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American Cancer Society Perspectives on Environmental Factors and Cancer

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Abstract

Cancer prevention is central to the mission of the American Cancer Society (ACS). The ACS's prevention activities take many forms, but are primarily focused on modifiable risk factors that have been demonstrated to have the largest impact on cancer risk in the general population (with particular emphasis on tobacco use because of its large impact on cancer), and well-proven policy and program interventions. The ACS addresses nutrition, physical inactivity and obesity, alcohol consumption, excessive sun exposure, prevention of certain chronic infections, and selected other environmental factors through a variety of venues, including consensus guidelines (eg, nutrition and physical activity, human papillomavirus vaccination) and developing educational materials for health care providers and the general public. In contrast to the broad definition of environmental factors used by the ACS and most other public health agencies, some members of the general public associate the term "environmental" only with toxic air and water pollutants and other, predominantly manmade, hazards that people encounter, often involuntarily, in their daily life. This article will provide an overview of the ACS's approach to the prevention of cancer associated with such toxic pollutants in the context of its mission and priorities with respect to cancer prevention. **CA Cancer J Clin 2009;59:0–0.** **©2009 American Cancer Society, Inc.**

Introduction

Fn1 Cancer prevention is central to the mission of the American Cancer Society (ACS). The ACS's prevention activities take many forms, but are primarily focused on modifiable risk factors that have been demonstrated to have a substantial impact on cancer risk in human populations. These environmental risk factors include tobacco use, poor nutrition, physical inactivity and obesity, alcohol consumption, excessive sun exposure, certain chronic infections, and exposures to other known carcinogens in various settings. All these factors are "environmental" in the sense that they are acquired, and potentially controllable, rather than being inherited genetic traits. Within the realm of primary prevention, the ACS places the greatest priority on tobacco control, both because of the large cancer burden associated with this exposure and the availability of effective policy and medical interventions that are documented to reduce tobacco use and the burden of tobacco-related cancers.[1-3] Nutrition and physical activity are also emerging priorities, due to evidence of the association between obesity and cancer incidence and mortality.[4,5] Exposure to all carcinogens cannot be eliminated. Many carcinogens occur naturally; some are generated inside our bodies, whereas others involve medications or diagnostic tests that are used in medical care when their benefits are believed to exceed their risks. Although certain exposures are unavoidable, the ACS supports minimizing or eliminating exposure to known or probable carcinogens and providing the public with

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information so that they can make informed choices. Although cancer screening is primarily a form of secondary prevention, access to and utilization of cancer screening tests is part of the ACS's prevention agenda, both because some tests (eg, cervical and colorectal cancer screening) can actually prevent cancer and because early detection and effective treatment prevent deaths from cancer and contribute to declining cancer mortality rates.[6]

In contrast to the broad definition of environmentally related causes of cancer used by the ACS and most other public health agencies, some members of the general public and scientific community use the term "environmental" to refer more specifically to toxic chemicals, environmental pollutants, radioactive exposures, and other predominantly manmade hazards that people encounter, often involuntarily, in their daily life. These exposures may occur from consumer products; old or new building materials; additives or contaminants in food or drinking water; and pollutants in indoor air, urban environments, and larger ecosystems. The exposure levels to the general public are typically orders of magnitude lower than those experienced historically in occupational or other settings in which cancer risks have been demonstrated. The resulting cancer risks are generally so low that they cannot be measured directly. Nevertheless, there is reason to be concerned about low-level exposures to carcinogenic pollutants because of the multiplicity of substances, the involuntary nature of many exposures, and the potential that even low-level exposures contribute to the cancer burden when large numbers of people are exposed.[7] Concerns about the toxic and carcinogenic potential of these exposures are amplified by broader public concerns regarding the effectiveness of hazard identification and the regulation of potentially toxic exposures in the United States and other economically developed countries, as well as high levels of exposures to known carcinogens that still occur in many developing countries.

To address ongoing and emerging issues relating specifically to environmental pollutants and cancer, the ACS has established a scientific advisory subcommittee on cancer and the environment. An initial undertaking of the committee was the development of a position statement to articulate the ACS's principles, objectives, and potential roles regarding the topic of environmental pollution within the context of cancer prevention. This position statement was developed to clarify how these issues relate to the overall mission of the ACS, to enhance understanding of their definition and scope, to improve coordination among the ACS's divisions and the National Home Office, and to identify actions by which the organization can contribute most effectively to addressing these issues. We hope that the document will be informative to the broader cancer control community as well.

How Carcinogens Are Identified and Evaluated

Studies in Humans

People have always been exposed to carcinogenic agents in their environment and cancer has been observed throughout human history. However, industrialization and growth of the chemical industry in the early 20th century created opportunities for concentrated, high-level exposures among working populations. Exposures included (1) naturally occurring substances that for the first time were mined and milled for industrial uses, such as asbestos and uranium; (2) substances extracted from natural sources, such as benzene from petroleum; and (3) newly synthesized substances, such as vinyl chloride. Due to the large increases in cancer risk associated with high-level industrial exposures from the middle to the end of the 20th century, case reports and epidemiologic studies documented high risks of cancer among workers exposed to concentrations of chemicals (organic compounds, metals, and dusts) at levels much higher than those that are acceptable today. Occupational studies have documented the carcinogenicity to humans of single chemicals (eg, arsenic, benzene, and vinyl chloride), physical agents (eg, solar radiation, radon, and radium), and mixtures (eg, coal tars and shale oils), as well as occupations and industries (eg, furniture and cabinet making, coke production from coal, and the rubber industry). Although exposures to most of these agents have been reduced in the United States and many other economically developed countries since the 1970s, workplace exposures continue to be high in many low- and medium-income countries.

In addition to the identification of human carcinogens through studies in occupational settings, epidemiologic studies in populations receiving medical

treatment have documented the carcinogenicity of many chemotherapeutic and immunosuppressive drugs, hormones, some antibiotics, and radiation therapy. Despite known risks for some of these drugs and therapies, some continue to be used because the benefits are believed to outweigh the risks and they remain the best options available. However, one of the goals of cancer treatment research is to identify treatments that more specifically target cancer cells without damaging healthy cells. This research has lead to a reduction in use and dose levels for some forms of cancer treatment that were associated with high risks of secondary cancers among cancer survivors.[8,9]

Studies in Experimental Animals

Although high-quality epidemiologic data provide a strong basis for hazard identification and risk assessment, it is often not possible to conduct definitive studies in humans. There are many animal carcinogens for which definitive epidemiologic studies cannot be performed due to multiple and/or poorly characterized exposures and other limitations. The prevention of cancer related to human exposure often relies on the extrapolation of findings in toxicologic studies. Because virtually all substances that are carcinogenic in humans are also carcinogenic in laboratory animals, the primary experimental approach used to test the carcinogenicity of chemicals is to conduct 2-year bioassays in mice and rats.[10] These assays typically expose 50 rats or 50 mice of each sex to 2 or 3 levels of the test agent for 2 years, representing most of the animals' lifespan.[11] The highest exposure level is set at the maximum tolerated dose, which has been shown to cause no more than a 10% decrement in weight and no clinical evidence of toxicity or increased mortality in a previous 90-day study. Careful pathologic studies are performed to identify benign and malignant tumors in the control and experimental animals after death so that the incidences of tumors can be compared. Often, the studies are designed to test several concentrations of the test chemical so that dose-response can be evaluated. Although the 2-year rodent bioassay is currently the "gold standard" for toxicologic testing of carcinogenicity, the time and expense of these assays limits the number of agents that can be tested. In addition, although positive results in such studies are important in hazard identification, they often do not address some questions relevant to predicting potential cancer risks in humans. For example, due to technical limitations and funding, the animal studies may have been conducted using only one route of exposure, which may or may not be the most common route of exposure or concern in humans. It may be difficult or impossible to generate exposures for animal studies that match those in environmental settings. This is a growing concern for evaluating the carcinogenicity of substances that are now being produced in the nanoparticle range, which may have different distributions and toxicities than larger particles of the same composition. To address these limitations, toxicologists have been working on alternative testing methods and approaches for identifying which substances should be prioritized for carcinogenicity testing. In its 2007 report, *Toxicity Testing in the 21st Century: A Vision and a Strategy*, the National Research Council set out a strategy for new approaches that include toxicity pathway analyses and targeted testing as central elements.[12] Tracking of population exposures and risks are part of the paradigm. In Europe, the European Union has also implemented a new approach to toxicity testing called REACH (Registration, Evaluation, Authorization and Restriction of Chemicals).[13] REACH gives new and greater responsibility to the chemical industry to establish the safety of their products and to provide information.

Evaluation and Classification of Carcinogens

There are national and international agencies that classify agents according to their carcinogenicity. Two independent agencies—The International Agency for Research on Cancer (IARC) of the World Health Organization and the National Toxicology Program (NTP) of the National Institute of Environmental Health Sciences (NIEHS)—systematically review all the epidemiologic, clinical, and toxicologic evidence on a given agent or exposure and classify this qualitatively in terms of the level of evidence. The ACS relies primarily on these 2 entities to classify substances as to their potential carcinogenicity.

The IARC has been producing monographs since 1969 that classify the evidence into 5 categories:

Group 1 (carcinogenic to humans), Group 2A (probably carcinogenic to humans), Group 2B (possibly carcinogenic to humans), Group 3 (not classifiable as to its carcinogenicity in humans), and Group 4 (probably not carcinogenic to humans). Using this classification, the IARC has evaluated more than 935 chemicals, industrial processes, and other exposures as of 2009. To date, the IARC has classified 108 agents, mixtures, and exposures in Group 1; 63 in Group 2A; 248 in Group 2B; 515 in Group 3; and 1 in Group 4. IARC policy is to recommend treating Group 2A and 2B chemicals as if they present a carcinogenic hazard to humans.[14] Among agents and exposure circumstances classified in Group 1 as human carcinogens by the IARC, approximately one-third are classified based on evidence from occupational settings, another one-third are classified based on medical exposures, and most of the remainder are infectious agents or substances classified as Group 1 based on sufficient evidence in animals and mechanistic data. In addition, in 2009, the ACS co-funded and planned a meeting with the IARC monograph program and leading scientists from around the world to identify information needs and gaps with regard to selected agents for which there is widespread human exposure and unresolved questions regarding carcinogenicity. The project was an outgrowth of work initiated by the US National Institute for Occupational Safety and Health's National Occupational Research Agenda (NORA) team to enhance occupational cancer research, and ultimately involved collaboration between the IARC, the ACS, the NIEHS, and the National Cancer Institute. A report on research priorities and gaps identified at this meeting for 20 agents is currently being prepared. Staff from the ACS research department regularly participate in IARC monograph working groups.

The NTP has a similar systematic process for evaluating the carcinogenicity of agents and exposures in the United States. It classifies exposures as "known to be human carcinogens" or "reasonably anticipated to be human carcinogens." The *11th Report on Carcinogens*, issued in 2004, listed 58 substances as "known to be human carcinogens" and 188 as "reasonably anticipated to be human carcinogens."[15] The NTP also is one of the leading organizations both nationally and internationally in the development and application of methods for carcinogenicity testing. A senior statistician from the ACS research department is currently serving as Chair of the NTP Board of Scientific Counselors as well as a legislatively mandated US Environmental Protection Agency (EPA) Science Advisory Board that reviews methodology for pesticide risk assessment.

In addition to exogenous carcinogens, endogenous processes such as inflammation and food metabolism generate reactive exposures that damage DNA and, therefore, may contribute to carcinogenesis. Although DNA damage plays an important role in carcinogenesis, DNA repair mechanisms and other protective cellular processes also exist.[16] Endogenous processes such as inflammation and food metabolism are not specifically evaluated by the IARC or the NTP, although they may contribute to the development of human cancer.

Limitations in Current Systems

Despite the value of the current systems for identifying and classifying evidence for carcinogenicity, there are major constraints due to both the limited resources allocated to operate these systems and the scientific complexity of the issues themselves. Many substances do not qualify for evaluation by the IARC and NTP because of a lack of available information. Carcinogen testing data are not available for many industrial and commercial chemicals and, ideally, such testing should be performed before products are introduced, rather than after there is widespread human exposure. Although the IARC and NTP publish qualitative judgments regarding the evidence for carcinogenicity, they do not provide quantitative estimates of the magnitude of risk resulting from a specified level of exposure. Quantitative risk assessment is a critically important and often mandatory next step for decision-making that is left primarily to regulatory agencies.

Quantitative risk assessments necessarily require assumptions to estimate the risk associated with low levels of exposure.[17] Some of these assumptions involve extrapolation from animal studies to humans and/or from the very high exposure levels in occupational studies to the much lower exposures experienced by the general public. Risk estimates at low levels of exposure are often quite sensitive to assumptions made to bridge uncertainties and, consequently, the magnitude of the expected risks and projected

costs and benefits of control approaches may be highly dependent on choices made in the analysis. Other scientific uncertainties that affect quantitative risk assessment relate to the susceptible populations, including children. Although risk estimates are subject to uncertainty, a formal risk assessment provides a framework within which to specify the sources of uncertainty and to assess the sensitivity of estimates to assumptions made to bridge knowledge gaps. Statistical methods that help to characterize uncertainty both quantitatively and qualitatively can be formally integrated into the risk assessment process. Quantitative estimates of risk are especially difficult to develop for mixtures, because the net effect of a mixture depends on the specific components of the mixture, their concentrations, and their interactions. In addition, the heterogeneity of mixtures limits broad generalizations concerning their risks. Despite the limitations of the existing systems that identify, classify, and regulate environmental and occupational pollutants, these systems have greatly reduced exposure to many pollutants over the past 30 to 40 years in high-resource countries such as the United States.

Estimates of Disease Burden

The fact that a substance is listed as a human carcinogen by the IARC or NTP is not in itself informative of the burden of human cancers that it causes. The next step, after determining that a correlation is causal, is to evaluate the extent of the public health problem. The disease burden in the overall population depends on both the level of risk among exposed people and the prevalence of exposure in the population. The risk to exposed individuals, in turn, varies according to the intensity, potency, and duration of the exposure, as well as other potential factors, including exposures to other carcinogens. The proportion of new cancers and deaths in both the United States and worldwide that are related to exposure to carcinogenic pollutants in the general environment is not precisely known. However, in 1981, it was estimated that approximately 4% of all cancer deaths in the United States were due to occupational exposures[18]; a more recent estimation was set at 2.4% to 4.8%.[19] In Great Britain, it was estimated that in 2004, approximately 8% of cancer deaths among men and 1.5% among women were attributable to occupational carcinogens.[20] Globally, an estimated 10% of lung cancer deaths, 2% of leukemia deaths, and nearly 100% of mesothelioma deaths are attributable to occupation.[21] Among the most important exposures associated with cancer in the general population are indoor radon exposures,[22] environmental tobacco smoke,[23] and, in developing countries, the use of solid fuels for cooking and heating,[24] all of which have been reported to be associated with lung cancer. A special section in *Cancer Facts and Figures* in 2006 addressed the role of environmental pollutants and cancer, with emphasis on air pollutants and lung cancer.[25]

Although the contribution of environmental and occupational pollutants to the human cancer burden is significant, it is much smaller than the impact of tobacco use, in part because such a large fraction of the population has used tobacco. In the United States, approximately half of all adult men reported smoking cigarettes regularly in 1965, and many of these had been smoking for more than 20 years. Because of the high prevalence of long-term smoking and the strength of smoking as a cause of disease, cigarette smoking accounts for both high individual risk in smokers and approximately 30% of all cancer deaths in the general population. It should be noted that tobacco smoke contains, in large quantities, many specific substances that are recognized as definite and probable carcinogens based on epidemiologic studies. Although tobacco smoking is well-recognized as a cause of human cancer and other chronic diseases, it remains an important exposure in the United States and globally, and the ACS contributes to prevention efforts with a spectrum of activities ranging from research to advocacy.

Infectious agents account for approximately 17% of new cancers worldwide and approximately 26% of cancers in low- and middle-resource countries.[26] Chronic infection with hepatitis B and C viruses, human papillomavirus (HPV), Epstein–Barr virus, certain other viruses, and *Helicobacter pylori* bacteria are significant globally. Infection with certain parasitic worms also accounts for specific cancers in more focal geographic regions. The IARC lists these biologic organisms among the other chemical and physical environmental agents known to cause cancer. The ACS has identified specific priorities for the prevention of cancers associated with infectious diseases in the United States and internationally. These include screening for cervical cancer,[27] hepatitis B

immunization, and HPV vaccination.[28] In addition, an overview of infections related to cancer was published as a special section in *Cancer Facts and Figures* in 2005.[29] Other issues related to the prevention of cancers related to infection have been addressed in specific research and cancer control projects.

ACS Position Statement on Cancer Prevention

1. The ACS recognizes the essential role of cancer prevention in reducing the burden of disease, suffering, and death from cancer.
2. The ACS targets its finite resources in cancer prevention on: (a) interventions that have been shown to be effective and (b) exposures that have a substantial impact on cancer risk.
3. The ACS is a science-based organization that sets its prevention priorities on: (a) the weight of the evidence that a particular exposure causes cancer; (b) the magnitude of the increased risk; (c) the certainty that a particular intervention will reduce exposure and thereby reduce risk; and (d) the evidence that substitution of an alternative product will not introduce new risks.
4. The ACS recognizes, however, that decisions regarding prevention must inevitably be made in the context of some degree of scientific uncertainty. The need to make decisions in the face of accruing but still incomplete evidence has long been recognized. In 1965, Sir Austin Bradford Hill, the British medical statistician wrote: "All scientific work is incomplete—whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have or to postpone the action that it appears to demand at a given time."[30]
5. The ACS endorses the position that occupational and community exposures should meet regulatory standards, and that research to identify and reduce carcinogenic hazards should be supported. Although regulations have reduced many hazardous exposures in workplaces having at least 10 employees in the United States, continued vigilance is needed to ensure that workers both in the United States and worldwide are protected against unacceptable risks from occupational carcinogens. The agencies that set and enforce environmental standards need to be appropriately funded and science-based to keep pace with scientific developments and to update their standards accordingly.
6. Because of the scope and complexity of identifying and classifying chemicals, the ACS relies on established national and international organizations that regularly conduct and publish such evaluations.

It is important to provide the public with information so that they can make informed choices. Communicating information to the public regarding manmade pollutants and other involuntary exposures is very difficult because the public is often more concerned about these exposures than about exposures perceived as natural and/or voluntary and because the underlying science often involves complex scientific concepts and high levels of uncertainty. It is important that communications acknowledge and not trivialize public concerns, but at the same time do not exaggerate the potential magnitude or level of certainty of the potential risk.[31]

The ACS supports the implementation of new strategies for toxicity testing, including the assessment of carcinogenicity, that will more effectively and efficiently screen the large number of chemicals to which people are exposed.

ACS Roles Regarding Environmental Pollutants and Cancer

Research

The ACS funds, conducts, and advocates for research on a broad range of issues ranging from basic research to cancer surveillance, prevention, and survivorship. This research has produced several landmark studies concerning environmental and occupational pollutants in relation to cancer. In the 1960s, intramural epidemiologists from the ACS collaborated with Dr. Irving Selikoff at the Mount Sinai School of Medicine to publish studies linking asbestos to the development of lung cancer and mesothelioma.[32–34] More recently, studies published since the mid-1990s have used the ACS's massive Cancer Prevention Study II (CPS-II) to make significant contributions to knowledge regarding cancer disparities[35,36] and the adverse effects of particulate air pollution and ozone on various disease outcomes. The latter studies influenced the US EPA to set more stringent limits on particulate air pollution.

The ACS has continuously supported pioneering epidemiology studies by its researchers, including the Hammond Horn Study (1955–1957), the Cancer Prevention Study I (CPS-I; 1959–1972), the CPS-II (1982 to the present), and the CPS-III (initiated in 2006). These studies have contributed to understanding the health effects of environmental tobacco smoke[42,43] and consumer products such as hair dye.[42,43] The ACS flagship publication, *Cancer Facts and Figures*, featured the topic of environmental pollutants and cancer as the banner section in 2007.[46] Trends in cancer sites for which the incidence has been increasing and the etiology is incompletely understood are monitored by the ACS's intramural program on Surveillance and Health Policy Research.[47] These sites include female breast cancer; testicular cancer; non-Hodgkin lymphoma; multiple myeloma; melanoma; and cancers of the thyroid, renal cortex, and liver. Further etiologic research is also needed to separate the effects of obesity, sun exposure, and screening from other potential risk factors for these cancers.

Each year, the ACS extramural research grants program provides greater than $100,000,000 in grants to young researchers at universities and cancer centers throughout the country. These extramural grants support highly innovative, peer-reviewed research. Examples of ACS-funded projects concerning chemical carcinogenicity include studies of dioxin,[48] cadmium in relation to breast cancer,[49] biomarkers of arsenic exposure,[50] and the structural effect of environmental mutagens on DNA repair.[51]

ACS staff scientists participate in expert committees convened by the IARC, NTP, NIEHS, and the Institute of Medicine.

Information Provider

The ACS is a trusted source of information regarding cancer. Information is regularly disseminated through original research and scientific reviews, media reports, materials posted on the ACS Web site (available at: http://cancer.org), and responses to inquiries received through the 24-hour call center (1-800-227-2345). Although not intended to be comprehensive, the reports posted on selected topics on the Web site provide unbiased summaries of major issues, help to put concerns about these issues into context, and direct readers who seek more detailed information to additional sources.

Communication

ACS representatives frequently comment on environmental issues to the media and when responding to requests from the public or the ACS divisions. The message in these communications can be improved by:

- Acknowledging public concern.
- Seeking to put these risks into context with respect to both their magnitude and the level of scientific certainty.[37–41]
- Differentiating between risk factors that strongly influence individual risk and those that may have a minor effect on any individual's risk yet have a significant impact on disease burden in the overall population. The latter may be candidates for tighter regulatory control, but not a major concern for individuals.
- Recognizing that concerned individuals may choose to avoid exposure to certain substances or products, even though the level of evidence is insufficient to make this recommendation to the general public.
- Recognizing that it is not feasible to eliminate exposure to carcinogens entirely, because many occur naturally or are produced endogenously through metabolic processes and inflammation.
- Referring interested parties to other credible sources of information.

Advocacy

The ACS advocates for legislation and policies to achieve its mission of eliminating cancer as a major health problem predominantly through its affiliate, the ACS Cancer Action Network (ACS CAN). ACS CAN is a nonprofit, nonpartisan affiliate that has been a national leader in advocating for prevention measures such as tobacco product regulation, smoke-free laws, and the expansion of early detection screenings for cancer. As part of the ACS's commitment to increasing attention on environmental issues, the ACS and ACS CAN work together on opportunities to promote coordinated policies and programs related to cancer. With regard to environmental carcinogens, the committee on Cancer and the Environment recommends several issues that merit further in-depth consideration by ACS CAN. We list these here, as part of the ACS's commitment to increasing attention on environmental issues:

1. Measures to accelerate the testing of new and existing chemicals for potential carcinogenicity.

2. Increase resources to improve surveillance systems that:
   - Monitor the bioaccumulation of chemicals in humans and in the food chain.
   - Monitor and evaluate trends in cancers for which incidence is increasing.
3. Increase resources for research focused on:
   - Circumstances in which risk may be influenced by the timing of exposures, particularly when exposures occur during critical periods of growth and development.
   - The effects of cumulative exposure to multiple substances with similar biologic effects on the development of cancer in humans.
   - The effects on humans of chemicals that mimic naturally occurring hormones or other processes in the body.
   - The effects on human health of chemicals purported to influence fundamental biologic processes, even at low doses and with transient exposures.

The ACS's National Home Office, ACS CAN, and the ACS divisions also provide a neutral forum for the exchange of information. The ACS will continue to convene meetings, such as the Cancer and the Environment symposium conducted in January 2008, and support the publication of articles in its scientific journals that explore the multifaceted issues related to environmental factors and cancer risk.

Conclusions

Over the last 50 years, the ACS has made major contributions to the primary prevention of cancer through research, education, and advocacy. Among the greatest accomplishments are the continuing reduction in cigarette smoking to levels not observed since World War II, the large decreases in incidence rates of tobacco-related cancers in men and the leveling off of the incidence rates of these cancers in women, and the transformation of cervical cancer from one of the most common cancers diagnosed in women in the United States to a rare disease. These successes have been achieved in large part through the ACS's commitment to scientifically proven prevention measures. Continuing this tradition, a key ACS objective in the current national debate on health care is to integrate scientifically based prevention services into standard medical care.

In developing this new initiative to increase understanding of how exposures to environmental pollutants may affect the risk of various cancers, the ACS will build on its long-term commitment to scientifically based prevention. The issues themselves are complex, as is the dynamic landscape of technologies used to evaluate the potential toxicity and/or carcinogenicity of chemicals, and the responsibilities and jurisdictions of the various research, regulatory, and public health agencies that have primary responsibility for these issues. Recognizing this complexity, the ACS is committed to exploring these issues further to identify ways in which it can contribute most effectively. ■

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