422] and among people whose drinking water comes from deeply drilled wells.[420] Little research has been conducted on radon workplace or drinking water exposures.

Comparative risk assessments by EPA [Environmental Protection Agency] and its Science Advisory Board... have consistently ranked radon among the top four environmental risks to the public.

SUSAN CONRATH
U.S. ENVIRONMENTAL PROTECTION AGENCY

Although some recent studies suggest there could be a hormetic (potentially beneficial stimulant) effect from low-dose residential radon exposures,[423,424] numerous human cohort and case-control studies have concluded that radon causes lung cancer.[425–430] Radon is the second leading cause of lung cancer in the United States and the leading cause of lung cancer among people who have never smoked. Radon-induced lung cancer is responsible for an estimated average of 21,000 deaths annually, though scientists believe the range could be as wide as 8,000–45,000 radon deaths per year.[431] People who smoke and also are exposed to radon have a higher risk of lung cancer than from either exposure alone

Table 9

Lifetime Risk of Lung Cancer Death (Per Person) from Radon Exposure in Homes[A]

RADON LEVEL (pCi/L)[B]	NEVER SMOKERS	CURRENT SMOKERS[C]	GENERAL POPULATION
20	36 out of 1,000	26 out of 100	11 out of 100
10	18 out of 1,000	15 out of 100	56 out of 1,000
8	15 out of 1,000	12 out of 100	45 out of 1,000
4	73 out of 10,000	62 out of 1,000	23 out of 1,000
2	37 out of 10,000	32 out of 1,000	12 out of 1,000
1.25	23 out of 10,000	20 out of 1,000	73 out of 10,000
0.4	73 out of 100,000	64 out of 10,000	23 out of 10,000

A. Estimates are subject to uncertainties as discussed in Chapter VIII of the sixth Biological Effects of Ionizing Radiation (BEIR VI) risk assessment.

B. Assumes constant lifetime exposure in homes at these levels; radon concentrations are measured in picocuries per liter of air (pCi/L).

C. Note: BEIR VI did not specify excess relative risks for current smokers.

Adapted from: U.S. Environmental Protection Agency. Assessment of risks from radon in the home [Internet]. [cited 2009 May 5] Available from http://www.epa.gov/radon/risk_assessment.html.

(Table 9). This combination may be deadly at least in part because tobacco contains, in addition to many carcinogens, considerable concentrations of radioactive polonium 210 (^{210}Po). When inhaled, ^{210}Po particles adhere to and damage parts of the lung where bronchial carcinomas frequently arise in smokers.[432]

The impact of long-term radon exposure may increase in the future as the population ages and exposure to radiation from medical sources escalates (see Chapter 4). Some evidence[433–435] suggests that in addition to lung cancer, protracted radon exposure may increase risks for leukemia, skin, stomach, and liver cancers, but well-designed analytic epidemiology studies are needed to examine these associations. One meeting speaker suggested that such studies could be conducted cost-effectively by including them as components of ongoing prospective cohort studies such as the National Children's Study[61] and the Agricultural Health Study,[212] or as new case-control studies that include assessment of multiple toxicant exposures. As with many types of environmental contaminants, assessing lifetime cumulative exposures retrospectively can be difficult. However, it now is possible to gather reliable retrospective data on decades of radon exposure by measuring embedded radon decay products on glass surfaces (e.g., the glass in picture frames) that individuals have carried from one residence to another.[436,437]

...about a third of the radon-attributable lung cancers are preventable at the current EPA action level.

JAY LUBIN
NATIONAL CANCER INSTITUTE

Current radon protection policies are based on a paradigm for radon risk assessment developed in the 1980s. The Indoor Radon Abatement Act of 1988[438] sets a national long-term goal of reducing radon levels in buildings to the levels of ambient outdoor air, but no regulations mandate specific radon levels for indoor residential buildings. The U.S. Environmental Protection Agency (EPA) action level for residential radon (the level at which remedial action is recommended) is four picocuries per liter of air (4 pCi/L), based both on risk considerations and the technical feasibility of remediation. Up to 6 percent of U.S. homes are estimated to have radon concentrations at or above the action level.[439] Yet most radon-induced lung

cancers arise from exposures below that level.[440] As with other types of potentially hazardous exposures, vigorous debate exists regarding the relative safety of low-dose exposures. Speakers at the PCP meetings questioned whether EPA's action level for radon should be lowered. An EPA representative emphasized that the current action level does not imply that levels below 4 pCi/L are safe; significant risk exists below the action level and, in fact, no safe exposure level has been identified.[441] In 2009, the World Health Organization (WHO) revised its recommendation for a maximum acceptable radon concentration in a residential dwelling to 2.7 pCi/L.[442]

Radon and its decay products account for 37 percent of the overall population radiation dose from natural sources.[308] As Figure 14 shows, radon levels vary considerably across the United States. EPA emphasizes that elevated radon levels can be found in homes in all three zones, and that all homes should be tested for radon.[443]

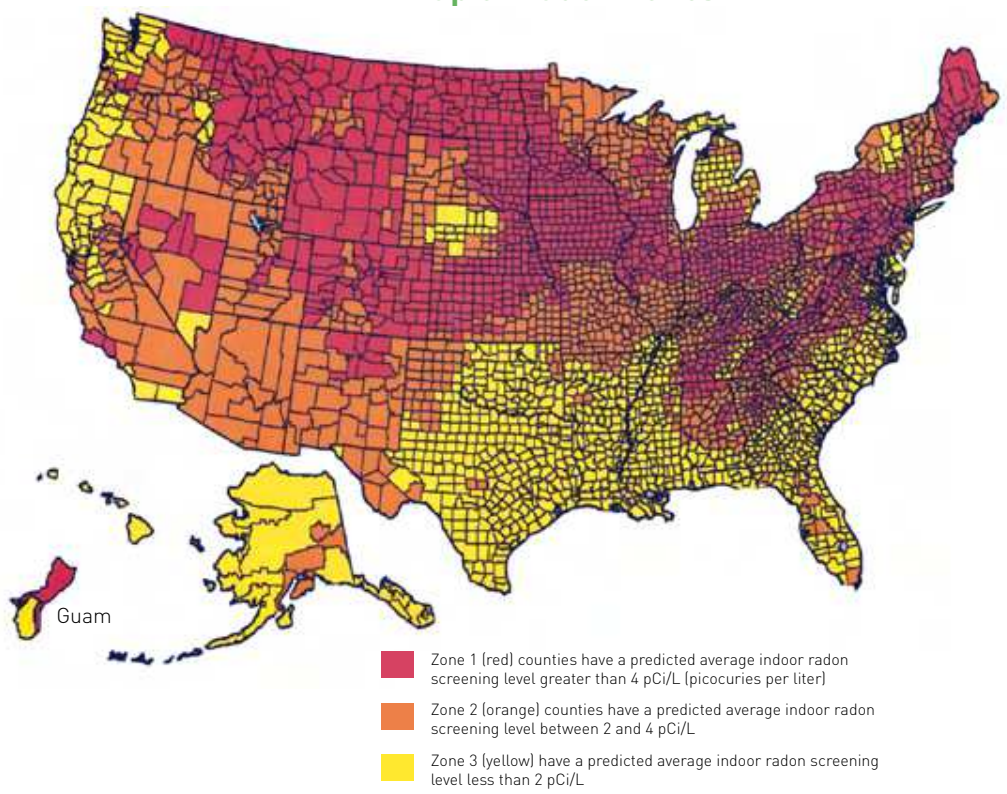
While the public may know that radon exists, relatively few people are aware of the levels at which radon concentration should cause significant concern. As a result of concerted efforts by EPA pursuant to the Indoor Air Abatement Act, most states now have radon reduction programs, yet as of December 2008, none require mandatory radon testing prior to a home sale.[444] More than half of states have residential real estate disclosure laws,[441] meaning that if the radon level of a home is known, it must be disclosed. If a home's radon level is not known, it is up to the prospective buyer to arrange for a radon test. In most states,

It's important to know that radon is naturally occurring, but in the home it's not naturally occurring; it's enhanced. We can build homes radon resistant. We just choose not to do so.

WILLIAM FIELD
UNIVERSITY OF IOWA

EPA Map of Radon Zones

Figure 14



Source: U.S. Environmental Protection Agency, April, 2009 [Internet]. [cited 2009 May 20] Available from: http://www.epa.gov/radon/zonemap.html.

a 48-hour radon test (in which a testing device is left undisturbed in the basement or other lower level(s) of the home for two days) is used most commonly. However, the sensitivity of the testing devices varies significantly and it is possible to intentionally or unintentionally compromise the accuracy of even the best devices used under ideal conditions.[445]

We have to go beyond a voluntary program [for radon mitigation] at this point. You can see all these homes in the future will need retrofitting and it's going to be three times, four times more expensive than doing it when we first build the homes.

WILLIAM FIELD
UNIVERSITY OF IOWA

Only a handful of states require radon testing in schools or day care facilities.[446] Such testing has the same accuracy issues as residential testing, and testing data may not be available to parents. Moreover, only a fraction of these states require mitigation if radon readings are high, and periodic retesting is not required. Only two states (RI and NH) require radon testing in all public buildings.

EPA provides guidance on radon testing[447] but does not provide oversight of radon testing accuracy or reliability. Its proficiency programs for radon testing device vendors and analysis laboratories (authorized under the Indoor Radon Abatement Act) were defunded in the late 1990s; it was intended that these programs would be replaced by a user fee system. According to the Office

of the Inspector General at EPA, most radon testing devices on the market require reevaluation to determine their accuracy.[445] Approximately 20 states have enacted legislation requiring professional certification or licensure of both testers and/or radon mitigation vendors,[444] but implementation varies widely.

Well-established methods are available to reduce radon concentrations to below the EPA action level in homes with elevated radon concentrations.[448–451] According to one speaker at a Panel meeting, radon venting for new home construction costs approximately $300–500. It is required in some states (WA, MN, MI, NJ, ME); only three states (CT, NJ, RI) require radon control in new school construction.[441] Retrofitting existing homes that have high radon concentrations with mitigation venting costs approximately $1,200; in one study, mitigation reduced average residential radon levels from more than 10 pCi/L to 1.2 pCi/L.[451] EPA recommends that homeowners consider mitigation if radon levels are at 2–4 pCi/L.[441]

Arsenic

Inorganic arsenic, a potent toxin, is found in bedrock at varying levels worldwide. Most inorganic arsenic in drinking water is from natural sources, but human activities such as mining, ore processing, use of arsenic-containing pesticides, and burning of fossil fuels are major contributors to waterborne arsenic in the U.S.[267] Both the EPA Maximum Contaminant Level (MCL)[452] and WHO[453] recommendations for inorganic arsenic limits in drinking water are 10 micrograms/liter. Organic arsenic compounds (those containing carbon) are found mainly in aquatic organisms, and are far less toxic than inorganic arsenic.

Ecologic, cohort, and case-control studies of highly exposed populations have linked inorganic arsenic in drinking water with skin, lung, bladder, and kidney cancer in both sexes and with prostate cancer in men.[267] Both EPA and the International Agency for Research on Cancer classify ingested inorganic arsenic as a known human carcinogen.[77,454] Inorganic arsenic also is associated with numerous non-cancer conditions, including gastrointestinal, vascular, neurologic, blood system, endocrine, respiratory, skin, reproductive, and developmental effects.[267,454]

Cancer risk related to low-level inorganic arsenic exposure has been estimated by extrapolation from high-exposure studies. Exposure is determined by the presence of arsenic and arsenic metabolites in urine. A large, NCI-led, collaborative case-control study underway in northern New England is assessing the carcinogenicity of arsenic exposure at lower doses. Other researchers are attempting to understand variations in individual susceptibility to carcinogenic effects of ingested arsenic. Some evidence suggests that diets deficient in micronutrients such as vitamins B-2, B-6, B-12, and folic acid may increase susceptibility to arsenic-induced cancers.[267]

PART 3

Taking Action to Reduce Environmental Cancer Risk: What We Can Do

In addition to exposures that directly or indirectly damage DNA, evidence suggests that some environmental agents may initiate or promote cancer by disrupting normal immune and endocrine system functions. The burgeoning number and complexity of known or suspected environmental carcinogens compel us to act to protect public health, even though we may lack irrefutable proof of harm. Action is possible at several levels: conducting scientific research to enhance our understanding and ability to prevent and respond to environmental carcinogens; taking personal action; enforcing existing policies and regulations that protect workers and the public; and implementing policy and regulatory changes that support public health and reduce the burden of cancer.

The following sections detail: (1) the Panel's conclusions based on the meeting testimony and subsequent additional information gathering; (2) recommendations for policy, research, program, industry, and other actions to minimize the influence of environmental factors on cancer; and (3) suggested actions individuals can take to reduce their risk of cancer due to harmful environmental exposures.

Just as there are many opportunities for harmful environmental exposures, ample opportunities also exist for intervention, change, and prevention to protect the health of current and future generations and reduce the national burden of cancer. The Panel concludes that:

We Need to Determine the Full Extent of Environmental Influences on Cancer.

At this time, we do not know how much environmental exposures influence cancer risk and related immune and endocrine dysfunction. Environmental contamination varies greatly by type and magnitude across the nation, and the lifetime effects of exposure to combinations of chemicals and other agents are largely unstudied. Similarly, the cancer impact of exposures during key "windows of vulnerability" such as the prenatal period, early life, and puberty are not well understood. Nonetheless, while these diverse effects often are difficult to quantify with existing technologies and research methods, in a great many instances, we know enough to act.

The Nation Needs a Comprehensive, Cohesive Policy Agenda Regarding Environmental Contaminants and Protection of Human Health.

Environmental health, including cancer risk, has been largely excluded from overall national policy on protecting and improving the health of Americans. It is more effective to prevent disease than to treat it, but cancer prevention efforts have focused narrowly on smoking, other lifestyle behaviors, and chemopreventive interventions. Scientific evidence on individual and multiple environmental exposure effects on disease initiation and outcomes, and consequent health system and societal costs are not being adequately integrated into national policy decisions and strategies for disease prevention, health care access, and health system reform.

Children Are at Special Risk for Cancer Due to Environmental Contaminants and Should Be Protected.

Opportunities for eliminating or minimizing cancer-causing and cancer-promoting environmental exposures must be acted upon to protect all Americans, but especially children. They are at special risk due to their smaller body mass and rapid physical development, both of which magnify their vulnerability to known or suspected carcinogens, including radiation. Numerous environmental contaminants can cross the placental barrier; to a disturbing extent, babies are born "pre-polluted." Children also can be harmed by genetic or other damage sustained by the mother (and in some cases, the father). There is a critical lack of knowledge and appreciation of environmental threats to children's health and a severe shortage of researchers and clinicians trained in children's environmental health.

Continued Epidemiologic and Other Environmental Cancer Research Is Needed.

Available evidence on the level of potential harm and increased cancer risk from many environmental exposures is insufficient or equivocal. The Panel is particularly concerned that the impact, mechanisms of action, and potential interaction of some known and suspected carcinogens are poorly defined.

- Meaningful measurement and assessment of the cancer risk associated with many environmental exposures is hampered by a lack of accurate measurement tools and methodologies. This is particularly true regarding cumulative exposure to specific established or possible carcinogens (e.g., radon, low-dose radiofrequency and electromagnetic energy, endocrine disrupting chemicals), gene-environment interactions, emerging technologies (e.g., nanoparticles), and the effects of multiple agent exposures.
- Single-agent toxicity testing and reliance on animal testing are inadequate to address the backlog of untested chemicals already in use and the plethora of new chemicals introduced every year. Some high-throughput screening (HTS) technologies are available to enable testing of many chemicals and other contaminants simultaneously, but many remain to be developed to meet chemical testing needs. Support also is needed to develop methods for interpreting the wealth of data that HTS technologies generate. At this time, incentives to encourage development of this research are nearly non-existent.
- Support for large, longitudinal studies to clarify the nature and magnitude of cancer risk attributable to environmental contaminants must continue. The capacity to collect biologic samples at the inception of studies is essential; even if current technologies do not allow these samples to be fully utilized at this time, it must be assumed that such technologies will evolve and enable use of collected biosamples to provide essential study baseline data. Personal health data privacy issues that currently limit research access to data and biosamples will need to be addressed.
- Cancer risk assessment also is hampered by lack of access to existing exposure data, especially for occupational/industrial exposures, and regarding levels of radon, asbestos, and other contaminants in schools and day care centers.

An Environmental Health Paradigm for Long-Latency Disease Is Needed.

Recognizing that results of laboratory and animal studies do not always predict human responses, an environmental health paradigm for long-latency diseases is needed to enable regulatory action based on compelling animal and *in vitro* evidence before cause and effect in humans has been proven.

Existing Regulations for Environmental Contaminants Need to Be Enforced and Updated; Stronger Regulation is Needed.

Weak laws and regulations, inefficient enforcement, regulatory complexity, and fragmented authority allow avoidable exposures to known or suspected cancer-causing and cancer-promoting agents to continue and proliferate in the workplace and the community. Existing regulations, and the exposure assessments on which they are based, are outdated in most cases, and many known or suspected carcinogens are completely unregulated. Enforcement of most existing regulations is poor. In virtually all cases, regulations fail to take multiple exposures and exposure interactions into account. In addition, regulations for workplace environments are focused more on safety than on health. Industry has exploited regulatory weaknesses, such as government's reactionary (rather than precautionary) approach to regulation. Likewise, industry has exploited government's use of the flawed and grossly outdated Doll and Peto methodology for assessing "attributable fractions" of the cancer burden due to specific environmental exposures. This methodology has been used effectively by industry to justify introducing untested chemicals into the environment.

Radiation Exposure from Medical Sources Is Underappreciated.

The use of computed tomography (CT) and other radiation-emitting tests is growing rapidly. Many physicians, other health care providers, and the public are unaware of the radiation dose delivered by specific imaging and nuclear medicine studies and the significant variation in radiation dose that can occur due to differences in equipment, technologist skill, application of dose-reduction strategies, and patient size, age, and gender. Moreover, many do not recognize that radiation exposure is cumulative, and that a single large dose and numerous low doses equal to the single large dose have much the same effect on the body over time. At least one initiative is underway to improve and disseminate radiation reduction strategies and educate physicians, device manufacturers, their training staff, and others about radiation doses associated with specific tests. Additional efforts are needed to eliminate unnecessary testing and improve both equipment capability and operator skill to ensure that radiation doses are as low as reasonably achievable without sacrificing image or test data quality. No mechanism exists to enable individuals to estimate their personal cumulative radiation exposure, which would help patients and physicians weigh the benefits and potential harm of contemplated imaging and nuclear medicine tests.

Medical Professionals Need to Consider Occupational and Environmental Factors When Diagnosing Patient Illness.

Physicians and other medical professionals ask infrequently about patient workplace and home environments when taking a medical history. Such information can be invaluable in discovering underlying causes of disease. Moreover, gathering this information would contribute substantially to the body of knowledge on environmental cancer risk.

Workers, Other Populations with Known Exposures, and the General Public Require Full Disclosure of Knowledge about Environmental Cancer Risks.

Individuals and communities are not being provided all available information about environmental exposures they have experienced, the cumulative effects of such exposures, and how to minimize harmful exposures. The disproportionate burden of exposure to known or suspected carcinogens experienced by specific populations (e.g., agricultural and chemical workers and their families, radiation-exposed groups such as uranium mine workers, nuclear industry workers, nuclear test site workers and "downwinders," residents of cancer "hot spots" or other contaminated areas) has not been fully acknowledged.

The Military Needs to Aggressively Address the Toxic Environmental Exposures It Has Caused.

Toxic materials produced for and used by the military have caused widespread air, soil, and water pollution across the United States and beyond our borders, including chemical and radiation contamination in and around current and former military installations, materiel production facilities, and mines. These contaminants, many of which may have serious long-term and latent effects including cancer, are a danger both to military personnel and civilians. Overall, the military has not responded adequately to health problems associated with its operations absent substantial pressure from those affected, advocacy groups, or the media. Of special concern, the U.S. has not met its obligation to provide for ongoing health needs of the people of the Republic of the Marshall Islands resulting from radiation exposures they received during U.S. nuclear weapons testing in the Pacific from 1946–1958.

Safer Alternatives to Many Currently Used Chemicals Are Urgently Needed.

The requisite knowledge and technologies exist to develop alternatives to many currently used chemical agents known or believed to cause or promote cancer. Many chemists require additional training to understand environmental hazards and reformulate products. Importantly, "green chemistry" alternative products themselves require longitudinal study to ensure that they do not pose unexpected health hazards.

Policy, Research, and Program Recommendations

Based on its conclusions, the Panel recommends:

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
1. A precautionary, prevention-oriented approach should replace current reactionary approaches to environmental contaminants in which human harm must be proven before action is taken to reduce or eliminate exposure. Though not applicable in every instance, this approach should be the cornerstone of a new national cancer prevention strategy that emphasizes primary prevention, redirects accordingly both research and policy agendas, and sets tangible goals for reducing or eliminating toxic environmental exposures implicated in cancer causation. The proposed Kid Safe Chemicals Act introduced in the 110th Congress, or similar legislation, has the potential to be an important first step toward a precautionary chemicals management policy and regulatory approach to reducing environmental cancer risk. Optimally, it should shift the burden of proving safety to manufacturers prior to new chemical approval, in mandatory post-market studies for new and existing agents, and in renewal applications for chemical approval.	President/Administration Congress Environmental Protection Agency (EPA) Department of Labor (DOL)/ Occupational Safety and Health Administration (OSHA) Department of Health and Human Services (HHS): • Food and Drug Administration (FDA) • National Institutes of Health (NIH) Department of Agriculture (USDA) State governments Industry

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
2. A thorough new assessment of workplace chemical and other exposures is needed to quantify current health risks. Previous estimates of occupational cancer risk are outdated and should no longer be used by government or industry.	Congress National Academy of Science/ Institute of Medicine National Science Foundation (NSF) General Accountability Office Other multidisciplinary group appointed for this task HHS/National Institute for Occupational Safety and Health (NIOSH) DOL: • OSHA • Mine Safety and Health Administration (MSHA)
3. In large measure, adequate environmental health regulatory agencies and infrastructures already exist, but agencies responsible for promulgating and enforcing regulations related to environmental exposures are failing to carry out their responsibilities. The following are needed:	
• A more integrated, coordinated, and transparent system for promulgating and enforcing environmental contaminant policy and regulations, driven by science and free of political or industry influence, must be developed to protect public health.	EPA HHS/FDA USDA DOL: • OSHA • MSHA
• Better concordance of exposure measures and standards is needed to facilitate interagency and international regulatory policy and enforcement and to identify research needs.	HHS/National Institute of Environmental Health Services (NIEHS) EPA DOL/OSHA
• The United States should carefully consider the potential impact on consumers and commerce of the Globally Harmonized System for classifying carcinogens.	President/Administration Congress

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
• Information sharing among the public, researchers, regulatory agencies, industry, and other stakeholders must be a bedrock component of the environmental health regulatory system mission.	EPA DOL: • OSHA • MSHA HHS: • FDA • Center for Disease Control and Prevention (CDC) USDA Department of Defense (DoD) Department of Energy (DOE) Environmental and cancer research communities Industry Media
• Environmental and public health advocates should be included in developing the environmental cancer research and policy agendas and in information dissemination.	Advocates EPA HHS: • FDA • CDC DOE
4. Epidemiologic and hazard assessment research must be continued and strengthened in areas in which the evidence is unclear, especially research on workplace exposures, the impact of *in utero* and childhood exposures, and exposures that appear to have multigenerational effects. Current funding for federally supported occupational and environmental epidemiologic cancer research is inadequate.	Congress EPA HHS: • National Cancer Institute (NCI) • NIEHS • National Institute for Child Health and Human Development • NIOSH EPA NSF Nongovernmental research funders

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
5. Measurement tool development and exposure assessment research, including the development of new research models and endpoints, should be accelerated to enable better quantification of exposures at individual, occupational, and population levels.	
• High-throughput screening technologies and related data interpretation models should be developed and used to evaluate multiple exposures simultaneously. It may be possible to screen apparently similar suspect chemicals together and regulate these as a group as indicated by findings.	HHS • NIEHS • NIOSH NSF DoD/Applied Research Projects Agency Industry
• Methods for long-term monitoring and quantification of electromagnetic energy exposures related to cell phones and wireless technologies are urgently needed given the escalating use of these devices by larger and younger segments of the population and the higher radiofrequencies newer devices produce.	DOE HHS/NIOSH EPA National Council on Radiation Protection and Measurements (NCRP)
6. The cancer risk attributable to residential radon exposure has been clearly demonstrated and must be better addressed. The following are needed:	
• The Environmental Protection Agency (EPA) should consider lowering its current action level (4 pCi/L) for radon exposure, taking into account data on radon-related cancer risk developed since the existing action level was established.	EPA
• Public and health care provider education should be developed and broadly disseminated to raise awareness of radon-related cancer risk.	HHS Health care provider professional organizations Media
• Improved testing methods for residential radon exposure and better methods for assessing cumulative exposure should be developed. Tax deductions or other incentives should be implemented to encourage radon mitigation retrofitting of existing housing. Building code changes should be made to require radon reduction venting in new construction.	Industry Congress Internal Revenue Service State and local governments
• All schools, day care centers, and workplaces should be tested at regular intervals for radon. Radon level data must be made available to the public. Buildings found to have levels in excess of the EPA action level should be mitigated.	State and local governments

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
7. Actions must be taken to minimize radiation exposure from medical sources. Specifically:	
• Health care providers, radiology technicians, and the public must be informed about the extent of radiation exposure from commonly used imaging and nuclear medicine examinations and the potential health risks of these procedures. Referring physicians are responsible for discussing with the patient the balance of benefit and risk associated with each imaging or nuclear medicine procedure being recommended. An educational/ decision-making tool that considers each patient's cumulative lifetime radiation exposure should be developed to facilitate these provider-patient communications.	Physicians and other health care providers Health professional organizations Advocates Media HHS: • Agency for Healthcare Research and Quality • NCI
• The estimated effective radiation dose of all imaging and nuclear medicine tests performed should be a required element in patient records and should be a core data element in all electronic health records systems. In addition, patients should be assisted to reconstruct an estimate of the total medical radiation dose they have received.	Joint Commission for Accreditation of Healthcare Organizations (JCAHO) HHS: • FDA • Centers for Medicare and Medicaid Services (CMS) • CDC • Health Resources and Services Administration (HRSA) • Indian Health Service (IHS) • Office of the National Coordinator for Health Information Technology (ONCHIT) Department of Veterans Affairs (VA) DoD Physicians and other health care providers
• Radiation dose-lowering techniques must be implemented consistently and to the maximum extent feasible.	Physicians and other health care providers
• Inspection of radiation-emitting medical equipment and pharmaceuticals must become more stringent, and uniform credentialing of technicians who administer scans is needed.	JCAHO Radiation technologist professional organizations HHS/FDA

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
8. The unequal burden of exposure to known and suspected carcinogens must be addressed.	
• Individuals exposed to nuclear fallout and other nuclear contamination by biologically important radionuclides must be provided all available information on these exposures. A system must be developed to enable affected individuals to reconstruct and add radiation doses received so that they can adequately assess their cumulative exposure and potential health risks, including cancer.	DoD DOE Nuclear Regulatory Commission HHS/NCI VA NCRP
• The Advisory Committee on Energy-related Epidemiologic Research (ACERER) should be rechartered, or a similar body convened, to enable individuals exposed to nuclear testing fallout and other nuclear exposures to participate in policy making and other decisions that will affect their access to health care and compensation related to those exposures.	DOE
• Geographic areas and vulnerable populations (including but not limited to children, migrant and other farm workers, and residents of high-poverty areas and cancer "hot spots") should be studied to determine environmental influences on cancer risk; identified risks must be remediated to the maximum extent possible.	EPA HHS/NIEHS DoD USDA
• The U.S. Government should honor and make payments according to the judgment of the Marshall Islands Tribunal.	President/Administration Congress

RECOMMENDATION	RESPONSIBLE AGENCIES, STAKEHOLDERS, AND OTHER ENTITIES*
9. Physicians and other medical personnel should routinely query patients about their previous and current workplace and home environments as part of the standard medical history. This information will increase the likelihood that environmental factors in cancer and other illnesses are considered and will strengthen the body of information on environmental exposures and disease. Data on workplace and home environmental history should be incorporated into existing and developing automated medical records systems.	Physicians and other health care providers HHS: • ONCHIT • NCI: Surveillance, Epidemiology, and End Results Program • CDC: National Program of Cancer Registries • CMS • HRSA • IHS DoD: TRICARE VA: Veterans Health Information System and Technology Architecture Private insurer patient databases
10. "Green chemistry" initiatives and research, including process redesign, should be pursued and supported more aggressively, but new products must be well-studied prior to and following their introduction into the environment and stringently regulated to ensure their short- and long-term safety.	HHS/NIEHS EPA NSF
11. Public health messages should be developed and disseminated to raise awareness of environmental cancer risks and encourage people to reduce or eliminate exposures whenever possible.	HHS: • FDA • CDC • HRSA • CMS USDA DOE Federal Communications Commission Advocates Media

* The Panel recognizes that entities other than those listed may have a vital role or interest in implementation of the recommendations.

What Individuals Can Do: Recommendations

Much remains to be learned about the effects of environmental exposures on cancer risk. Based on what is known, however, there is much that government and industry can do now to address environmental cancer risk. The Panel's recommendations in this regard are detailed above. At the same time, individuals can take important steps in their own lives to reduce their exposure to environmental elements that increase risk for cancer and other diseases. And collectively, individual small actions can drastically reduce the number and levels of environmental contaminants.

CHILDREN
1. It is vitally important to recognize that children are far more susceptible to damage from environmental carcinogens and endocrine-disrupting compounds than adults. To the extent possible, parents and child care providers should choose foods, house and garden products, play spaces, toys, medicines, and medical tests that will minimize children's exposure to toxics. Ideally, both mothers and fathers should avoid exposure to endocrine-disrupting chemicals and known or suspected carcinogens prior to a child's conception and throughout pregnancy and early life, when risk of damage is greatest.
CHEMICAL EXPOSURES
2. Individuals and families have many opportunities to reduce or eliminate chemical exposures. For example: • Family exposure to numerous occupational chemicals can be reduced by removing shoes before entering the home and washing work clothes separately from the other family laundry. • Filtering home tap or well water can decrease exposure to numerous known or suspected carcinogens and endocrine-disrupting chemicals. Unless the home water source is known to be contaminated, it is preferable to use filtered tap water instead of commercially bottled water. • Storing and carrying water in stainless steel, glass, or BPA- and phthalate-free containers will reduce exposure to endocrine-disrupting and other chemicals that may leach into water from plastics. This action also will decrease the need for plastic bottles, the manufacture of which produces toxic by-products, and reduce the need to dispose of and recycle plastic bottles. Similarly, microwaving food and beverages in ceramic or glass instead of plastic containers will reduce exposure to endocrine-disrupting chemicals that may leach into food when containers are heated.

- Exposure to pesticides can be decreased by choosing, to the extent possible, food grown without pesticides or chemical fertilizers and washing conventionally grown produce to remove residues. Similarly, exposure to antibiotics, growth hormones, and toxic run-off from livestock feed lots can be minimized by eating free-range meat raised without these medications if it is available. Avoiding or minimizing consumption of processed, charred, and well-done meats will reduce exposure to carcinogenic heterocyclic amines and polyaromatic hydrocarbons.
- Individuals can consult information sources such as the Household Products Database to help them make informed decisions about the products they buy and use.
- Properly disposing of pharmaceuticals, household chemicals, paints, and other materials will minimize drinking water and soil contamination. Individuals also can choose products made with non-toxic substances or environmentally safe chemicals. Similarly, reducing or ceasing landscaping pesticide and fertilizer use will help keep these chemicals from contaminating drinking water supplies.
- Turning off lights and electrical devices when not in use reduces exposure to petroleum combustion by-products because doing so reduces the need for electricity, much of which is generated using fossil fuels. Driving a fuel-efficient car, biking or walking when possible, or using public transportation also cuts the amount of toxic auto exhaust in the air.
- Individuals can reduce or eliminate exposure to secondhand tobacco smoke in the home, auto, and public places. Most counseling and medications to help smokers quit are covered by health insurance or available at little or no cost.

RADIATION

3. Adults and children can reduce their exposure to electromagnetic energy by wearing a headset when using a cell phone, texting instead of calling, and keeping calls brief.

4. It is advisable to periodically check home radon levels. Home buyers should conduct a radon test in any home they are considering purchasing.

5. To reduce exposure to radiation from medical sources, patients should discuss with their health care providers the need for medical tests or procedures that involve radiation exposure. Key considerations include personal history of radiation exposure, the expected benefit of the test, and alternative ways of obtaining the same information. In addition, to help limit cumulative medical radiation exposure, individuals can create a record of all imaging or nuclear medicine tests received and, if known, the estimated radiation dose for each test.

6. Adults and children can avoid overexposure to ultraviolet light by wearing protective clothing and sunscreens when outdoors and avoiding exposure when the sunlight is most intense.

SELF-ADVOCACY

7. Each person can become an active voice in his or her community. To a greater extent than many realize, individuals have the power to affect public policy by letting policymakers know that they strongly support environmental cancer research and measures that will reduce or remove from the environment toxics that are known or suspected carcinogens or endocrine-disrupting chemicals. Individuals also can influence industry by selecting non-toxic products and, where these do not exist, communicating with manufacturers and trade organizations about their desire for safer products.

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APPENDIX A

President's Cancer Panel Meetings
Environmental Factors in Cancer—Participants

MEETING DATES AND LOCATIONS		
September 16, 2008	Industrial and Occupational Exposures	East Brunswick, NJ
October 21, 2008	Agricultural Exposures	Indianapolis, IN
December 4, 2008	Indoor/Outdoor Air Pollution and Water Contamination	Charleston, SC
January 27, 2009	Nuclear Fallout, Electromagnetic Fields, and Radiation Exposure	Phoenix, AZ

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APPENDIX B

Recommendations of NIOSH Expert Panel for Enhancing Occupational Cancer Research Methods

FOCUS AREA	RECOMMENDATIONS
Identification of Occupational Carcinogens	**Improve surveillance of occupational cancer with inclusion of workplace factors in national surveillance system.** **Improve workplace exposure assessment and characterization for prioritization of carcinogenicity testing.** **Improve simulation of occupational exposure circumstances for experimental studies.** **Develop new strategies for predicting and testing the adverse effects of mixtures.** **Develop and validate experimental and computational methods for carcinogenicity.**
Epidemiologic Research in Occupational Cancer	**Improve methods to:** • Characterize extent of occupational and environmental exposures by all routes; • Identify populations for study; • Estimate levels of exposure retrospectively; • Conduct surveillance of occupationally related cancer; • Identify, validate, and utilize biological markers as surrogate endpoints; and • Determine the relationship between maternal and paternal occupational exposure and cancer in offspring. **Increase emphasis on:** • Prospective studies with collection of biological samples and use of archival samples; • Multicenter case-control studies; • Applying advances in genetic research to better understand the etiology of occupational cancer and the basis for inter-individual differences in susceptibility; and • Studies of occupational cancer in women and minorities.

FOCUS AREA	RECOMMENDATIONS
Improvements in Risk Assessment for Occupational Carcinogens	**Develop approaches to foster collaboration between human and animal researchers by:** • Improving communication and interaction; • Integrating modes and mechanisms; and • Setting national priorities. **Develop and validate risk assessment models by incorporating modes and mechanisms of action (biomarkers):** • Use biologically based risk models for hypothesis framing and testing; and • Study sensitive subpopulations and lifestyles. **Explore improved methods of communicating risk assessment information to risk managers, decision makers, and the public.**
Prevention of Occupational Cancers	**Emphasize methods for primary prevention through elimination or reduction of exposure to suspected carcinogens, which will include:** • Greater emphasis on front-end designs to reduce exposures in industrial processes; • Research on effective prevention of primary exposures; and • Research on effective communication of prevention strategies. **Enhance methods for secondary prevention through:** • Intervention research in high-risk occupational cohorts that includes screening studies, early diagnosis, and treatment (chemoprevention); and • Inclusion of high-risk cohorts in future cancer research. **Evaluate high-risk notification and intervention research programs.** **Address ethical issues of secondary prevention studies.**

Source: Schulte PA, Schnorr TM. Priorities for research and prevention of occupational cancer. Presented at the President's Cancer Panel meeting. East Brunswick, NJ: 2009 Sep 16. Adapted from: Ward EM, Schulte PA, Bayard S, Blair A, Brandt-Rauf P, et al. Priorities for development of research methods in occupational cancer. Environ Health Perspec. 2003; 111(1):1-12.

Selected International, U.S., and European Carcinogen Classification Systems

GLOBALLY HARMONIZED SYSTEM (GHS)	
Category 1A	**Known human carcinogen**: Based on human evidence.
Category 1B	**Presumed human carcinogen**: Based on demonstrated animal carcinogenicity.
Category 2	**Suspected carcinogen**: Limited evidence of human or animal carcinogenicity.

EUROPEAN UNION (EU)	
Category 1	**Substances known to be carcinogenic to man**: There is sufficient evidence to establish a causal association between human exposure to a substance and the development of cancer.
Category 2	**Substances which should be regarded as if they are carcinogenic to man**: There is sufficient evidence to provide a strong presumption that human exposure to a substance may result in the development of cancer, generally on the basis of: • Appropriate long-term animal studies; or • Other relevant information.
Category 3	**Substances which cause concern for man owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment**: There is some evidence from appropriate animal studies, but this is insufficient to place the substance in Category 2.

U.S. NATIONAL TOXICOLOGY PROGRAM (NTP)	
Known to Be a Human Carcinogen	There is sufficient evidence of carcinogenicity from studies in humans that indicates a causal relationship between exposure to the agent, substance, or mixture and human cancer.
Reasonably Anticipated to Be Carcinogenic	There is limited evidence of carcinogenicity from studies in humans that indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded, *or* There is sufficient evidence of carcinogenicity from studies in experimental animals that indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) in multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset, *or* There is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous NTP Report on Carcinogens as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH)	
A1	**Confirmed human carcinogen**: Based on the weight of evidence from epidemiological studies. Requires convincing epidemiological evidence to support carcinogenesis.
A2	**Suspected human carcinogen**: Human data are accepted as adequate in quality but are conflicting or insufficient to classify the agent as A1, *or* The agent is carcinogenic in experimental animals at doses, by routes of exposure, at sites, of histological types, or by mechanisms considered relevant to worker exposure.
A3	**Animal carcinogen**: The agent is carcinogenic in experimental animals at relatively high doses, by routes of administration, at sites, of histological types, or by mechanisms that may not be relevant to worker exposure. Available epidemiological studies do not confirm an increased risk of cancer in exposed humans. Available evidence does not suggest that the agent is likely to cause cancer in humans except under uncommon or unlikely routes or levels of exposure.
A4	**Not classified as a human carcinogen**: The agent causes concern that it could be carcinogenic for humans but cannot be assessed conclusively because of a lack of data. In vitro or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.
A5	**Not suspected as a human carcinogen**: The agent is not suspected to be a human carcinogen on the basis of properly conducted epidemiological studies in humans. These studies have sufficiently long follow-up, reliable exposure histories, sufficiently high dose, and adequate statistical power to conclude that exposure to the agent does not convey significant risk to humans.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC)	
Group 1	**Carcinogenic to humans:** There is sufficient evidence of carcinogenicity in humans. However, an agent or mixture may be placed in this category when evidence of carcinogenicity in humans is less than sufficient but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent or mixture acts through a relevant mechanism of carcinogenicity.
Group 2A	**Probably carcinogenic to humans:** There is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent or mixture may be classified in this category when there is inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. In addition, an agent, mixture, or exposure circumstance may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans.
Group 2B	**Possibly carcinogenic to humans:** There is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. An agent, mixture, or exposure circumstance may be included in this category when there is inadequate evidence of carcinogenicity in humans but there is sufficient evidence of carcinogenicity in experimental animals. In some instances, an agent, mixture, or exposure circumstance for which there is inadequate evidence of carcinogenicity in humans but limited evidence of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.
Group 3	**Not classifiable as to carcinogenicity to humans:** The evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals. In some cases, agents or mixtures for which the evidence of carcinogenicity is inadequate in humans but sufficient in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans. Agents, mixtures, and exposure circumstances that do not fall into any other group are also placed in this category.
Group 4	**Probably not carcinogenic to humans:** This category is used for agents or mixtures for which there is evidence suggesting lack of carcinogenicity in humans and in experimental animals. In some instances, agents or mixtures for which there is inadequate evidence of carcinogenicity in humans but evidence suggesting lack of carcinogenicity in experimental animals, consistently and strongly supported by a broad range of other relevant data, may be classified in this group.

U.S. ENVIRONMENTAL PROTECTION AGENCY (EPA)	
Carcinogenic to Humans	This descriptor indicates strong evidence of human carcinogenicity. It covers different combinations of evidence. • This descriptor is appropriate when there is convincing epidemiologic evidence of a causal association between human exposure and cancer. • Exceptionally, this descriptor may be equally appropriate with a lesser weight of epidemiologic evidence that is strengthened by other lines of evidence. It can be used when **all** of the following conditions are met: (a) There is strong evidence of an association between human exposure and either cancer or the key precursor events of the agent's mode of action but not enough for a causal association, *and* (b) There is extensive evidence of carcinogenicity in animals, *and* (c) The mode(s) of carcinogenic action and associated key precursor events have been identified in animals, *and* (d) There is strong evidence that the key precursor events that precede the cancer response in animals are anticipated to occur in humans and progress to tumors, based on available biological information.
Likely to Be Carcinogenic to Humans	This descriptor is appropriate when the weight of the evidence is adequate to demonstrate carcinogenic potential to humans but does not reach the weight of evidence for the descriptor "Carcinogenic to Humans." Adequate evidence consistent with this descriptor covers a broad spectrum. As stated previously, the use of the term "likely" as a weight of evidence descriptor does not correspond to a quantifiable probability. The examples below are meant to represent the broad range of data combinations that are covered by this descriptor; they are illustrative and provide neither a checklist nor a limitation for the data that might support use of this descriptor. Moreover, additional information (e.g., on mode of action) might change the choice of descriptor for the illustrated examples. Supporting data for this descriptor may include: • An agent demonstrating a plausible (but not definitively causal) association between human exposure and cancer, in most cases with some supporting biological, experimental evidence, though not necessarily carcinogenicity data from animal experiments; • An agent that has tested positive in animal experiments in more than one species, sex, strain, site, or exposure route, with or without evidence of carcinogenicity in humans; • A positive tumor study that raises additional biological concerns beyond that of a statistically significant result—for example, a high degree of malignancy, or an early age at onset; • A rare animal tumor response in a single experiment that is assumed to be relevant to humans; or • A positive tumor study that is strengthened by other lines of evidence—for example, either plausible (but not definitively causal) association between human exposure and cancer **or** evidence that the agent or an important metabolite causes events generally known to be associated with tumor formation (such as DNA reactivity or effects on cell growth control) likely to be related to the tumor response in this case.

Suggestive Evidence of Carcinogenic Potential

This descriptor of the database is appropriate when the weight of evidence is suggestive of carcinogenicity; a concern for potential carcinogenic effects in humans is raised, but the data are judged not sufficient for a stronger conclusion. This descriptor covers a spectrum of evidence associated with varying levels of concern for carcinogenicity, ranging from a positive cancer result in the only study on an agent to a single positive cancer result in an extensive database that includes negative studies in other species. Depending on the extent of the database, additional studies may or may not provide further insights. Some examples include:

- A small, and possibly not statistically significant, increase in tumor incidence observed in a single animal or human study that does not reach the weight of evidence for the descriptor "Likely to Be Carcinogenic to Humans." The study generally would not be contradicted by other studies of equal quality in the same population group or experimental system (see discussions of *conflicting evidence* and *differing results*, below);
- A small increase in a tumor with a high background rate in that sex and strain, when there is some but insufficient evidence that the observed tumors may be due to intrinsic factors that cause background tumors and not due to the agent being assessed. (When there is a high background rate of a specific tumor in animals of a particular sex and strain, then there may be biological factors operating independently of the agent being assessed that could be responsible for the development of the observed tumors.) In this case, the reasons for determining that the tumors are not due to the agent are explained;
- Evidence of a positive response in a study whose power, design, or conduct limits the ability to draw a confident conclusion (but does not make the study fatally flawed), but where the carcinogenic potential is strengthened by other lines of evidence (such as structure-activity relationships); or
- A statistically significant increase at one dose only, but no significant response at the other doses and no overall trend.

Inadequate Information to Assess Carcinogenic Potential

This descriptor is appropriate when available data are judged inadequate for applying one of the other descriptors. Additional studies generally would be expected to provide further insights. Some examples include:

- Little or no pertinent information;
- Conflicting evidence—that is, some studies provide evidence of carcinogenicity but other studies of equal quality in the same sex and strain are negative. Differing results—that is, positive results in some studies and negative results in one or more different experimental systems—do not constitute *conflicting evidence*, as the term is used here. Depending on the overall weight of evidence, differing results can be considered either suggestive evidence or likely evidence; or
- Negative results that are not sufficiently robust for the descriptor "Not Likely to Be Carcinogenic to Humans."

Not Likely to Be Carcinogenic to Humans

This descriptor is appropriate when the available data are considered robust for deciding that there is no basis for human hazard concern. In some instances, there can be positive results in experimental animals when there is strong, consistent evidence that each mode of action in experimental animals does not operate in humans. In other cases, there can be convincing evidence in both humans and animals that the agent is not carcinogenic. The judgment may be based on data such as:

- Animal evidence that demonstrates lack of carcinogenic effect in both sexes in well-designed and well-conducted studies in at least two appropriate animal species (in the absence of other animal or human data suggesting a potential for cancer effects);
- Convincing and extensive experimental evidence showing that the only carcinogenic effects observed in animals are not relevant to humans;
- Convincing evidence that carcinogenic effects are not likely by a particular exposure route; or
- Convincing evidence that carcinogenic effects are not likely below a defined dose range.

A descriptor of "not likely" applies only to the circumstances supported by the data. For example, an agent may be "Not Likely to Be Carcinogenic" by one route but not necessarily by another. In those cases that have positive animal experiment(s) but the results are judged to be not relevant to humans, the narrative discusses why the results are not relevant.

Selected Federal Laws Related to Environmental Hazards

FEDERAL LAWS REGARDING AIR QUALITY			
Bill	**Year**	**Background**	**Authorizations**
Air Pollution Control Act (APCA) **P.L. 84-159**	1955	The first federal air pollution legislation. Prompted by air inversion events: • Air pollution cloud in Donora, PA, 1948; lingered for 5 days, 20 dead, 6,000 sick; and • "Killer Fog" in London, 1952; 3,000 dead.	Funded research for scope and sources of air pollution.
Clean Air Act (CAA) **P.L. 88-206**	1963	The first federal legislation regarding air pollution control.	Developed a national program to address air pollution related to environmental problems. Supports research into techniques to minimize air pollution.
Motor Vehicle Air Pollution Control Act (MVAPCA) **P.L. 89-272**	1965	Amended the 1963 CAA.	Developed federal emissions standards for new vehicles.
Air Quality Act (AQA) **P.L. 90-148**	1967	Expanded federal government activities.	Developed enforcement procedures for air pollution problems involving interstate transport of pollutants. Expanded research to prevent and control air pollution.

Bill	Year	Background	Authorizations
CAA Extension **P.L. 91-604**	1970	The first comprehensive federal response to address air pollution. A major shift in the federal government's role in air pollution control.	Established National Ambient Air Quality Standards (NAAQS). Established requirements for State Implementation Plans to achieve NAAQS. Established New Source Performance Standards for new and modified stationary sources. Established National Emission Standards for Hazardous Air Pollutants (HAPs). Increased enforcement authority. Developed requirements for control of motor vehicle emissions.
CAA Amendments (CAA77) **P.L. 95-95**	1977	Amended the 1963 CAA.	Developed provisions related to the Prevention of Significant Deterioration. Developed provisions for areas considered non-attainment for NAAQS.
CAA Amendments (CAA90) **P.L. 101-549**	1990	Amended the 1963 CAA.	Developed programs for Acid Deposition Control (acid rain). Developed a program to control 189 toxic pollutants, including those previously regulated by the National Emission Standards for HAPs. Established permit program requirements. Expanded and modified provisions concerning the attainment of NAAQS. Expanded and modified enforcement authority to include Indian Tribes.

FEDERAL LAWS REGARDING WATER QUALITY

Bill	Year	Background	Authorizations
Federal Water Pollution Control Act (FWPCA) **P.L. 80-845**	1948	Objective: to restore and maintain the chemical, physical, and biological integrity of the nation's waters. Amended in 1956, 1961, 1966, 1970, 1972, 1977, and 1987 to strengthen enforcement provisions.	Established comprehensive programs for eliminating or reducing the pollution of interstate waters and tributaries and improving the sanitary condition of surface and underground waters. Provided assistance to states, municipalities, and interstate agencies in constructing treatment plants to prevent discharges of inadequately treated sewage and other wastes into interstate waters or tributaries.

Bill	Year	Background	Authorizations
Safe Drinking Water Act (SDWA) **P.L. 93-523**	1974	The main federal law ensuring the quality of Americans' drinking water. Excludes private wells. Amended in 1986 and 1996.	Established U.S. Environmental Protection Agency (EPA) health-based standards for drinking water quality to protect against microbial, disinfection by-product, and other contaminants. Required EPA protection of drinking water sources such as rivers, lakes, reservoirs, springs, and groundwater wells. Initiated funding to state water systems to make infrastructure or management improvements or to help systems assess and protect their source water. Required EPA oversight of states, localities, and water suppliers who implement standards. Required EPA conducted cost-benefit analyses for every new standard.
Clean Water Act (CWA) **P.L. 95-217**	1977	The principal statute governing water quality. Goals: • To end all discharges entirely and to restore, maintain and preserve the integrity of the nation's waters; and • To provide water that is both fishable and swimmable.	Regulated direct and indirect pollutant discharge into the nation's waters. Mandated permits for wastewater and storm water discharges. Regulated publicly owned treatment works for municipal and industrial wastewater. Required states to establish site-specific water quality standards for navigable bodies of water. Regulated other activities that affect water quality, such as dredging and the filling of wetlands.
Oil Pollution Act (OPA) **P.L. 101-380**	1990	The principal statute governing oil spills into the nation's waterways. Prompted by the Exxon Valdez oil spill in March of 1989. Amended the 1977 CWA. Includes the Oil Terminal and Oil Tanker Environmental Oversight and Monitoring Act.	Established liability and limitations on liability for damages resulting from oil pollution, and establishes a fund for the payment of compensation for such damages. Mandated a "National Oil and Hazardous Substances Pollution Contingency Plan (NCP)" to provide the organizational structure and procedures for preparing for and responding to discharges of oil and releases of hazardous substances, pollutants, and contaminants. Required preparation of spill prevention and response plans by coastal facilities, vessels, and certain geographic regions.

FEDERAL LAWS REGARDING NUCLEAR MATERIALS, FACILITIES, AND REGULATION

Bill	Year	Background	Authorizations
Atomic Energy Act (AEA) **P.L. 79-585**	1946	Shifted nuclear power management from military to civilian control.	Established the Atomic Energy Commission (AEC) and gave it responsibility for the development and production of nuclear weapons and for both the development and the safety regulation of the civilian uses of nuclear materials.
AEA Amendments **P.L. 83-703**	1954	The fundamental U.S. law on use of nuclear materials and facilities. Amended the 1946 AEA.	Regulated the development and use of nuclear materials and facilities.
The Price-Anderson Nuclear Industries Indemnity Act **P.L. 85-256**	1957	Objective: to ensure the availability of a large pool of funds to provide prompt and orderly compensation of members of the public who incur damages from a nuclear or radiological incident despite liability.	Provided the same protection available for a covered licensee or contractor, through indemnification, for persons who may be legally liable, regardless of identity or relationship to the licensed activity. Later amended to require Nuclear Regulatory Commission (NRC) licensees and Department of Energy contractors to enter into agreements of indemnification to cover personal injury and property damage to those harmed by a nuclear or radiological incident.
Reorganization Plan No. 3 of 1970 **35 F.R. 15623**	1970	Issued by President Nixon to organize the government's environmentally related activities rationally and systematically.	Established the U.S. Environmental Protection Agency and gave it a role in establishing "generally applicable environmental standards for the protection of the general environment from radioactive material." Established the National Oceanic and Atmospheric Administration.
Energy Reorganization Act (ERA) **P.L. 95-601**	1974	Superseded the 1954 AEA.	Established the Nuclear Regulatory Commission. Split the functions assigned by the AEA to the Atomic Energy Commission. • Assigned to the Department of Energy the responsibility for the development and production of nuclear weapons, promotion of nuclear power, and other energy-related work; and • Assigned to the NRC the regulatory work, which does not include regulation of defense nuclear facilities.

Bill	Year	Background	Authorizations
Uranium Mill Tailings Radiation Control Act **P.L. 95-604**	1978	Objective: to prevent or minimize, among other things, the diffusion of radon into the environment.	Established programs for the stabilization and control of mill tailings at active and inactive uranium or thorium mill sites. Gave the NRC regulatory authority over mill tailing at sites under NRC license.
Reorganization Plan No. 1 of 1980 **45 F.R. 40561**	1980	Issued by President Carter in response to a Government Accountability Office (GAO) report stating that the NRC needed more aggressive leadership.	Strengthened the executive and administrative roles of the NRC Chairman, particularly in emergencies, transferring to the Chairman "all the functions vested in the Commission pertaining to an emergency concerning a particular facility or materials ... regulated by the Commission." Provided that all policy formulation, policy-related rulemaking, and orders and adjudications would remain vested with the full Commission.

FEDERAL LAWS REGARDING PESTICIDES

Bill	Year	Background	Authorizations
Federal Insecticide Act (FIA) **P.L. 61-152**	1910	Passed in response to concerns from the United States Department of Agriculture (USDA) and farm groups about the sale of fraudulent or substandard pesticide products. Superseded by FIFRA.	Ensured the quality of pesticide chemicals purchased by consumers. Set standards for the manufacture of Paris Green, lead arsenate, insecticides, and fungicides. Provided for inspections, seizure of adulterated or misbranded products, and prosecution of violators.
Federal Food, Drug and Cosmetic Act (FFDCA) **P.L. 75-717**	1938	Includes various other regulations not related to pesticides. Supersedes the 1906 Federal Food and Drug Act, which did not address pesticides.	Authorized the Food and Drug Administration (FDA) to oversee safety of food, drugs, and cosmetics. Required coloring for certain pesticides to prevent their use as flour.
Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) **P.L. 80-104**	1947	The basic system of pesticide regulation to protect applicators, consumers and the environment. Supersedes the 1910 FIA.	Granted pesticide regulatory authority to U.S. Department of Agriculture (USDA).

Bill	Year	Background	Authorizations
Miller Amendment **P.L. 83-518**	1954	Also known as The Pesticide Residues Amendment. Amended the 1938 FFDCA.	Established EPA health-based standards (tolerances) for pesticides used in or on foods or animal feed. Allowed exemptions for pesticides from the requirement of a tolerance. Required pesticide residue levels in foods to be monitored and enforced by FDA (fruits, vegetables, seafood) and USDA (meat, milk, poultry, eggs, aquacultural foods).
Food Additives Amendment **P.L. 85-929**	1958	Amended the 1938 FFDCA.	Established zero tolerance for cancer-causing food additives (i.e. pesticides).
The Federal Environmental Pesticide Control Act **P.L. 92-516**	1972	Amended the 1947 FIFRA. Amended in 1996 by the Food Quality Protection Act (FQPA).	Moved pesticide regulatory authority to EPA. Established registration for all pesticides. Proscribed pesticide labeling requirements. Required pesticide applicants to show proper pesticide use "will not generally cause unreasonable adverse effects on the environment." Established a system of examination and certification at the private and commercial levels for applicators who wish to purchase and use restricted use pesticides. Established review processes for antimicrobials, biopesticides, and conventional pesticides.
Federal Advisory Committee Act (FACA) **P.L. 92-463**	1972	The legal foundation defining how federal advisory committees operate. Has special emphasis on open meetings, chartering, public involvement, and reporting.	Allowed EPA to charter the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) to advise EPA on establishing a program to: • Develop a flexible process to select and prioritize pesticides for screening; • Develop a process for identifying new and existing screening tests; • Agree on a set of available, validated screening tests for early application; and • Develop a process and criteria for deciding when additional tests beyond screening are needed and how any of these additional tests will be validated.

Bill	Year	Background	Authorizations
Food Quality Protection Act (FQPA) **P.L. 104-170**	1996	Represents an effort to update and resolve the inconsistencies between FIFRA and FFDCA. Fundamentally changed the way EPA regulates pesticides.	Mandated a single, health-based standard for all pesticides in all foods. Provided special protections for infants and children. Expedited approval of safer pesticides. Created incentives for the development and maintenance of effective crop protection tools for American farmers. Required periodic reevaluation of pesticide registrations and tolerances to ensure pesticide registrations will remain up to date with current science. Directed EPA to develop a screening program to determine whether certain substances may have hormonal effects in humans.

FEDERAL LAWS REGARDING ENVIRONMENTAL POLICY

Bill	Year	Background	Authorizations
National Environmental Policy Act (NEPA) **P.L. 91-190**	1970	The basic national charter for the protection of the environment. Objective: to "encourage productive and enjoyable harmony between man and the environment; to promote efforts which will prevent or eliminate damage to the environment and biosphere and stimulate the health and welfare of man; and to enrich the understanding of the ecological systems and natural resources important to the Nation." Trustees have integrated Oil Pollution Act restoration planning with the NEPA process.	Required the government to consider the consequences of major federal actions on human and natural aspects of the environment in order to minimize, where possible, adverse impacts. Established the Environmental Assessment (EA) process of environmental review and public notification for federal planning and decision making.
Environmental Justice **Executive Order 12898**	1994	Issued by President Clinton to address environmental justice in minority and low-income populations.	Required each federal agency to identify and address, as appropriate, disproportionately high and adverse human health or environmental effects of its programs, policies and activities on minority and low income populations.

FEDERAL LAWS REGARDING COMPENSATION OF SPECIAL COHORTS			
Bill	**Year**	**Background**	**Authorizations**
The Radiation-Exposed Veterans Compensation Act (REVCA) **P.L. 100-321**	1988	Objective: to provide compassionate compensation for service-based radiation exposure. Applies to World War II veterans who served in Hiroshima or Nagasaki, were prisoners of war in Japan, or who participated in tests of nuclear devices and who developed certain cancers.	Bypassed the requirement for demonstration of a connection between a veteran's disability and the veteran's military service in eligible veterans.
Radiation Exposure Compensation Act (RECA) **P.L. 101-426**	1990	Implementing regulations were issued by the Department of Justice in 1992. Revisions to the regulations in 1999 served to greater assist claimants in establishing entitlement to an award.	Provided for compassionate payments to individuals who contracted certain cancers and other serious diseases as a result of: • Residing or working "downwind" of The Nevada Test Site ($50,000); • Worker participation in above-ground nuclear weapons tests ($75,000); or • Working in uranium mines ($100,000).
RECA Amendments **P.L. 106-245**	2000	Amended the 1990 RECA to increase the number of individuals covered by RECA and to improve the ability of individuals to establish entitlement to an award.	Added uranium mill workers and ore transporters to the claimant categories. Provided additional compensable illnesses. Lowered the radiation exposure threshold for uranium miners. Included above-ground miners within "uranium miner" category. Modified medical documentation requirements. Removed certain lifestyle restrictions. Added geographic areas to the downwinder claimant category.

Bill	Year	Background	Authorizations
Energy Employees Occupational Illness Compensation Program Act (EEOICPA) **P.L. 106-398**	2000	Objective: to provide lump-sum compensation and health benefits to eligible Department of Energy (DOE) nuclear weapons workers or, if deceased, their survivors.	Part B, effective 2001: • Guaranteed compensation of $150,000 and payment of medical expenses for workers who meet requisite criteria and have developed Chronic Beryllium Disease, radiation-induced cancer, or chronic silicosis; • Guaranteed compensation of $50,000 and payment of medical expenses for uranium workers (or their survivors) previously awarded benefits by the Department of Justice under RECA; and • Ensured workers who develop beryllium sensitivity will receive medical monitoring to check for Chronic Beryllium Disease. Part E, effective 2004: • Guaranteed compensation and payment of medical expenses to employees of DOE contractors, subcontractors, uranium miners, millers, and ore transporters (or their survivors) who develop an illness due to exposure to toxic substances, not limited to radiation, at certain DOE facilities; and • Allowed variable compensation up to $250,000 based on wage loss, impairment, and survivorship.

Bill	Year	Background	Authorizations
Providing Compensation to America's Nuclear Weapons Workers **Executive Order 13179**	2000	Issued by President Clinton in response to the difficulties experienced by workers seeking compensation. Built upon the framework of EEOICPA.	Set out federal agency responsibilities to: • Provide necessary information and help to DOE employees and its contractors to determine if their illnesses are associated with conditions of their nuclear weapons-related work; • Provide workers and their survivors with all pertinent and available information necessary for evaluating and processing claims; and • Ensure that this program minimizes the administrative burden on workers and their survivors, and respects their dignity and privacy.
21st Century Department of Justice Appropriation Authorization Act **P.L. 107-273**	2002	Contained several technical revisions to RECA.	Reinserted a previously covered area for downwinder claimants that had erroneously been removed by the 2000 Amendments. Clarified the requirement that lung cancer must be "primary" for all claimant categories. Provided uranium miners the option of establishing exposure to 40 working level months of radiation or establishing employment in a mine for 1 year. Eliminated the requirement for uranium workers diagnosed with lung cancer to submit evidence of a nonmalignant respiratory disease.

OTHER RELEVANT FEDERAL LAWS			
Bill	**Year**	**Background**	**Authorizations**
Resource Conservation and Recovery Act (RCRA) **P.L. 94-580**	1976	Regulates hazardous and nonhazardous wastes. Regulates facilities that generate, treat, store, or dispose of hazardous waste.	Established a system for controlling hazardous waste from the time it is generated until its ultimate disposal. Prevented environmental problems by ensuring that wastes are well managed from "cradle to grave", reducing the amount of waste generated, conserving energy and natural resources. Required clean up of environmental problems caused by the mismanagement of wastes.
Toxic Substances Control Act (TSCA) **P.L. 94-469**	1976	Addresses the production, importation, use, and disposal of specific chemicals. Excludes foods, drugs, cosmetics, and pesticides.	Required pre-manufacture notification for "new chemical substances." Required testing of chemicals by manufacturers, importers and processors where risks or exposures of concern are found. Issued Significant New Use Rules (SNURs) when EPA identifies a "significant new use" that could result in exposures to, or release of, a substance of concern. Maintained the TSCA Inventory—an inventory that contains more than 83,000 chemicals. As new chemicals are commercially manufactured or imported, they are placed on the list. Required those importing or exporting chemicals to comply with certification reporting. Required reporting and recordkeeping by persons who manufacture, import, process, and/or distribute chemical substances in commerce. Required that any person who manufactures, imports, processes, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment to immediately inform EPA.

Bill	Year	Background	Authorizations
Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) **P.L. 96-510**	1980	The principal statute governing the cleanup of sites contaminated with hazardous substances and responses to spills of those substances.	Established liability for site cleanup. Prescribed a procedure for identifying and ranking contaminated sites. Provided funding for site cleanups. Reduced uncontrolled releases of hazardous substances. Established cleanup procedures that provide protection for humans and the environment. Restored injured natural resources through provisions administered by the natural resource trustees. Set forth penalties and fines for failure to notify the U.S. Government when a hazardous substance is released into the environment. Established environmental taxes on petroleum and petroleum products. Created the Hazardous Substance Response Trust Fund (Superfund).
Superfund Amendments and Reauthorization Act (SARA) **P.L. 99-499**	1986	Reauthorized the 1980 CERCLA to continue cleanup activities around the country.	Stressed the importance of permanent remedies and innovative treatment technologies in cleaning up hazardous waste sites. Required Superfund actions to consider the standards and requirements found in other state and federal environmental laws and regulations. Provided new enforcement authorities and settlement tools. Increased state involvement in every phase of the Superfund program. Increased the focus on human health problems posed by hazardous waste sites. Encouraged greater citizen participation in making decisions on site clean-up. Increased the size of the trust fund to $8.5 billion. Required EPA to revise the Hazard Ranking System (HRS) to ensure it accurately assessed the relative degree of risk to human health and the environment posed by waste sites.

Bill	Year	Background	Authorizations
Emergency Planning and Community Right-to-Know Act (EPCRA) **P.L. 99-499**	1986	Created under the 1986 SARA. Designed to improve community access to information about chemical hazards and to facilitate the development of chemical emergency response plans by state/tribe and local governments.	Established four types of reporting obligations for facilities that store or manage specified chemicals: • Required facilities to notify emergency response commissions of the presence of any "extremely hazardous substance" if such substance is in excess of the substance's threshold planning quantity; • Required a facility to notify emergency response commissions in the event of a release exceeding the reportable quantity of CERCLA hazardous substance or an EPCRA extremely hazardous substance (excludes proper application of pesticide products, as well as handling and storage of those pesticide products by an agricultural producer); • Required facilities at which a hazardous chemical is present in an amount exceeding a specified threshold must submit material safety data sheets and hazardous chemical inventory forms to the state/tribe emergency planning committee, the local emergency planning committee and the fire department (excludes hazardous chemicals used in routine agricultural operations and fertilizers held for resale by retailers); and • Required certain manufacturing facilities to submit an annual toxic chemical release report if they have 10 or more employees and if they manufacture, process, or use specified chemicals in amounts greater than threshold quantities.

Federal Agencies Involved in Environmental Regulation or Research

REGULATION/ENFORCEMENT	
Environmental Protection Agency—EPA	Establishes air quality standards and regulates emissions of hazardous air pollutants, including radioisotopes. Establishes quality standards for surface waters and drinking water and regulates discharges of pollutants into water (includes standards for radioisotopes). Enforces cleanup of uncontrolled or abandoned hazardous-waste sites by responsible parties and cleans up orphan sites (CERCLA/ Superfund). Regulates generation, transportation, treatment, storage, and disposal of hazardous waste. Licenses pesticides for distribution/sale within the U.S. and establishes and enforces tolerances for pesticide residues on foods. Authorized to regulate production, importation, and use of "new chemicals" that may pose a threat to human health or the environment. Specific authority to regulate PCBs, asbestos, radon, and lead-based paint. Tobacco, certain tobacco products, nuclear materials, munitions, foods, food additives, drugs, cosmetics, and pesticides are exempt from EPA oversight. Authorized to require producers/importers/processors to test existing chemicals for health and environmental effects if there is evidence of substantial exposure levels and/or unreasonable risk to health or the environment and/or submit unpublished data related to health and safety of chemicals. Establishes standards for release of radioactive material from nuclear waste stored in deep geological repositories (waste sites are identified, built, and operated by DOE and licensed by NRC).

Food and Drug Administration—FDA (Department of Health and Human Services—HHS)	Establishes standards for radiation-emitting electronic products (medical and nonmedical) such as lasers, X-ray systems, ultrasound equipment, microwave ovens, and color televisions. Accredits and enforces standards for mammography facilities. Monitors the food supply to ensure that pesticide residues do not exceed allowable levels (established by EPA). Regulates the labeling and safety of bottled water. Oversees food safety, including the safety of food additives, foods/ingredients developed through technology, and food contact substances (FDA does not regulate traditional meats and poultry, which are the purview of USDA). Authorized to regulate the manufacture, marketing, and distribution of tobacco products.
Nuclear Regulatory Commission	Regulates civilian use and storage of nuclear materials (e.g., nuclear power plants, research reactors, and other medical, industrial, and academic licensees). Regulates the manufacture and distribution of nuclear by-product materials for medical use.
Department of Energy—DOE	Conducts nuclear energy research and development. Maintains and enhances the safety, reliability, and performance of the U.S. nuclear weapons stockpile and oversees the design, production, and testing of nuclear products for military application. Produces and sells many stable and radioactive isotopes that are widely used in medicine, industrial, and research applications. Supplies radioisotope power systems to NASA. Oversees occupational radiation protection and conduct of DOE employees and contractors at DOE sites and enforces contractor compliance with DOE worker and safety, nuclear, and security requirements.
Department of Agriculture	Manages the collection, analysis, data entry, and reporting of pesticide residues on agricultural commodities in the U.S. food supply, with an emphasis on those highly consumed by infants and children.
Occupational Safety and Health Administration—OSHA (Department of Labor—DOL)	Conducts investigations and enforces standards to maintain safe and healthful working conditions for most people employed in the U.S. (excluding miners, transportation workers, many public employees, and the self-employed). Standards limit worker exposure to ionizing radiation and carcinogenic chemicals, among other things.

Mine Safety and Health Administration (DOL)	Develops and enforces safety and health standards that apply to all U.S. mines. Standards exist for asbestos, diesel particulate, and dust as well as potentially hazardous chemicals.
Federal Communications Commission	Authorizes and licenses communications devices, transmitters, and facilities that generate radiofrequency electromagnetic fields.
Chemical Safety Board	Investigates causes of industrial chemical accidents and makes recommendations to plants, industrial organizations, labor groups, OSHA, and EPA to avoid future incidents.
Consumer Product Safety Commission	Protects consumers from products that pose fire, electrical, chemical (including potential carcinogens), or mechanical hazard by developing voluntary or mandatory standards, issuing product recalls, conducting research on potential product hazards, and informing and educating consumers. Does not have jurisdiction over automobiles, tires, boats, tobacco, firearms, food, drugs, cosmetics, pesticides, and medical devices.
RESEARCH/SERVICE	
Agency for Toxic Substances and Disease Registry (HHS)	Identifies sites contaminated with hazardous substances and makes recommendations to EPA, state regulatory agencies, or private organizations regarding ways to prevent or reduce further exposure and illness. Conducts studies in communities near Superfund sites to determine the health effects of exposure to hazardous substances. Funds similar research by universities, state agencies, and others. Maintains registries of people who have been exposed to trichloroethane, trichloroethylene, benzene, and dioxin. Conducts public health assessments of legitimate hazardous waste storage or destruction facilities at the request of EPA, states, or individuals. Provides technical assistance to federal agencies, states, and local governments that respond to accidental spills or releases of hazardous substances.
National Center for Toxicological Research (FDA, HHS)	Conducts toxicology research to inform regulatory decisions and reduce risks associated with FDA-regulated products.
National Center for Environmental Health (Centers for Disease Control and Prevention—CDC, HHS)	Conducts research and surveillance to investigate effects of the environment on human health. Provides information, resources, and technical assistance to other agencies/organizations that are implementing interventions or preparing for/responding to environmental emergencies. Develops and optimizes laboratory tests to help measure and treat persons exposed to toxic substances.

National Institute for Occupational Safety and Health—NIOSH (CDC, HHS)	Conducts research and makes recommendations for the prevention of work-related illness and injury. Establishes dose reconstruction algorithms used to determine occupational radiation exposure for workers with cancer who may be eligible for compensation.
National Cancer Institute (National Institutes of Health—NIH, HHS)	Conducts and supports research, training, health information dissemination, and other programs with respect to cancer, including activities related to the contributions of tobacco, radiation, and environmental factors to cancer.
National Institute of Environmental Health Sciences—NIEHS (NIH, HHS)	Conducts and supports research to improve understanding of how the environment influences the development and progression of human disease.
National Toxicology Program (NIEHS, NIH, HHS) (National Center for Toxicology Research, FDA, HHS) (NIOSH, CDC, HHS)	Coordinates toxicology testing within the Federal Government. Conducts toxicological research and develops and validates improved toxicology testing methods. Provides information about potentially toxic chemicals to health, regulatory, and research agencies; scientific and medical communities; and the public.

Summary of Environmental and Occupational Links with Cancer

CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
Aromatic Amines	**Benzidine, 2-naphylamine, 4,4'-methylenebis 2-choloraniline (MOCA), Chlornaphazine, Heterocyclic Aromatic Amines**	Used as antioxidants in the production of rubber and cutting oils, as intermediates in azo dye manufacturing, and as pesticides. Common contaminant in chemical and mechanic industries and aluminum transformation and an air contaminant from tobacco smoking. Used widely in the textile industry and as hair dyes.	Bladder (Benzidine, 2-naphylamine, 4,4'-methylenebis 2-choloraniline (MOCA), chlornaphazine)	Prostate (heterocyclic aromatic amines)
Chlorination By-Products	**Trihalomethanes**	Trihalomethanes include chloroform, bromodichloromethane, chlorodibromomethane, and bromoform. Result from the interaction of chlorine with organic chemicals. Several halogenated compounds may form from these reactions, although trihalomethanes are the most common. Brominated by-products are also formed from the reaction of chlorinated by-products with low levels of bromide in drinking water.	Bladder	Colorectum, Esophagus

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
Environmental Tobacco Smoke	**Contains more than 50 known carcinogens**	Also known as passive smoke, environmental tobacco smoke is a combination of smoke emitted from the burning end of a cigarette, cigar, or pipe, and smoke exhaled by the smoker.	Lung, Breast	
Metals	**Arsenic**	Produced commercially as a by-product of nonferrous metal production, primarily from copper production. Comprises greater than 10% of dust content in some smelter operations. Inorganic arsenic is primarily used to preserve wood, but also is used as a pesticide, mainly on cotton plants.	Bladder, Kidney, Lung, Skin, Soft Tissue Sarcoma (angiosarcoma of the liver)	Brain/Central Nervous System, Liver/Biliary, Prostate, Soft Tissue Sarcoma
	Beryllium	Used in the nuclear, aircraft, and medical devices industries. Used also as an alloy or in specialty ceramics for electrical and electronic applications. Found as a contaminant in the combustion of coal and fuel oil.	Lung	
	Cadmium	Occurs naturally in ores together with zinc, lead, and copper. Used as stabilizers in polyvinyl chloride products, color pigment, several alloys, and now most commonly in rechargeable nickel-cadmium batteries. Also present as a pollutant in phosphate fertilizers.	Lung	Pancreas, Kidney, Prostate
	Chromium	Used in steel and other alloy production. Chromium III and Chromium VI are used in chrome plating, the manufacture of dyes and pigments, leather tanning, and wood preserving.	Lung, Nasal/ Nasopharynx	

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
	Lead	Used primarily in the production of batteries, ammunition, metal products such as solder, and pipes and devices to shield X-rays. Lead also is found in gasoline, paints, ceramic products, caulking, and pipe solder, but has been reduced dramatically in the U.S.		Brain/Central Nervous System, Lung, Kidney, Stomach
	Mercury	Used to produce chlorine gas and caustic soda. Mercury also is used in thermometers, dental fillings, and batteries. Mercury salts are sometimes used in skin lightening creams and as antiseptic creams and ointments. Elemental mercury is transformed into methylmercury by microorganisms in water and soil.		Brain/Central Nervous System
	Nickel	Used primarily as an alloy in stainless steel. Also used in nickel plating and battery production.	Lung, Nasal/ Nasopharynx	Larynx, Pancreas, Stomach
Metalworking Fluids and/or Mineral Oils	**Straight Oils, Soluble Oils, Synthetic and Semi-synthetic Fluids**	Used in a variety of industries including metal machining, print press operating, and cotton and jute spinning.	Bladder, Larynx, Lung, Nasal/ Nasopharynx (mineral oils), Rectum, Skin, Stomach	Esophagus, Pancreas, Prostate
Natural Fibers/Dust	**Asbestos**	An inorganic naturally occurring fibrous silicate particle used primarily in acoustical and thermal insulation. Asbestos fibers can be divided into two groups: chrysotile (most widely used) and amphibole, which includes amosite, crocidolite, anthophyllite, actinolite, and tremolite fibers.	Larynx, Lung, Mesothelioma, Stomach	

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
	Silica	An inorganic particle used in foundries, brick-making, and sandblasting.	Lung	
	Talc containing asbestiform fibers	A mineral used in the manufacture of pottery, paper, paint, and cosmetics.	Lung	Ovary
	Wood Dust	Used primarily in carpentry, joinery, and in furniture and cabinetry making.	Lung, Nasal/ Nasopharynx	Larynx
Pesticides	**Herbicides, Fungicides, and Insecticides**	Used for preventing, destroying, repelling, or mitigating pests. Also used as plant regulators, defoliants, or desiccants. The majority of pesticides as registered with the U.S. Environmental Protection Agency (EPA) are used in agricultural applications, although residential application also is an important source.		Brain/Central Nervous System, Breast, Colon, Hodgkin Lymphoma, Leukemia, Lung, Multiple Myeloma, Non-Hodgkin Lymphoma, Ovary, Pancreas, Kidney, Soft Tissue Sarcoma, Stomach, Testicle

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
Petrochemicals and Combustion By-Products	**Petroleum Products, Motor Vehicle Exhaust (including diesel), Polycyclic Aromatic Hydrocarbons (PAHs), Soot, and Dioxins**	Petrochemicals are derived from natural gas or petroleum and used to produce a variety of other chemicals and materials including pesticides, plastics, medicines, and dyes. Substances can be produced as the building blocks for other products, but mainly result from the incomplete combustion of burning coal, oil, gas (diesel exhaust), household waste, tobacco, and other organic substances. Dioxins are a class of chemical that are the by-products of combustion processes containing chlorine and carbon-based chemicals such as polyvinyl chloride plastics. Dioxins also are created during the chlorine-bleaching processes for whitening paper and wood pulp and are a contaminant in the herbicide, Agent Orange, used in Vietnam.	Lung (PAHs, air pollution including diesel exhaust, soot, dioxin), Non-Hodgkin Lymphoma (dioxin), Soft Tissue Sarcoma (dioxin), Skin (PAHs)	Bladder (PAHs, diesel exhaust), Breast (dioxin, PAHs), Esophagus (soot), Larynx (PAHs), Multiple Myeloma (dioxin), Prostate (dioxin, PAHs)
Radiation	**Ionizing Radiation**	Any one of several types of particles and rays given off by radioactive material, high-voltage equipment, nuclear reactions, and stars. Alpha and beta particles, X-rays, and gamma rays are radiation particles of concern to human health.	Bladder, Bone, Brain/Central Nervous System, Breast, Colon, Leukemia, Liver/Biliary, Lung, Multiple Myeloma, Nasal and Nasopharynx, Ovary, Soft Tissue Sarcoma, Skin, Stomach, Thyroid *Note: Based on combined evidence from A-bomb survivor, occupational and medical irradiation evidence.*	

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
	Non-ionizing Radiation	Microwaves and electromagnetic frequencies, including radio waves and extremely low-frequency electromagnetic fields.		Brain, Breast, Leukemia, Salivary Gland
	Ultraviolet Radiation	Ultraviolet radiation is part of the solar radiation emitted by the sun.	Skin	
Reactive Chemicals	**Butadiene**	Used in the production of polymers for the manufacture of styrene-butadiene rubber for tires; nitrile rubber for hoses, gaskets, adhesives, and footwear; styrene-butadiene latexes for paints and carpet backing; and acrylonitrile-butadiene-styrene polymers for parts, pipes, and various appliances.		Leukemia
	Ethylene Oxide	Used as a sterilant, disinfectant, and pesticide. Also used as a raw ingredient in making resins, films, and antifreeze.	Leukemia	Breast
	Formaldehyde	Used primarily in the production of urea, phenol, or melamine resins for molded products such as appliances, electric controls, and telephones. Also used in particle-board, plywood, and in surface coatings.	Nasal/ Nasopharynx	Leukemia
	Mustard Gas	Produced and used primarily during World War I as a chemical warfare agent.	Lung	Larynx
	Sulfuric Acid	Used widely in industry for the production of isopropanol, ethanol, treatment of metals, and the manufacture of soaps, detergents, and batteries.	Larynx	Lung

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
	Vinyl Chloride	Used in polyvinyl resins for the production of plastic pipes, floor coverings, and in electrical and transportation applications.	Liver/Biliary, Soft Tissue Sarcoma (angio-sarcoma of the liver)	
Solvents	**Benzene**	Used as an intermediate in the production of plastics, resins, and some synthetic and nylon fibers. Also used to make some types of rubbers, lubricants, dyes, detergents, drugs, and pesticides. Also found in crude oil, gasoline, and cigarette smoke.	Leukemia, Multiple Myeloma, Non-Hodgkin Lymphoma	Brain/Central Nervous System, Lung, Nasal/ Nasopharynx
	Carbon Tetrachloride	Used primarily in various industrial applications. Before being banned, was used in the production of refrigeration fluid and propellants for aerosol cans, as a pesticide, as a cleaning fluid and degreasing agent, in fire extinguishers, and in spot removers.		Leukemia
	Methylene Chloride	Used primarily as a solvent in industrial applications and as a paint stripper. Also found in some aerosol and pesticide products and in the production of photographic film.		Brain/Central Nervous System, Liver/ Biliary
	Styrene	Used in the production of rubber, plastic, insulation, fiberglass, pipes, automobile parts, food containers, and carpet backing.		Non-Hodgkin Lymphoma
	Toluene	Used in the production of paints, paint thinners, fingernail polish, lacquers, adhesives, and rubber. Also used in some printing and leather tanning processes.		Brain/Central Nervous System, Lung, Colorectum

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
	Trichloroethylene (TCE)	Used mainly for degreasing metal parts. Previously used as a dry cleaning agent. May be found in printing inks, varnishes, adhesives, paints, and lacquers. Important contaminant in the general environment as a result of emissions and leakage from industrial settings.	Liver/Biliary	Cervix, Hodgkin Lymphoma, Kidney, Leukemia, Non-Hodgkin Lymphoma
	Tetrachloroethylene (PCE)	Used to degrease metal parts and as a solvent in a variety of industrial applications. Since the 1930s, used by an increasingly large percentage of U.S. dry cleaning operations.		Bladder, Cervix, Esophagus, Kidney, Non-Hodgkin Lymphoma
	Xylene(s)	Used as a cleaning agent, a thinner for paint, and in paints and varnishes. Used in printing, rubber, and leather industries, and found in small amounts in gasoline and airplane fuel.		Brain/Central Nervous System, Colorectum
Other	**Creosotes**	Includes coal tar and coal tar pitch formed by high-temperature treatment of wood, coal, or from the resin of the creosote bush. Wood creosote historically was used as a disinfectant, laxative, and cough treatment. Coal tar products are used in medicine, animal and bird repellents, and pesticides. Coal tar creosote is widely used as a wood preservative. Coal tar, coal tar pitch, and coal tar pitch volatiles are used in roofing, road paving, aluminum smelting, and coking.	Bladder (coal tars), Lung, Skin	

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CATEGORY	CARCINOGENIC AGENT	SOURCE/USES	STRONG*	SUSPECTED**
	Endocrine Disruptors	A number of natural and synthetic chemicals capable of mimicking the body's natural hormones. See detailed list at: http://www.ourstolenfuture.org/Basics/chemlist.htm.	Breast (DES), Cervix (DES)	Breast (bisphenol A), Prostate (bisphenol A), Testicle (chlorinated insecticides)
	Hair Dyes	Coloring products used on hair. Hair dyes usually fall into one of four categories: temporary, semi-permanent, demi, and permanent. Chemical agents used in dyes are specific to the color and the degree of permanency.		Bladder, Brain/Central Nervous System, Leukemia, Multiple Myeloma, Non-Hodgkin Lymphoma
	Nitrosamines and N-nitroso Compounds	Chemicals that form when amines and nitrosating agents chemically react. Found in the rubber, metal, and agricultural industries, and in cosmetics and foods such as fried bacon and cured meats.		Brain/Central Nervous System, Kidney
	Polychlorinated Biphenyls (PCBs)	Used as coolants and lubricants in transformers, capacitors, and other electrical equipment. PCBs were banned in the U.S. in 1977.	Liver/Biliary	Breast, Non-Hodgkin Lymphoma

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Updated from: Clapp RC, Jacobs M, Loechler EL. Environmental and Occupational Causes of Cancer; New Evidence 2005-2007. Reviews on Environmental Health. 2008;23(1):1-37.

APPENDIX G

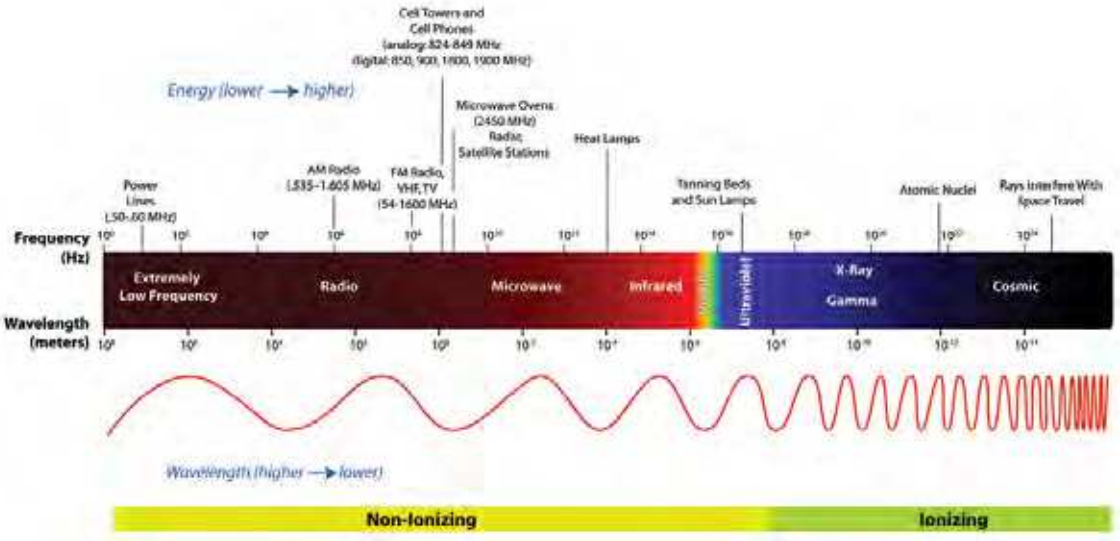
Electromagnetic Energy—Overview

Humans are exposed to electromagnetic energy from numerous sources every day. These sources pose varying levels of risk to health, depending upon the type of radiation, individual dose, cumulative exposure, age at exposure, gender, smoking history, and other factors. As Figure 15 illustrates, radiation is divided into two major categories: ionizing and non-ionizing radiation. Ionizing radiation is any form of radiation with enough energy to detach electrons from atoms or molecules. This type of radiation can cause DNA damage that, if not repaired, can result in gene mutations that lead to cancer or other health conditions. Ionizing radiation includes alpha and beta particles, neutrons, X-rays, gamma rays, and cosmic rays. These differ in energy level and extent to which they can penetrate cells and tissues. Sources of ionizing radiation include background cosmic radiation, radon, medical diagnostic X-rays, computed tomography (CT) scans, fluoroscopy, other medical and dental radiologic procedures, nuclear power plant emissions and waste, uranium mines and unusable mine waste, and nuclear weapon facilities.

Non-ionizing radiation, also referred to as electromagnetic radiation (EMR) or electromagnetic fields (EMF)—including extremely low-frequency (ELF) electromagnetic fields—is lower frequency radiation such as radio waves, microwaves, and infrared, visible, and ultraviolet (UV) light that lacks sufficient energy to detach and ionize electrons. It should be noted that one form of ultraviolet light, UVR, can alter DNA and is mutagenic, but penetrates tissues only superficially. However, UV light is a well established carcinogen and some evidence suggests that EMR/EMF may also have deleterious effects on human health with prolonged exposure. Sources of non-ionizing radiation include electric power lines, radio and television transmissions, radar, cell phones and other wireless communication devices, cell phone towers, microwave ovens, other home appliances, the sun, and artificial tanning devices.

Figure 15

Electromagnetic Spectrum



Adapted from:
NASA, Regions of the Electromagnetic Spectrum. Accessed online: http://imagine.gsfc.nasa.gov/docs/science/know_l1/spectrum_chart.html.

Georgia State University, Department of Physics and Astronomy. Hyperphysics-Electricity and Magnetism. Accessed online: http://hyperphysics.phy-astr.gsu.edu/hbase/ems2.html

Little question exists that intermediate and high doses of ionizing radiation (greater than 100 millisieverts, mSv), delivered either as an acute dose or over a prolonged period, result in significant harm to human health, including cancer development. Less certainty exists, however, regarding lower doses of radiation. Compared with higher doses, low-dose radiation is likely to confer less cancer risk, but requires progressively larger epidemiologic studies to quantify such risk to a useful degree of precision.

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Electromagnetic Energy Units of Measure

	SI UNIT	MEASURE	DEFINITION	OTHER COMMON UNITS	CONVERSIONS
Ionizing Radiation	**Becquerel (Bq)**	Radioactivity	The rate of radiation emission from a source.	Kilobecquerel (kBq) Gigabecquerel (GBq) Curies (Ci) Microcurie (μCi) Picocurie (pCi)	1 Bq = 10^{-3} kBq 1 Bq = 10^{-9} GBq 1 Bq = 2.7 x 10^{-11} Ci 1 Bq = 2.7 x 10^{-5} μCi 1 Bq = 27 pCi
	Gray (Gy)	Absorbed Dose	The amount of energy absorbed per unit weight of the organ or tissue.	Milligray (mGy) Rads	1 Gy = 1000 mGy 1 Gy = 100 Rads
	Sievert (Sv)	Equivalent Dose	The *absorbed dose* multiplied by a radiation weighting factor, which accounts for variability of harm in radiation type.	Millisievert (mSv) Rem Millirem (mRem)	1 Sv = 1000 mSv 1 Sv = 100 Rem 1 Sv = 10^5 mRem
		Effective Dose	The *absorbed dose* multiplied by a tissue weighting factor, which accounts for variability of harm in tissue type.	Millisievert (mSv) Rem Millirem (mRem)	1 Sv = 1000 mSv 1 Sv = 100 Rem 1 Sv = 10^5 mRem
		Collective Effective Dose	The total estimated amount of radiation to all members of a population over a specified period of time.	Millisievert (mSv) Rem Millirem (mRem)	1 Sv = 1000 mSv 1 Sv = 100 Rem 1 Sv = 10^5 mRem
Non-Ionizing Radiation	**Tesla (T)**	Magnetic Field	The magnetic force exerted on a moving charged particle.	Nanotesla (nT) Gauss (G)	1 T = 10^{-9} nT 1 T = 10^4 G
	Hertz (Hz)	Frequency	The number of energy wave cycles per second.	Megahertz (MHz)	1 Hz = 10^{-6} MHz

Sources:

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Research Recommended by PCP Meeting Participants

Participants at the President's Cancer Panel 2008–2009 meetings on environmental influences on cancer identified several areas in which environmental cancer research is needed, as well as specific studies that would improve our understanding of environmental cancer and support environmental cancer hazard assessment and control:

Conduct new or updated assessments of current occupational and environmental exposures:

- Update exposure assessments in U.S. workers, particularly those with body burdens of persistent pollutants; the most recent study was conducted in the 1980s.
- Assess children's exposures to agricultural pesticides, considering drift, inadvertent parental "take-home" of occupational chemicals, and ingestion.
- Assess cancer risks attributable to exposures and specific occupations where current, scientifically sound assessments do not exist. Such assessments should correct flaws in the methodology used by Doll and Peto and must consider synergistic effects of multiple exposures.
- Improve quantitative radiation risk estimates, including dose reconstruction, and develop new research tools.

Improve toxicity testing methods and technologies for new and existing chemicals:

- Develop high throughput screening (HTS) technologies to enable simultaneous testing for molecular, biochemical, and functional impacts of multiple possible carcinogens. Specifically, develop HTS tools and assays that will support the National Toxicology Program's three-tiered testing program now under development. The program and supporting technologies should reflect current scientific knowledge (e.g., about environmental and occupational carcinogens, immunotoxicants, and developmental toxicants).
- Conduct mechanistic studies to determine whether perturbed biological mechanisms that cause cancer in animals have the same effect in humans.
- Identify and validate biological markers that can be used as surrogate endpoints for cancer to accelerate research results.
- Develop alternative methods for assessing carcinogenicity; studies currently are limited to substances that are believed to be genotoxic or mutagenic. Research is needed to improve methods and technologies for assessing the impact of epigenetic changes, gene-environment interactions, and other non-genotoxic mechanisms (e.g., telomere length) on cancer risk.

Increase focus on understudied exposure mechanisms:

- Assess the effects of exposure to chemical mixtures.
- Determine the effects of chronic low-dose exposures.
- Elucidate the effects of gene-environment interactions on individual susceptibility to environmental cancer.
- Identify determinants of susceptibility to radiation-related cancer.

Increase research on understudied population groups:

- Elucidate epigenetic and other relationships between parental exposure and childhood cancer.
- Determine why rates of childhood leukemia, brain, and testicular cancer are rising. The National Children's Study is a good foundation on which to build the knowledge base in this area.
- Design and conduct other large prospective studies to further explore "windows of susceptibility" to environmental carcinogens; research to date shows that the same exposures at different ages may lead to different cancers.

Conduct research on understudied environmental chemical exposures:

- Follow up existing leads on associations between individual pesticides and specific cancers. In addition, conduct studies to assess the carcinogenic potential of inert as well as active ingredients in pesticides. Inert ingredients often are considered proprietary and do not undergo toxicological testing.
- Conduct additional research on the effects of nitrate in drinking water. Few studies have been conducted to determine associations between nitrate in drinking water and specific cancer sites. In addition, the impact of early life exposure is not well understood. Cross-sectional biomonitoring studies of nitrate ingestion will enhance understanding of adverse effects of nitrate, N-nitroso compounds, and other nitrogen compounds on vulnerable populations.
- Identify cancer risk (other than bladder cancer) associated with water disinfection by-products. In particular, colon and rectal cancer studies to date have been inconclusive; these potential links need further research.
- Determine the mechanism of arsenic carcinogenesis.
- Further investigate links between endocrine-disrupting chemicals and breast and other cancers.
- Conduct research on the carcinogenicity of emerging air pollutants not included in the National Air Toxics Assessment, such as nanomaterials.
- Investigate the suspected link between polycyclic aromatic amines and breast cancer, especially in populations that may be genetically susceptible.

Conduct research on understudied radiation exposures:

- Quantify workplace radon exposures.
- Resolve controversies regarding the safety or harm of low doses of various forms of radiation in adults and children. Identify circumstances under which low-dose radiation may have a hormetic effect.
- Develop radiation dose and risk estimates that better reflect the current and future U.S. population. Existing dose and risk estimates have been based on adult males; estimates should account for population diversity, including children. In addition, develop medical radiation risk estimates that are not based on acute doses received by atomic bomb survivors.
- Expand research on possible harmful effects of cell phone use, especially in children. Cell phone use still is relatively recent, and studies to date have had mixed findings; most involve users of older equipment. Findings from cohort studies now underway are anticipated, but longer-term studies of individuals using current equipment are needed.
- Conduct additional research on possible links between electromagnetic fields (EMF) and cancer; identify mechanism(s) of EMF carcinogenesis.
- Monitor changing patterns of radiation exposure.

Conduct research on toxins and endocrine disrupting chemicals in personal care products and cosmetics; only 11 percent of the ingredients in these products have been tested for safety.

Raise the priority of and investment in research to develop non-toxic products and processes:

- Increase research on sustainable production, such as:
  - Green chemistry initiatives, including new product development and redesign of products or processes to eliminate harmful substances rather than mechanical engineering tactics to reduce exposures;
  - Compostable bio-based plastics; and
  - Solar, wind, and hydroelectric power.

Develop, test, and evaluate prevention communication strategies and interventions, especially in high-risk occupations and populations.


President's
Cancer
Panel

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