**A Consensus Statement on Cancer and the Environment**

**Creating a National Strategy to Prevent the Preventable Environmental Factors in Cancer Causation**

DRAFT August 19, 2008

## Introduction

More effective cancer treatments. Improved access to care. Raising the quality of life for cancer survivors. Discouraging smoking and reducing obesity. These important goals have been the primary foci of the major national voluntary and governmental cancer organizations. When prevention has been added to these objectives, the word has sometimes been used as a synonym for early detection, like mammograms and colon cancer screenings and sometimes been used only to describe the actions individuals can take to prevent cancer like smoking cessation, exercise and maintaining a healthy weight.

As organizations and individuals concerned with cancer and other illnesses, we affirm the significant accomplishments that these strategies have brought to the American people: The number of cancer deaths and the incidence of lung cancer, colo-rectal cancers and breast cancer have dropped. These are remarkable achievements. But our recognition of these successes should not obfuscate that the incidence of childhood cancer has steadily increased since 1975.[1] In men, the rates of multiple myeloma, cancers of the kidney, liver and esophagus went up from 1975 to 2004. Over that same time period, melanoma, non-Hodgkin's lymphoma, leukemia and cancers of the bladder, thyroid and kidney have increased in women.[2]

Declining cancer mortality is good. But declining cancer incidence is even better. The signers of this statement share the belief that a new, additional focus on the environmental contributors to cancer causation and a new additional focus on prevention strategies to mitigate these environmental contributors will add great value to the existing foci on cancer treatment, access to care and quality of life for cancer survivors. We define "environmental exposures" as all chemical contaminants (or environmental chemicals), ionizing and non-ionizing radiation including electromagnetic fields, diet/nutrition, social stressors or circumstances, and various infectious agents. We believe that by reducing these environmental contributors to cancer, we will be able to protect more men, women and children from ever receiving a cancer diagnosis.

So we welcome the decision of the National Cancer Institute to focus the hearings of the President's Cancer Panel this year on cancer and the environment. This is a momentous opportunity for the three distinguished Panel Members to review the scientific evidence on the contribution of environmental exposures to cancer causation and on the strategies that can reduce the environment's role in causing cancer. The Panel Members will have the unique opportunity to present their findings and conclusion to a new President at a time when an expanded

[1] Ries LAG, Melbert D, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2004, National Cancer Institute. Bethesda, MD; based on November 2006 SEER data submission, posted to the SEER web site, 2007. Accessed 12/17/07 at: http://seer.cancer.gov/csr/1975_2004/

[2] Espey DK, Wu X, Swan J, et al. Annual report to the nation on the status of cancer, 1975-2004, featuring cancer in American Indians and Alaska Natives, Cancer. 2007; 110(10):2119-2152.

perspective on cancer causation and prevention could significantly contribute to research, policy and education agenda that lessens our nation's cancer burden.

The American public cares about cancer and the environment. Opinion polls repeatedly show that Americans are very concerned about exposures in air, water, and food, and in the home, the workplace, and schools that may contribute to cancer incidence. And, as this consensus statement will show, a growing body of scientific evidence supports the American people's concern.

As organizations and individuals concerned with environmentally mediated cancers and other illnesses, we offer the following consensus statement to inform and inspire a national dialogue on cancer prevention. This consensus statement first describes four significant findings from the most recent scientific evidence and then, based on those findings, proposes five cancer prevention strategies. It is not intended to be an exhaustive review of all of the evidence linking environmental factors to many different types of cancer. Instead, this statement is intended as a summary for policymakers, scientists, medical professionals and public health advocates. It is also written for the women, men and children who are living with cancer today, hoping for better treatment options and cures for themselves and for a future in which prevention strategies have effectively decreased the incidence of all cancers in adults and children.

## I. Although cancer deaths have decreased, the burden of cancer in the United States continues to grow. But we are learning through experience that reducing exposure to environmental cancer risk factors [i] saves lives.

The lifetime risk (up to age 95) of being diagnosed with cancer has increased. Data from the National Cancer Institute's Surveillance Epidemiology End Results Program (SEER) estimates that 45% percent of men and 40% of women in the U.S. will be diagnosed with cancer at some point in their life. The number of people living with cancer in the U.S. is now over 10 million; this burden has been steadily increasing and will continue to increase in the coming decades. Moreover, the risk of secondary cancers later in life is a concern for people living with cancer, especially for survivors of childhood cancer.

The age-adjusted cancer incidence rate in the U.S. has begun to decline, mostly because of the recent decline in lung cancer in males, colo-rectal cancer in males and females, and very recently, breast cancer in females. However, incidence rates of several less common types of cancer have continued to rise or have remained steady from previous levels. Among the top 15 cancers in men, multiple myeloma, cancers of the kidney, liver and esophagus increased from 1975-2004.[3] Over that same time period and among the top 15 cancers in women, melanoma, non-Hodgkin's lymphoma, leukemia and cancers of the bladder, thyroid and kidney have increased.[1] Notable increases in the last decade include a near tripling of thyroid cancer among women.[1] In addition, the incidence of childhood cancer has steadily increased since 1975.[4]

With few exceptions, improved diagnostic techniques and changes in disease coding/ classification do not explain these increased rates of cancer. Moreover, many of the types of

[3] Espey DK, Wu X, Swan J, et al. Annual report to the nation on the status of cancer, 1975-2004, featuring cancer in American Indians and Alaska Natives, Cancer. 2007; 110(10):2119-2152.
[4] Ries LAG, Melbert D, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2004, National Cancer Institute. Bethesda, MD; based on November 2006 SEER data submission, posted to the SEER web site, 2007. Accessed 12/17/07 at: http://seer.cancer.gov/csr/1975_2004/

cancer that have been rising in the past decade are not related to cigarette smoking but are caused by viral exposures, ionizing radiation, ultraviolet radiation or other environmental and occupational exposures. However, the national investment in tobacco-related cancers and the subsequent decline or stabilization of lung cancer and several other tobacco-related cancers shows us that preventing exposure to risk factors saves lives.

## II. Current cancer goals in the U.S. focus on reducing death and changing individual behaviors to reduce cancer incidence and should be expanded to include changing the conditions that contribute to cancer.

Both governmental and non-governmental organizations have put forth targets to reduce cancer incidence and mortality. The Centers for Disease Control and Prevention (CDC) set a goal as part of its Healthy People 2010 initiative to "reduce the number of new cancer cases as well as the illness, disability and death caused by cancer."[5] Although a target of a 21% reduction in cancer mortality was outlined in addition to targets for the reduction of cancer deaths associated with seven specific cancer types, no target was outlined for reduction of cancer *incidence* nor was there a target for the reduction of specific disparities in cancer incidence. The CDC through multiple programs and initiatives has a prevention agenda that includes objectives and strategies for lung cancer (tobacco cessation), and melanoma/skin cancer (sun exposure education) but does not set goals for environmental and occupational exposures that increase cancer risk more broadly.[6] However, some states such as Maryland, which receive CDC funding through its National Cancer Control Program are implementing a model program for cancer prevention associated with environmental and occupational exposures.[7] The CDC's Health Protection Goals take a step in the right direction by focusing on the health of workplaces and communities.[8] Other countries are far ahead of the U.S. and actively track progress toward more upstream goals, emphasizing the importance of creating conditions that foster health and reduce the risk of disease.[9] Cancer prevention strategies are more likely to be effective if, in the aggregate, they address a collection of factors at multiple levels that collectively create the conditions out of which cancer patterns emerge.

## III. The methods that have been used to attribute cancer risk to environmental exposures are out of date and should no longer be used to set policy or determine research priorities.

In 1981 Richard Doll and Richard Peto[10] estimated the percentage of cancer deaths that would be avoided if certain individual factors were addressed, including occupational, environmental,

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[5] Centers for Disease Control and Prevention. Healthy People 2010. Accessed 12/13/07 at: http://www.healthypeople.gov/Document/HTML/Volume1/03Cancer.htm

[6] Centers for Disease Control and Prevention. Preventing and Controlling CancerThe Nation's Second Leading Cause of Death At A Glance 2008. Accessed 8/11/08 at: http://www.cdc.gov/nccdphp/publications/aag/dcpc.htm

[7] Maryland Family Health Administration, Maryland Department of Health and Mental Hygiene. The Maryland Comprehensive Cancer Control Plan Our Call to Action 2004-2008. Chapter 8: Environmental Issues and Cancer. Accessed 8/11/08 at: http://www.fha.state.md.us/cancer/cancerplan/plan/Ch8_Environmental_Issues%20and%20Cancer.pdf

[8] Centers for Disease Control and Prevention. Health Protection Goals. Accessed 7/10/08 http://www.cdc.gov/osi/goals/places.html

[9] Canadian Public Health Association. Public Health Goals for Canada: A Federal, Provincial and Territorial Commitment to Canadians. Accessed http://www.healthycanadians.ca/index_e.html

[10] Doll R and R Peto. The Causes of Cancer: Quantitative estimates of Avoidable Risks of Cancer in the United States Today, Journal of the National Cancer Institute. 1981; 66: 1191-1308.

tobacco smoking, diet, alcohol consumption, viruses, etc. The Harvard Center for Cancer Prevention[11] used this same method of calculating attributable fractions in 1996 and used again by Doll in 1998.[12] These well cited sources estimated that only a very small percentage of cancer deaths could be prevented by reducing exposure to cancer risks in the environment (~2%) or in workplaces (~4%-5%) while the majority of cancers would be avoided by improvements in diet and steering clear of tobacco smoke—results which are reflected in over half of our statewide cancer prevention programs.[13] These estimates of attributing cancer risk do not reflect our new understanding of the complexity of cancer causation. As acknowledged later by Sir Richard Doll, the calculation of attributable fractions fails to account for the fact that exposures interact with each other, that the true sum of attributable risks would have to be more than 100%, but that this is impossible to estimate as all avoidable causes are still unknown. National cancer priorities are highly influenced by these attributable fractions and need to be reset to reflect our new understanding of the complex causes of cancer.

**IV. Cancer is most often the result of a complex set of accumulated stressors and reducing the number and severity of these stressors will reduce the incidence of cancer.**

For over a decade, carcinogenesis has been generally understood as a complex multistage process that may begin as early as embryonic development and unfold over a person's life. It includes tumor initiation, promotion and progression. Risk factors for cancer can act alone or through the interaction with other factors to either directly or indirectly initiate one or more of these stages of carcinogenesis.

We now know that complex interactions among genetic inheritance, diet, social circumstances and exposures to a variety of environmental agents – including chemicals known to cause cancer, radiation, and some biological organisms – influence cancer risk. We emphasize the interaction of these variables and note that the presence of one or more risk factors, such as exposure to dioxin,[14] or agents such as bisphenol A that disrupt endocrine signaling,[15] can profoundly influence the extent of risk posed by other factors.

Given this complex cancer model more accurate estimates are required that move us from simple pie charts (as with attributable risk), which result in misleading conclusions, to a multidimensional causal web of disease in which we acknowledge the cumulative interplay among risk factors at various levels of organization (biological, social and ecological) and scales (individual, family, community, society, ecosystem). While on a population-level, there are certainly risk factors such as tobacco smoke that increase the risk of disease dramatically, more often we are challenged by many concurrent exposures each of which may pose only modest increases in cancer risk but which can collectively add up to harm and represent significant

[11] Harvard Reports on Cancer Prevention, Vol 1: Human Causes of Cancer. Cancer Causes & Control, November 7, 1996. Accessed June 9, 2008 at: www.hsph.harvard.edu/cancer/resources_materials/reports.index.htm

[12] Doll R. Epidemiological Evidence of the Effects of Behavior and the Environment on the Risk of Human Cancer, Recent Results in Cancer Research. 1998; 154: 3-21.

[13] Centers for Disease Control and Prevention. Comprehensive Cancer Control Plans: A Content Review. December 2005.

[14] Webster TF and Commoner B. Overview: the dioxin debate. In Dioxins and Health, 2nd Edition. John Wiley & Sons, Inc (Hoboken, NJ) 2003.

[15] Ho S-M, Tang W-Y, Belmonte de Frausto J et al. Developmental Exposure to Estradiol and Bisphenol A Increases Susceptibility to Prostate Carcinogenesis and Epigenetically Regulates Phosphodiesterase Type 4 Variant 4, Cancer Research. 2006; 66 5624-5632.

threats to public health.[16] Whereas it is true that mitigating the risk of cancer from tobacco smoke can be achieved through policy and individual behavior changes, it is also true that successful cancer prevention will depend on addressing other co-occurring and interactive risk factors[17] [18] along with the broader set of social conditions that influence these exposures and contribute to disparities.

**The following goals have emerged from the scientific literature linking environmental factors to cancer. An effective national cancer prevention strategy will incorporate these goals prominently into research, policy and education agendas.**

**Goal 1: Take action now on what we already know by supporting policy and market-based efforts to reduce exposures to risk factors for cancer. We cannot wait to do something until we know everything.**

Identifying all of the necessary new research modalities to determine the cumulative stress of millions of possible mixtures in the environment will take many, many generations of research. Waiting for incontrovertible proof that a chemical contributes to cancer does not allow us to apply what we know. While this research is critically important, a national cancer prevention strategy should also identify ways to take action now to reduce exposures to chemicals and other contaminants of concern. These contaminants should be prioritized based on preliminary evidence of harm, shared mechanisms with chemicals known to be harmful and potential exposures to vulnerable populations. The most direct way to achieve primary prevention of cancer is to avoid the introduction of environmental risk factors into indoor and outdoor environments in the first place. To that end, a significant investment in green chemistry and alternatives development is required. National goals must be set that aim to reduce the upstream causes of cancer.

Among the major known risk factors that we can begin to act on now, we can identify reducing socioeconomic disparities, improving lifelong fitness and nutrition, and reducing exposures to harmful chemicals and radiation.

While not established risk factors, we also have a serious concern with the dramatic increases in exposures to electromagnetic fields, especially cell phones, and the equally dramatic increases in exposure to nanoparticles that are being widely added to consumer products. Both contaminants may contribute to cancer risk.[19] [20] We believe nanoparticles require a prudent safety testing regime before they are widely introduced. We believe that emerging evidence points to a sufficient cancer hazard from cell phones to urgently increase independent research reviews and to recommend reducing cell phone use and exposure, especially for children.

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[16] Accumulative stress/exposures and cancer citation needed???

[17] Hardell L. Pesticides, soft-tissue sarcoma and non-Hodgkin lymphoma - historical aspects on the precautionary principle in cancer prevention, Acta Oncologica. 2008; 47(3): 347-354. Appropriate citations

[18] Coombs NJ, Taylor R, Wilcken N, et al. HRT and breast cancer: impact on population risk and incidence, European Journal of Cancer. 2005; 41(2): 1775-1781. Appropriate citation?

[19] Hardell L, Carlber M, Hansson Mild K. Pooled analysis of two case-control studies on use of cellular and corless telephones and the risk for malignant brain tumours diagnosed in 1997-2003, International Archives of Occupational and Environmental Health. 2006; 79(8): 630-639.

[20] Takagi A, Hirose A, Nishimura T, et al. Induction of mesothelioma in p53+/- mouse by intraperitoneal application of multi-wall carbon nanotube, Journal of Toxicological Sciences. 2008;33(1):105-116.

**Goal 2: Support the creation of new research methodologies that capture the complex web of cancer causation including multiple exposures, low dose effects and how early life exposures and other critical windows of vulnerability can increase cancer risk.**

It is important to distinguish between cancer causation and cancer prevention. It is impossible to be really smart about cancer prevention – reducing the incidence of cancer – if we are stuck in old assumptions about what causes cancer. And the old paradigm of cancer prevention research is in urgent need of repair.

In the past, epidemiologic research has focused on measuring the cancer risk of one contaminant or exposure at a time. Yet in our daily lives, we are not exposed to single agents, but rather to combinations of a large number of agents. Rather than assessing the combined effect of exposure to multiple cancer risk factors, most epidemiologic studies control for the effect of those considered confounders. Where studies examine the effect of multiple exposures, practical limitations in epidemiology often mean that researchers can examine only two or three agents at a time. New methods are needed to understand the cancer risks associated with exposure to chemical and other contaminant mixtures.

Science has shown the inadequacy of the well-known dictum "the dose makes the poison." We know from many new studies that very low levels of exposure may correspond to an increased cancer risk and sometimes have even more of an effect than higher levels.[21] [22] Linear dose-response modeling does not capture all cancer risk.

Research has repeatedly documented examples of differential cancer risk with age at exposure.[23] [24] [25] [26] These examples and others[27] also demonstrate that early life exposures are likely to significantly impact later cancer risk, and exposure may even convey risk on future generations.[28] [29] [30] Cancer prevention must start very early in life and continue throughout life. Understanding the timing of exposures that increase cancer risk later in life is critical to our success in prevention. Large prospective studies like the National Children's Study and the

[21] Hertz-Picciotto and Smith AH. Observations on the dose-response curve for arsenic and lung cancer, Scandinavian Journal of Work, Environment and Health. 1993; 19: 217-226.
[22] Durando M, Kass L, Piva J, et al. Prenatal bisphenol-A exposure induces preneoplastic lesions in the mammary gland in wistar rats, Environmental Health Perspectives. 2007; 115(1):80-86.
[23] Kneale GW, Stewart AM. Reanalysis of Hanford data: 1944-1986, American Journal of Industrial Medicine. 1993; 23(2):371-389.
[24] Richardson DB, Wing S. Greater sensitivity to ionizing radiation at older age: follow-up of workers at Oak Ridge National Laboratory through 1990, International Journal of Epidemiology. 1999; 28:428-436.
[25] Gilman EA, Kneale, GW, Knox EG, et al. Pregnancy x-rays and childhood cancers: effects of exposure age and radiation dose, Journal of Radiological Protection. 1988; 8(1):2-8.
[26] Cohn, BA, Wolfe MS, Cirillo PM, et al. DDT and breast cancer in young women: new data on the significance of age at exposure, Environmental Health Perspectives. 2007;115:1406–1414.
[27] Durando M, Kass L, Piva J, et al. Prenatal bisphenol-A exposure induces preneoplastic lesions in the mammary gland in wistar rats, Environmental Health Perspectives. 2007; 115(1):80-86.
[28] Anway MD, Leathers C and Skinner MK. Endocrine disruptor vinclozolin induced epigenetic transgenerational adult onset disease, Endocrinology. 2006; 147(12): 5515-5523.
[29] Newbold RR, Padilla-Banks E, Jefferson WN. Adverse effects of the model environmental estrogen diethylstilbestrol are transmitted to subsequent generations, Endocrinology. 2006; 147:s11-s17.
[30] Newbold R. Lessons learned from perinatal exposure to diethylstilbestrol, Toxicology and Applied Pharmacology. 2004; 199:142-150.

biomonitoring activities of CDC's National Center for Environmental Health will shed light on these exposures.

But even recognizing the complexity of interactive cancer risk factors is not sufficient to understand cancer causation. An important body of research points to the importance of understanding the systemic conditions that contribute to cancer.[31] [32] This approach is well recognized in social epidemiology where researchers examine how different forms of social organization impact health as well as the ecological sciences, where ecologists regularly study the conditions that lead to systemic resilience or system collapse. We need research paradigms that recognize how important system conditions are to preventing cancer and many other diseases. Because the truth is, the systemic conditions that will reduce cancer incidence are the same as those that will reduce the incidence of the many other epidemic diseases of our time.

**Goal 3: Take action to reduce cancer disparities in low income communities, communities of color, and workers with high exposures to cancer-causing agents.**

The incidence of most cancers, with the exception of breast cancer and melanoma, increases with declining socioeconomic status (SES). Studying this phenomenon is complex and challenging but there are clear associations that can guide inquiry and direct prevention efforts. For example, low income communities and communities of color are generally exposed to more environmental contaminants, poorer nutrition and poorer health care than more affluent communities in the U.S. According to the American Cancer Society, lower-income workers and communities are disproportionately affected by environmental pollutants and occupational exposures.[33] Recent studies have shown that people of color, recent immigrants and the poor are far more likely to work with carcinogens, have less access to institutions that protect them and suffer disproportionately from exposure to environmental contaminants where they live.[34] [35] Moreover, studies report increased levels of markers of inflammation and oxidative stress that are almost certain to be linked to increased cancer risk, as well as a variety of other degenerative diseases, in people of lower socioeconomic status.[36] [37]

Socioeconomic status, ethnicity and gender can significantly influence cancer risk in a variety of inter-related ways at the individual, community, and societal levels and must therefore be addressed collectively, at multiple levels. Genetic inheritance and environmentally mediated gene expression may also impact the biological effects of single and mixed exposures on the populations being studied. We encourage more research using this approach as part of the effort to find new ways to prevent cancer.

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[31] Krieger N. Theories for social epidemiology in the 21st century: an ecosocial perspective, International Journal of Epidemiology. 2001; 30:668-677.

[32] Karpati A, Galea S, Awebuch T et al. Variability and vulnerability at the ecological level: implications for understanding the social determinants of health, American Journal of Public Health. 2002;92(11): 1768-1772.

[33] American Cancer Society. *Cancer Facts and Figures 2006.* Atlanta, GA: American Cancer Society; 2006.

[34] Morello-Frosch R, Pastor M, Porras C, Sadd J. Environmental justice and regional inequality in Southern California: implications for future research, *Environmental Health Perspectives. 2002; 110(2):149-154.*

[35] Brulle RJ and Pellow DN. Environmental Justice: Human Health and Environmental Inequalities, Annual Reviews of Public Health. 2006; 27:103-124.

[36] Harris RE. Cyclooxygenase-2 (cox-2) and the inflammogenesis of cancer. Subcell Biochem. 2007;42:93-126.

[37] Pollitt RA, Kaufman JS, Rose KM, Diez-Roux AV, Zeng D, Heiss G. Cumulative life course and adult socioeconomic status and markers of inflammation in adulthood. J Epidemiol Community Health. 2008 Jun;62(6):484-91.

Disparities in income have increased markedly in the United States in recent decades and represent a major contributor to cancer incidence and mortality. No serious cancer prevention agenda can overlook the importance of returning to a more equitable society.

**Goal 4: Create a new way of managing chemicals so we can determine which chemicals are safe and which are harmful.**

With specific respect to chemical contaminants, the National Toxicology Program has published long-term carcinogenicity studies of only 556 chemicals,[38] a very small portion of the total number in use today. The Toxic Substances Control Act (TSCA), the basis of U.S. chemical policy today, has allowed more than 60,000 chemicals to be in use without requiring the research necessary to determine their safety. Comprehensive chemical policy reform that requires chemical manufacturers to adequately test their products to determine if they can cause cancer or other harm is essential to the prevention of cancer and other environmentally mediated disease. Simultaneously, we need to promote alternatives assessment and green chemistry to expedite the "sunsetting" of carcinogenic and endocrine disrupting chemicals.

**Goal 5: Implement a new cancer prevention strategy that sets the course for new directions in research, policy and individual action.**

We need a comprehensive U.S. cancer prevention strategy that promotes health, reduces the incidence of cancer, and protects the most vulnerable members of society. The current cancer prevention work in the U.S. focuses primarily on smoking cessation, reducing obesity, and early detection. Current policies call for increases in the screening rates for breast cancer, colon cancer and prostate cancers.

But early detection is not prevention. While early detection strategies are critically important because they allow treatment to begin early in the course of disease, true cancer prevention strategies aim to reduce the incidence of cancer by lessening the number of stressors that cause disease. An effective prevention strategy should embrace the inherent complexity and integrate current knowledge on the role of ionizing and non-ionizing radiation, biological organisms, genetic inheritance, endocrine disruptors and chemical carcinogens in water, air, sediment food and consumer products and the role of psychosocial factors like stress, socioeconomic status and income disparities.

A new cancer prevention strategy should set the course for new directions in research, policy and individual action and should set concrete goals for reduction in the exposures that have already been implicated in cancer causation. We owe it to the people who are living and dying with cancer to expand our efforts to prevent every possible preventable cause of this devastating disease.

**The following scientists, researchers, health professionals and advocates affirm that they each agree with content of the Consensus Statement on Cancer and the Environment:**

[38] National Toxicology Program. Long-term study reports and abstract. Accessed on June 16, 2008 at: http://ntp.niehs.nih.gov/index.cfm?objectid=0847DDA0-F261-59BF-FAA04EB1EC032B61

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[i] The term "risk factor" is used throughout this statement to capture the spectrum of causal and mechanistic pathways (tumor promotion, tumor initiation, tumor enabling, developmental disruption, endocrine disruption, developmental susceptibility, etc.) by various agents are known or suspected to contribute to cancer. The more commonly used "carcinogen" is a subset of "risk factor" and does not adequately capture the complexity of cancer causation.