Policy and Research Recommendations Emerging from the Scientific Evidence Connecting Environmental Factors and Breast Cancer

JANET NUDELMAN, MA, BRYNN TAYLOR, MPH, MEM, NANCY EVANS, JEANNE RIZZO, RN, JANET GRAY, PHD, CONNIE ENGEL, MA, MARISA WALKER

A substantial body of evidence links environmental exposures to increases in breast cancer incidence over the past decades. State and federal legislative initiatives that could help prevent breast cancer include: federal standards to achieve consistency in radiation-emitting medical and dental equipment; improved state quality assurance standards for radiation-emitting equipment; federal and state exposure limits for electromagnetic radiation; an overhaul of the federal Toxic Substances Control Act to reduce unsafe chemical exposures; strengthened premarket health and safety testing and regulation of pesticides; a federal ban on the manufacture, distribution and sale of consumer products containing bisphenol A and phthalates; and strengthened oversight and regulation of the cosmetics industry. We recommend public and private investment in research on low dose exposures, mixtures, and the timing of chemical exposures, as well as the development of health tracking and biomonitoring programs designed to link data from pollution surveillance systems with disease registries. *Key words*: breast cancer, chemical regulation, radiation policy, cosmetics, biomonitoring.

INT J OCCUP ENVIRON HEALTH 2009;15:79–101

Worldwide, breast cancer affects more women than any other type of cancer except skin cancer. In the United States, a woman's lifetime risk of breast cancer has increased steadily and dramatically over the decades of the 20th century.[1,2] Between 1973 and 1998, breast cancer incidence rates in the United States increased by more than 40 percent.[3] Recent data (2003-2004)[4,5] suggest that the decreased use of hormone replacement therapy (HRT) has been associated with a decrease in the incidence of the estrogen-receptor-positive (ER+) form of breast cancer in white, postmenopausal women.[6–8] Nevertheless, today, a woman's lifetime risk of breast cancer in the United States is one in eight.[9]

The increasing incidence of breast cancer over decades following World War II paralleled the proliferation of synthetic chemicals. An estimated 80,000 synthetic chemicals are used in commerce today in the United States; another 1,000 or more are added each year.[10] Complete toxicological screening data are available for just 7% of these chemicals.[11] Many of these chemicals persist in the environment,[12,13] accumulate in body fat and may remain in breast tissue for decades.[14] Many have never been tested for their effects on human health.

Among the 216 compounds identified as mammary carcinogens in animals in a recent study on the environment-breast cancer connection, 73 are found in food or consumer products, 35 are air pollutants, and 29 are produced in the U.S. in large amounts.[15] Many other chemicals, especially those classified as endocrine-disrupting compounds (EDCs) are not listed by the regulatory agencies, yet the scientific evidence linking EDCs to breast cancer risk is substantial and growing.[16,17]

In a companion piece to this article, we examine the increasingly sophisticated and compelling data linking radiation and many chemicals in our environment to the current high rates of breast cancer incidence. While we acknowledge the importance of commonly discussed risk factors for breast cancer—primary genetic mutations,[18] reproductive history[19] and lifestyle factors such as weight gain,[20] alcohol consumption[21,22] and lack of physical exercise[23]—we assert that these commonly discussed factors alone do not address a large portion of the risk for the disease.[24]

An important body of scientific evidence demonstrates that exposure to common chemicals and radiation contributes to the incidence of breast cancer. In our daily lives, we are rarely exposed to these substances in isolation. The pervasiveness of many of these substances means we likely have multiple, low-level

Received from the Breast Cancer Fund, San Francisco, California (JN, BT, NE, JR, CE, MW) and the Program in Science, Technology, and Society, Vassar College, Poughkeepsie, New York (JG). This article is based on a Breast Cancer Fund report entitled "State of the Evidence: The Connection Between Breast Cancer and the Environment." Address correspondence and reprint requests to Connie Engel, Breast Cancer Fund, 1388 Sutter St., Suite 400, San Francisco, CA 94109; telephone: +1 415-346-8223; e-mail: cengel@breastcancerfund.org.

Disclosures: The authors report no conflict of interest.

exposures over the course of weeks, months, even years. There are several examples in recent scientific literature demonstrating that *mixtures* of environmental chemicals, chemicals and radiation, or complex combinations of chemicals and particular genetic or hormonal profiles may alter biological processes and possibly lead to increases in breast cancer risk.[18]

When examining the effects of lifestyle factors, environmental chemicals and radiation on future breast cancer induction, scientists now know that the *timing, duration, and pattern of exposure* are at least as important as the dose. A growing body of evidence from both human and animal models indicates that exposures of fetuses, young children, and adolescents to radiation and environmental chemicals put them at higher risk for breast cancer in later life.[16,17] This evidence reflects the fact that mammary cells are more susceptible to the carcinogenic effects of hormones, chemicals, and radiation during early stages of development, from the prenatal period through puberty, adolescence and on until the first full-term pregnancy.[25]

Together, these new data show that we need to begin to think of breast cancer causation as a complex web of often interconnected factors, each exerting direct and interactive effects on cellular processes in mammary tissue.

The current paper builds on the data suggesting that recent declines in cancer incidence rates are associated with decreases in HRT use. At the same time, it recognizes that over the past 30 years there have been significant improvements in reducing some environmental contaminants associated with breast cancer risk. By decreasing exposures to carcinogens, such as exogenous estrogens, estrogen mimics, and endocrine disruptors, we may continue to lower breast cancer levels—and actually prevent the disease—in the future. Toward that end, this paper was written for breast cancer prevention, women's health and environmental health and justice advocates as well as others interested in developing policy and research agendas at the state and federal levels that call for the identification and elimination of the environmental links to breast cancer. It is not meant to provide an exhaustive list of public policy and research initiatives but rather to present a variety of policy options for breast cancer prevention.

REDUCE EXPOSURE TO RADIATION

Ionizing Radiation

Exposure to ionizing radiation is the longest-established environmental cause of human breast cancer in both women and men. In 2005, the National Toxicology Program (NTP) classified X-radiation and gamma radiation as known human carcinogens, because "exposure to these kinds of radiation causes many types of cancer including leukemia and cancers of the thyroid, breast and lung."[27] Also in 2005, a report from the National Research Council established that there is no safe dose of radiation, that "the smallest dose has the potential to cause a small increase in risk [of cancer] to humans."[28] Multiple exposures to low-dose radiation may cause the same harm as a single high-dose exposure. Radiation exposure in combination with exposure to certain synthetic chemicals, including estrogens, can magnify the effect of radiation and/or result in greater susceptibility to chemical insults in the future.[29]

Exposure to ionizing radiation occurs during medical and dental X-rays, computed tomography (CT) scans, fluoroscopy and other imaging procedures. Diagnostic and therapeutic radiation are invaluable in the practice of medicine and dentistry today. Yet, not all equipment or procedures are subject to the same standards, even though legislation to establish federal standards has been introduced in every Congress since 1999. Mammography equipment has a higher quality assurance standard than other radiological equipment as a result of the Mammography Quality Standards Act. Currently, seven states do not license radiation technologists and four more only partially license.[30] Because most states only have recommended quality assurance (QA) standards—if they have standards at all—many medical and dental offices do not perform the required tests that ensure the standards are maintained.

Federal Policy Recommendations. The highest possible standards should be established at the federal level to achieve consistency among the states. Advocates should support the 2007 Consistency, Accuracy, Responsibility and Excellence in Medical Imaging and Radiation Therapy bill (CARE bill), which requires:

1. People performing medical imaging and radiation therapy meet federal education and credential standards in order to participate in federal health programs such as Medicare, Medicaid and other programs administered by the Department of Health and Human Services; and
2. Medical imaging examinations and procedures, as well as radiation therapy treatments for patients covered under these programs, would need to be performed by personnel meeting the federal standards to be eligible for reimbursement.

State Policy Recommendations. States should adopt quality assurance standards for all radiation-emitting equipment that meet or exceed standards currently in place for mammography equipment. State QA standards should require physicians and technologists to use the smallest dose of radiation possible to capture the highest quality image. All states should require licensing of radiation technologists.

Standards should be established by appropriate state agencies so health care providers can more effectively

measure and track their patients' lifetime cumulative exposure to ionizing radiation. Ideally, electronic medical records should include patients' exposure to diagnostic and therapeutic radiation.

States should mandate the use of educational materials in health care facilities to improve patient and physician awareness of the benefits and risks of radiological procedures. Radiation tracking cards should be provided to patients so they can track their cumulative exposure to ionizing radiation and make better-informed decisions about optional procedures.

Research Required. Research is needed to develop safer, noninvasive technologies for breast cancer screening, diagnosis and treatment. In addition, research is needed to better understand the possible cumulative, additive, and synergistic effects that could result from combined exposure to toxic chemicals and ionizing radiation.

Non-Ionizing Radiation (Electromagnetic Fields)

Continuous daily exposure to electromagnetic fields (EMF) is a fact of life for everyone living in the industrialized world. EMF is a type of low-intensity, non-ionizing radiation that has insufficient energy to break off electrons from their orbits around atoms and ionize (charge) the atoms. EMF includes extremely low-frequency radiation (ELF-EMF) from electrical appliances and power lines, and radiofrequency (RF) radiation from wireless technologies such as cell phones, cordless phones, personal data assistants, laptops, the towers and antennas that support these technologies, and broadcast transmission towers.

Decades of research indicate that exposure to EMF is associated with many adverse health effects including breast cancer (in both men and women) and other cancers, neurodegenerative diseases, and impaired immune function.[31,32] Existing public exposure standards for EMF are inadequate to protect public health because they are based on the assumption that unless heating of tissue occurs within 30 minutes (short-term thermal effect), no harm can result.

There are no federal guidelines for nonthermal effects or long-term chronic exposure. A growing body of international research challenges that assumption, and experts around the globe are debating the need to strengthen the standards based on newer science showing health risks of chronic, widespread low-level exposure. In September 2007, Germany's Federal Office for Radiation Protection advised citizens to avoid WiFi wherever possible because of the risks it may pose to health.[33] In the same month, the European Environmental Agency (EEA) called for immediate action to reduce exposure to radiation from WiFi and mobile phones and their masts[34] based on an international scientific review which concluded that safety limits set for these types of radiation are "thousands of times too lenient."[35] In the U.S., there has been little federally funded research on EMF despite the expansion of wireless technologies, particularly cell phones. Rapid deployment of wireless technologies is outpacing the policy decisions necessary to protect public health.

Breast Cancer Fund supports *The BioInitiative Report* statement that the scientific evidence is sufficient to warrant regulatory action for extremely low-frequency electromagnetic fields (ELF-EMF) and preventive actions for radiofrequency (RF) radiation.[35]

Existing government limits do not protect the public from the adverse health effects of electromagnetic radiation emanating from devices such as power lines, cell phones, wireless internet, radar, and TV and FM broadcast towers.[35,36] Most of the existing limits on this form of radiation are 1,000–4,000 times too lenient to prudently protect against cancers in children and adults, Alzheimer's and other neurodegenerative diseases, reproductive problems, immune function disruption, electrohypersensitivity and symptoms such as insomnia, headaches, memory loss, concentration and attention difficulties.[31,35]

Federal Policy Recommendations. The federal government should set exposure limits for electromagnetic radiation based on the scientific evidence set forth in *The BioInitiative Report*[35] and a growing body of additional research. Limits should be set for:

1. Extremely low-frequency electromagnetic fields (ELF-EMF) including those created by power lines, appliances, interior electric wiring and other devices, and
2. Long-term and cumulative radiofrequency (RF) radiation from outdoor pulsed sources including cell phone antennas, radar, TV and FM broadcast antennas and wireless internet antennas; and from indoor sources including cell phones, wireless internet equipment and radiation that permeates buildings from outdoor sources.[37]

With the setting of federal limits for non-ionizing radiation, special protections should be required for homes, schools and places where children spend large amounts of time.

Research Required. Research is needed to quantify and monitor the levels and characteristics of ELF-EMF and RF radiation present in schools, workplaces, and residential neighborhoods now and into the future. In addition, research is needed to determine the effects of chronic exposure to ELF-EMF on women recovering from breast cancer and other cancers.

REDUCE EXPOSURE TO TOXIC CHEMICALS

There is consensus around the globe that our failure to adequately assess and regulate chemicals is taking a

toll on the health of humans and the environment. Evidence of public and environmental health problems related to chemical exposures continues to grow. With the passage of its new law on chemicals management, REACH (Registration, Evaluation, Authorization and Restriction of Chemicals), the European Union is leading the way on the international stage to protect human health and the environment through the better and earlier identification of the toxicological properties of chemical substances.

Although there are 80,000 chemicals commercially used in the U.S. and 1,000 new chemicals entering the market each year, little is known about the toxicity of the majority of these chemicals.[38,39] The federal statute intended to regulate chemicals before and after they enter commerce is the Toxic Substances Control Act of 1976 (TSCA).[40]

Studies by the National Academy of Sciences, U.S. Government Accountability Office and U.S. Environmental Protection Agency, among others, have concluded that TSCA does not adequately help the public, industry or government assess the hazards of chemicals in commerce or control those of greatest concern.[41–44] Attempts to reform this inadequate chemicals policy are underway in Congress. The most recent and promising is the Kids' Safe Chemical Act of 2008,[45] which would amend TSCA. Also important are smaller, chemical- or product-specific bills such as the recently passed Consumer Product Safety Improvement Act, which included legislation introduced by U.S. Senator Dianne Feinstein and U.S. Representative Darlene Hooley to ban six toxic phthalates from children's toys and childcare articles.[46]

Along with activity in Congress and efforts at the federal level by nongovernmental research and advocacy organizations, there have been important state-level efforts to better understand and regulate unsafe chemical exposures, such as Proposition 65 in California. Passed in 1986, Proposition 65 requires the governor to publish, at least annually, a list of chemicals known to the state to cause cancer or birth defects.[47] Businesses are required to provide a "clear and reasonable" warning before knowingly and intentionally exposing anyone to a listed chemical, unless exposure is low enough to pose no significant risk of cancer, birth defects, or other reproductive harm.

While these efforts are a step in the right direction, they are not comprehensive enough to fix the broken chemical regulatory system. More promising are efforts at the state level on chemical policy reform through the State Alliance for Federal Reform of Chemicals Policy (SAFER). SAFER is a strategic campaign whose long-term vision is to establish a new precautionary federal chemicals policy as the basis of a clean, green economy by 2020.[48] SAFER is composed of environmental health and justice coalitions in eight states including California, Connecticut, Maine, Massachusetts, Michigan, Minnesota, New York, and Washington.

Federal Policy Recommendations. TSCA should be amended to adhere to the recommendations of the Louisville Charter for Safer Chemicals, a set of principles agreed upon in Louisville, Kentucky in May 2004 by a network of environmental health and justice organizations working to reform the way chemicals are regulated in the U.S.[49] According to the Louisville Charter, a full-scale overhaul of TSCA is needed that (1) requires safer substitutes and solutions, (2) phases out persistent, bio-accumulative or highly toxic chemicals, (3) gives the public and workers the full right to know and participate, (4) acts on early warnings, (5) requires comprehensive safety data for all chemicals, and (6) takes immediate action to protect communities and workers.

Federal legislation should require manufacturers to provide health and safety information to government agencies before releasing a chemical into commerce, instead of presuming a substance is safe until proven dangerous.[50] Comprehensive federal chemical policy reform should protect the most vulnerable (children, women of childbearing age, people with weakened immune systems, and the elderly) and those who bear an unequal burden of chemical exposures (workers, fence-line communities, etc.). Legislation should also require chemical manufacturers to pay a fee to register their chemicals to offset the financial burden, similar to the model of the Federal Insecticide, Fungicide, Rodenticide Act/Food Quality Protection Act (FIFRA/FQPA), in which pesticide manufacturers pay a fee to register pesticides.[51] Proceeds could offset the costs of monitoring and data collection to evaluate the direct impacts of chemicals in commerce on human health.

Finally, federal tax incentives are needed to stimulate investments in green chemistry and safe alternatives.

State Policy Recommendations. In the absence of comprehensive federal reform, states should assume the regulatory authority the federal government has been unwilling to accept to protect the public from chemical exposures including, as listed above, the core components of the Louisville Charter. States should prioritize protection of the most vulnerable populations by requiring the phase-out of chemicals that can cross the placenta and harm developing fetuses. State policies should require that manufacturers provide comprehensive health and safety data for chemicals, information about where and how chemicals are used in consumer products and industrial processes, and the availability of safer alternatives. This information should be made readily available to the public and should also be made available for data-sharing among states. States should require the labeling of chemicals linked to adverse health effects in consumer products. If health data is not available for a chemical ingredient, labeling should state that the health and safety of that chemical ingredient is unknown and/or cannot be substantiated.

In addition, states should institute producer-take-back rules requiring manufacturers of computers and other products made with toxic materials to take back and reuse or recycle their products to reduce the quantity of waste that goes to landfills, where it can leach into soil and water. They should encourage market innovation and reform by mandating the purchase of nontoxic products by all state agencies through procurement policies. Finally, states should augment undergraduate and graduate chemistry curricula with green chemistry classes such as coursework in toxicology, exposure assessment, ecology and environmental science.

Research Required. Premarket testing of new chemicals and postmarket testing of legacy chemicals (such as PCBs, DDT, etc.) are needed to assess the impacts of all chemicals on human health, worker health, and environmental health. Green chemistry research is required to identify or create safer alternatives to toxic chemicals used in manufacturing and industrial processes.

Air Contaminants

According to a comprehensive scientific review of environmental links to breast cancer, 216 chemicals have been associated with increases in mammary gland tumors in animals.[15] Of those, 35 are air pollutants. There is widespread public exposure to many of these chemicals in outdoor air, as well as offices, homes, restaurants and schools. Another review of studies of human populations found that the evidence generally supports an association between breast cancer and ubiquitous air pollutants called polycyclic aromatic hydrocarbons (PAHs).[52] And, while human studies are limited in number, evidence also points to an association between breast cancer and two other chemical families of air pollutants: dioxins and organic solvents.[53,54]

Most of the air pollutants can be found in primary and secondhand tobacco smoke, diesel exhaust and/or in specific occupational settings (see Table 1). According to the California Air Resources Board, there are 20 mammary carcinogens in tobacco smoke alone.[55] In 2006, the California EPA determined that "overall, the weight of evidence . . . is consistent with a causal association between [environmental tobacco smoke] exposure and breast cancer in younger, primarily premenopausal women."[56]

Federal and State Policy Recommendations. States should adopt environmental (second-hand) tobacco smoke bans in all public locations, including restaurants and bars. There are 26 states/commonwealths plus the District of Columbia with laws in effect that require 100% smoke-free workplaces and/or restaurants/bars.[57]

States should follow California's lead and adopt tough emission standards for off-highway diesel vehicles like bulldozers, airport baggage trucks and ski resort snowcats.[58] Diesel engine exhaust contains, among other toxic substances, PAHs. Evidence in both animal[15] and human[52] studies links PAH exposures to increased risk for breast cancer.

A number of U.S. organizations are working on reducing air pollution. They have developed a number of recommendations—both personal and political—for reducing air contaminants like PAHs, tobacco smoke and diesel exhaust.[59–61]

Research Required. State and federal agencies should increase the number of chemicals that are monitored in ambient air. Currently, the Clean Air Act requires tracking of six "criteria pollutants."[62] Air toxicants (188 hazardous air pollutants as defined by the EPA) should also be tracked. This data should be supplemented with personal monitoring (for example, devices used on children to monitor their exposure to diesel exhaust from school buses) and biomonitoring studies in disproportionately impacted communities, occupational settings, and communities with disease clusters. Occupational studies that look at workers regularly exposed to air pollutants like PAHs, tobacco smoke, diesel exhaust, and organic solvents should be prioritized.

Pesticides

Some pesticides and herbicides have been labeled as human or animal carcinogens and many are found in water supplies as well as in air and dust in homes. Though banned in the U.S. in 1972, dichloro-diphenyl-trichloroethane (DDT) and its metabolite, dichloro-ethylene (DDE), are still found in the body fat of humans and animals, as well as in human breast milk and placenta. The triazine herbicides—atrazine, simazine and cyanazine—have all been shown to cause mammary cancer in rats. Atrazine, the most studied of the three, is of particular concern for breast cancer because it disrupts—in fact increases—the activity of aromatase, which can lead to increased estrogen levels. Through different mechanisms, three other pesticides—heptachlor, dieldrin and aldrin—have also been shown to increase estrogen levels and/or stimulate growth of breast cancer cells.

Of particular concern is the health of agricultural workers and their families, and communities affected by pesticide drift. Biomonitoring studies of children of agricultural workers revealed that high levels of pesticides can be found in the children's urine soon after application in the fields near their homes.[63] Many pesticides are endocrine disruptors; children's exposures pose a special concern as chidren are at a susceptible point in their development.[64–66]

Federal Policy Recommendations. Advocates should pressure the EPA to follow the lead of the EU and ban the use of atrazine in the U.S. In addition, advocates should pressure the EPA to ensure that the Endocrine

TABLE 1 Air Contaminants Associated with Breast Carcinogenesis

Air Pollutant(s)	Description	Sources of Exposure
Polycyclic Aromatic Hydrocarbons (PAHs)	Class of chemicals produced in combustion Example: benzo(a)pyrene	• Outdoor and indoor air pollution • Tobacco smoke • Coal and coke-burners • Auto exhaust (diesel) • Diet —Smoked and grilled foods —Foods contaminated by outdoor air pollution • Occupational exposures
Dioxins	Class of chemicals produced in combustion of PVC, PCBs and other chlorinated compounds Example: tetra chlorodibenzo-p-dioxin (TCDD)	• Outdoor air pollution • Waste incineration • Pulp and paper manufacturing and other industrial processes • Diet (indirect, primary exposure) —Dietary fat, especially in milk, eggs, fish, meat —Foods contaminated by outdoor air pollution • Occupational exposures
Organic Solvents	Class of chemicals that include chlorinated and other solvents Examples: toluene, methylene chloride, trichloroethylene, formaldehyde	• Outdoor and indoor air pollution • Waste incineration • Used in manufacture of computer parts • Used in manufacture of cleaning products and some cosmetics • Occupational exposures
Alkylphenols	Industrial chemicals used in manufacturing of consumer products Example: 4-nonylphenol	• Indoor air and dust • Personal care products —Hair products —Spermicides • Used in manufacture of cleaning products and detergents • Occupational exposures
Vinyl Chloride	Released when PVC is produced. PVC is used extensively in food packaging, cars, toys, credit cards, rainwear and other products	• Outdoor and indoor air pollution • Tobacco smoke • Air near hazardous waste sites and landfills • Occupational exposures during PVC manufacture
Benzene	High production volume petrochemical	• Outdoor and indoor air pollution • Tobacco smoke • Gasoline fumes • Auto exhaust (diesel) • Industrial burning/combustion • Occupational exposures
Ethylene Oxide	Chemical used to sterilize medical equipment and in some cosmetics	• Primarily indoor air pollution • Possibly from cosmetics • Occupational exposures in sterilization facilities or cosmetics manufacturing
Aromatic Amines	Class of chemicals found in the chemical and plastic industries. Combustion byproducts of manufacturing. Types: monocyclic, polycyclic, heterocyclic	• Outdoor or indoor air pollution • Tobacco smoke • Combustion of wood chips or rubber • Formed in production of polyurethane foams, dyes, pesticides, and pharmaceuticals • Auto exhaust (diesel) • Diet—grilled meats and fish • Occupational exposures
Pesticides	Class of chemicals used residentially or in agriculture to kill plant and animal pests Examples: atrazine, heptachlor, dieldrin, DDT	• Outdoor or indoor air pollution • Dust in households • Diet—non-organic food • Occupational exposures
1,3-Butadiene	Product of internal combustion engines and petroleum refineries	• Outdoor or indoor air pollution • Tobacco smoke • In manufacture of rubber products and some fungicides • Occupational exposures

Sources: Brody JG, Moysich KB, Humblet O, Attfield KR, Beehler GP, Rudel RA. Environmental pollutants and breast cancer: epidemiologic studies. Cancer 2007;109(S12):2667-711; Rudel RA, Attfield KA, Schifano JN, Brody JG. Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. Cancer. 2007;109(S12):2635-66.

ATRAZINE, FROGS AND BREAST CANCER

Atrazine, a triazine herbicide, has been banned in the European Union since 2005.[73] The U.S. EPA concluded it was an endocrine disruptor in 2000. However, farmers used 77 million pounds of it in the U.S. in 2003.[74]

Atrazine has been shown to cause mammary cancer in lab rats.[75,76] Recent data suggest that the major mechanism by which atrazine exerts its endocrine-disrupting effects is by increasing the activity of the enzyme aromatase.[77,78] Aromatase facilitates the conversion of testosterone and other androgens to estrogens, including estradiol.

This pathway of estrogen production is of great enough importance to the development of breast cancer that a current class of breast cancer drugs aims to block this activity of aromatase. Femara (Letrozole) is one of these drugs. It targets aromatase, which in turn reduces estrogen and keeps breast cancer cells from growing initially.[79,80]

Dr. Tyrone Hayes at the University of California at Berkeley has spent his career examining atrazine and its effect on the growth and development of frogs. He has shown that atrazine chemically castrates and feminizes male amphibians in the wild and in the lab. He suggests that atrazine-induced deformities result from the depletion of androgens and production of estrogens, perhaps after atrazine increases the activity of aromatase.[81]

When Dr. Hayes presents his research, he often tells this story: The maker of atrazine is Syngenta, a multinational agrichemical corporation. Syngenta was formed in 2000, when another multinational called Novartis merged their Crop Protection and Seeds businesses with Astra Zeneca's Agrochemicals.[82] What is interesting and very disturbing, he argues, is that Novartis is also the producer of Femara, the breast cancer drug discussed above. And so, Dr. Hayes points out, the very company that produces atrazine (that "turns on" aromatase, thereby increasing estrogen which can lead to breast cancer cell growth) is also producing—and selling at great profit—a medication that has the opposite effect (to "turn off" aromatase).

Sixty percent of Americans are regularly exposed to atrazine, an herbicide that may be negating the positive effects of breast cancer medications. The company that stands to profit from sales on both sides of the equation is headquartered in Switzerland, where atrazine is banned.

Disruptor Screening Program gets underway as mandated by Congress,[67] and that the EPA screens these chemicals and makes the results readily available to the public without delay.

Strengthened premarket health and safety testing and regulation of pesticides should be included in comprehensive chemical policy reform, as discussed above.

State Policy Recommendations. In the absence of federal legislation, states should either ban the use of or require adequate labeling of home-use pesticides containing chemicals linked to endocrine disruption, carcinogenesis, central nervous system disruption, and reproductive disorders, and encourage the use of safer substitutes.

States should ban the use of pesticides on or near school grounds, including day care centers and nurseries. In addition, states and municipalities should ban the use of "cosmetic" pesticides and the use of pesticides in parks. In Canada, support is growing (mostly at the municipal level) for bans on cosmetic—purely aesthetic—use of pesticides, where the weed or pest poses no danger to human health, the environment, or property.[68,69] The cities of San Francisco and Oakland, California have banned the use of pesticides in their parks for years.[70–72] Such efforts to end the nonessential uses of pesticides should be supported and ultimately written into state legislation.

Research Required. More research is needed on the cumulative exposures of agricultural workers and their families to first, protect their health, and second, gain a greater understanding of the role of pesticides in the development of breast cancer and other diseases.

Moving away from toxic, endocrine-disrupting pesticides will require a just transition strategy and viable alternatives. A significant national investment in integrated pest management research is essential and long overdue.

Consumer Exposures

Each day, consumers use products that contain chemicals untested for impacts on human health and the environment. Reducing human exposure will also help keep these chemicals out of air, waterways, soil, ice caps, and wildlife.

Plastics

Plastics are widely used in consumer products and packaging of all kinds. There are, however, serious risks to human health and the environment from the widespread use of plastics. Most plastics are made from petroleum, a nonrenewable resource. Not all plastic is recycled and millions of bottles go to landfills every year.[83] In addition, many plastic products end up in the ocean where they have formed enormous flotillas, harming plankton and the entire food chain of fish, turtles, and birds that depend on these tiny creatures.[84]

The three plastics that have been shown to leach toxic chemicals when heated, worn or put under pressure are polycarbonate (leaches bisphenol A), polystyrene (leaches styrene) and PVC (leaches phtha-

TABLE 2 Pesticides Associated with Breast Cancer

Pesticide	Carcinogenic: Animal Mammary Gland Carcinogen[a]	Carcinogenic: Human Carcinogenic Risk Classification[b]	Hormone Disrupting: Disrupts Endocrine System/ Estrogenic[c]	Source of Exposure/ Scope of Use
1,2-Dibromo-3-chloropropane	X	IARC Possible; NTP Reasonably Anticipated		Pesticide: banned as soil fumigant in 1985, air pollutant, exposure through ingestion of previously contaminated food and water
2,4-Dichloro-phenoxyacetic acid			X	Pesticide: herbicide
Atrazine (a triazine herbicide)	X	IARC Not Classifiable	X	Pesticide: herbicide, air pollutant, found widely in water bodies, exposure through ingestion of food or water, banned in European Union in 2005, 75 million pounds used annually in U.S., mainly on corn and sorghum
Captafol	X	IARC Probable		Pesticide: fungicide, not currently registered for use in U.S.
Chlordane	X		X	Pesticide: insecticide (ticks and mites), veterinary pharmaceutical, air pollutant, use as insecticide has been banned, persists in meat and fish, found in household dust
Chlorpyrifos			X	Pesticide: insecticide (ticks and mites)
Clonitralid	X			Pesticide: exposure through dermal contact or ingestion of water treated with clonitralid (for water snail and sea lamprey control) or contaminated fish
Cypermethrin			X	Pesticide: insecticide
DDT (Dichloro-diphenyl-trichloroethane)		NTP Reasonably Anticipated	X	Pesticide: contact insecticide, banned in many countries, used for malaria control in others, DDT and metabolite DDE still found in body fat of humans and animals though banned in U.S. in 1973
Dichlorvos	X	IARC Possible		Pesticide: air pollutant, inhalation of air and dermal contact with no-pest strips, sprays or flea collars, ingestion of food prepared where dichlorvos has been used
Dieldrin, Aldrin, Endrin (-drin pesticides)			X	Pesticide: insecticide, 1950s to 1970s dieldrin and aldrin used on corn and cotton, 1987 both were banned, still persist in environment
Fenvalerate	X	IARC Not Classifiable		Pesticide: landscaping/yard products, pet care products
Heptachlor		IARC Possible	X	Pesticide: insecticide, used for termite control through 1980s in U.S., agricultural use continued until 1993 (especially on pineapple)
Lindane		NTP Reasonably Anticipated	X	Pesticide: insecticide
Malathion			X	Pesticide: insecticide
Methoxychlor			X	Pesticide: insecticide, veterinary pharmaceutical
Nifurthiazole	X	IARC Possible		Pesticide
Pentachlorophenol			X	Pesticide: insecticide (termites), wood preservative
Permethrin, Sumithrin			X	Pesticide: insecticide
Simazine (a triazine herbicide)	X	IARC Not Classifiable		Pesticide: air pollutant, widely used to control weeds in food crops and in ponds, algae control in pools and fountains, detected at low levels in air, rainwater and surface water
Sulfallate	X	IARC Possible; NTP Reasonably Anticipated		Pesticide: herbicide, used until early 1990s in U.S., exposure through ingestion of residues in food crops
Toxaphene		NTP Reasonably Anticipated	X	Pesticide: insecticide
Tributyl Tin (chloride)			X	Pesticide: biocide, rodent, repellent
Vinclozolin			X	Pesticide: agricultural fungicide, used in vineyards

[a]Rudel RA, Attfield KA, Schifano JN, Brody JG. Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. Cancer. 2007;109(S12):2635-66.
[b]International Agency for Research on Cancer (IARC) carcinogenic risk classification is based on evaluation of potential tumor development at all sites, not only breast/mammary tissue. Categories include: known, probable, possible and others. The National Toxicology Program (NTP), within the National Institute of Environmental Health Sciences of the National Institutes of Health, provides carcinogenicity ratings based on scientific evidence in both animals and humans. Categories include: known, reasonably anticipated, and others (Report on Carcinogens, 11th edition; US Department of Health and Human Services, Public Health Service, National Toxicology Program.) Not all chemicals have been rated by IARC or NTP.
[c]To date, neither the NTP nor IARC have classified most endocrine disruptors as carcinogens in humans. List of endocrine disruptors from: Brody JG, Rudel RA. Environmental pollutants and breast cancer. Environ Health Perspect. 2003;111:1007-19.

lates).[85] Bisphenol A (BPA) is the building block of polycarbonate plastic and is used to manufacture baby bottles, sports water bottles, and dental sealants. BPA is also a component of the epoxy resins used to line infant formula and food cans. The evidence on BPA and its many effects on human health is convincing and growing. Studies funded by the chemical industry say it is harmless; nonindustry studies show it is a powerful hormone disruptor linked to breast cancer.[86–88]

Phthalates, another chemical family of concern, are used to soften plastics, especially PVC. They are found in many consumer products including children's bath toys and teething toys. Phthalates are endocrine disruptors that increase the risk of early puberty (and therefore, breast cancer) in girls, and have been linked to reduced testosterone levels, lowered sperm counts, and genital defects in baby boys, and testicular cancer in young men.[89–92]

Federal Policy Recommendations. U.S. EPA should fully implement the Endocrine Disruptor Screening Program, as mandated by Congress, to effectively and efficiently screen chemicals for hormonal activity and to make the results readily available to the public without delay. Congress should also ban the manufacture, distribution and sale of consumer products containing BPA and phthalates.

State Policy Recommendations. In the absence of federal regulation, states should either ban endocrine-disrupting chemicals like BPA and phthalates in all consumer products, or require that consumer products containing these plastics be adequately labeled. In the meantime, advocates should support legislation (as in California, other states, and at the federal level[93–95]) that bans endocrine disruptors like phthalates and BPA in children's toys and childcare articles such as baby bottles and "sippy cups."

Research Required. Funding is needed to support green chemistry research on bio-based plastics that can be composted after they have been used in consumer products. Another need is for human studies of exposure to endocrine-disrupting chemicals—like BPA and phthalates—and breast cancer outcomes. This may require an investment in new methodologies because exposure to these chemicals is widespread in the population, challenging currently available testing methods. Limited (and expensive) human studies should both inform and be informed by targeted animal studies. Coordination of these two research models is critical to moving the research forward.

Household Cleaning Products

Although there are thousands of household cleaning products on the market, the products' labels provide little information about risks to the environment and human health. The government provides very little oversight of these products and yet consumers and their children are exposed to them every day.

Certain occupations are especially vulnerable to the effects of toxic cleaning products. Housekeepers and custodians are heavily exposed to cleaning chemicals and are often not given any information about health effects or safety precautions. Little exposure assessment has been done in these occupations. Critical information needed to inform public health interventions has not been collected.

Federal and State Policy Recommendations. The federal government should either ban the use of chemicals linked to cancer and other long-term health effects in cleaning products (e.g., phthalates in synthetic fragrance formulations), or require labeling adequate to allow consumers to make informed and safer purchases. In the absence of federal regulation, state governments should ban these substances or adopt strong labeling guidelines.

Research Required. Research is needed on safe alternatives to toxic chemicals in cleaning products. Occupational research should look at workers regularly exposed to cleaning products and the possible linkage to breast cancer later in life. Use of biomarkers of exposure and early disease should be explored as soon as possible to shorten the length of the study and allow for occupational health interventions.

Hormones in Meat and Milk

Modern food production methods have introduced new environmental exposures to carcinogens and endocrine-disrupting compounds. Pesticides on crops, antibiotics in poultry, and hormones in cattle, sheep and hogs expose consumers to unsafe contaminants every day. Consumption of animal products may hold inherent risks because animal fat can retain pesticides and other environmental toxicants consumed by the animal, and research suggests that some of these exposures increase breast cancer risk.[133,134]

Since its introduction in 1993, bovine growth hormone (rBGH/rBST) has proven controversial because of its potential carcinogenic effects. Several studies have shown an association between dairy consumption and breast cancer in premenopausal women. rBGH has been shown to raise insulin-like growth factor 1(IGF-1) levels in the body, which have, in turn, been associated with an increased risk of breast cancer.[135–140] Another food additive of concern is zeranol, a growth promoter used in the beef industry that mimics the effects of natural estradiol in the body.

Federal and State Policy Recommendations. The federal government should ban the use of hormones in meat and

BPA AND DES: A TALE OF TWO ESTROGENS

Bisphenol A (BPA) is one of the most widely used chemicals today. It is found in baby bottles, other food and beverage containers, linings of metal food cans, dental sealants and countless other products. It is also found in air, dust, rivers and estuaries—and in Americans of all ages, including newborns.[96] More than 2 billion pounds of BPA are produced in the United States each year; more than 6 billion pounds are produced worldwide. BPA generates enormous annual revenues for corporations such as Bayer, Dow, GE Plastics and Sunoco.[97]

BPA is a result of the search for cheap synthetic estrogens, compounds designed to keep postmenopausal women "feminine forever" and to promote the rapid growth of cattle and poultry industry profits. Synthesized in 1936,[98] BPA was shunted aside two years later by a more potent synthetic estrogen: diethylstilbestrol (DES), now known to cause cancer and reproductive abnormalities in both males and females.[99]

Though they differ in potency, DES and BPA share striking similarities in their structures, functions and histories. Both chemicals:

- were developed when the health effects of estrogen were poorly understood. Early animal studies linked both chemicals with increased risk of mammary and other cancers and reproductive abnormalities.
- entered the food chain: DES as a livestock drug and BPA through food containers and packaging. DES was prescribed to pregnant women to prevent miscarriage (which it failed to do[100]), and BPA is associated with recurrent miscarriage as seen in a recent study from Japan.[101]
- were aggressively marketed, despite scientific evidence suggesting the need for caution. BPA is still marketed globally. The Food and Drug Administration (FDA) ignored animal evidence of DES reproductive toxicity and approved the drug for medical use in humans in 1941, then for use during pregnancy and for use in livestock and chickens in 1947.[102,103] When male agricultural workers exposed to DES suffered sterility and breast cancer, FDA banned the use of DES in poultry, but not in cattle or in women.[104] Between 1938 and 1971, an estimated 5–10 million women in the U.S. were prescribed DES.[105] Use of DES in cattle continued into the 1980s.

In 1970, doctors noted an unprecedented number of rare vaginal cancers in young women whose mothers had taken DES during their pregnancy. Ultimately, DES proved to be a transgenerational carcinogen and a reproductive toxicant, resulting in an FDA alert on the drug. Subsequent research showed an indisputable cause-effect relationship between maternal use of DES and clear cell vaginal carcinoma in daughters.[105–107] DES also increased the risk of breast cancer in the mothers, and studies now show that increased breast cancer risk extends to DES daughters.[108–112] Decades of research on DES daughters and sons have shown that animal studies can be useful in predicting effects in people.

Discarded as an estrogen replacement therapy pharmaceutical, BPA was rediscovered by polymer scientists in the late 1940s and quickly became a mainstay of the plastics industry.[97,113] It is the building block of polycarbonate plastic and is also used in the manufacture of epoxy resins and other plastics, such as polyester and styrene.

Although never prescribed as a drug or deliberately added to foods, BPA enters the food chain by leaching from plastic packaging or containers as the plastic ages or is heated. Once in food, BPA moves quickly into people, including placental tissue and umbilical cord blood, where it can disrupt normal prenatal development, even at low levels—parts per billion or parts per trillion.[114]

BPA exposure during critical windows of development has been linked with increased risk of breast, prostate and testicular cancer. It is also linked to birth defects, including neurobehavioral disorders, increased risk of miscarriage, decreased sperm production, early puberty in females, obesity and insulin-resistant diabetes.[115–118]

One recent study showed that neonatal exposure to low levels of BPA causes uterine fibroids, cystic ovaries and precancerous lesions in female middle-aged mice. These results closely parallel the effects of comparable DES exposure.[119] In women, such effects are major contributors to infertility and the most common reasons for hysterectomy.

Many scientists and the public are increasingly concerned about BPA because of (1) high production volume, (2) widespread human exposure, and (3) evidence of reproductive toxicity in laboratory animals.[120] Much of the research indicating health risks of early life exposure to BPA has occurred since 1995, and the accumulated evidence is compelling. However, the chemical is regulated based on research findings prior to 1984. The U.S. EPA standard for BPA safety, called a reference dose, is 50 micrograms per kilogram of body weight, per day. [121] Although considerable variability in body burdens of BPA have been found, studies consistently indicate significant levels of the chemical in most people in the U.S., with levels at or above those shown to induce damaging effects in animal models.[122,123]

Manufacturing Doubt

Manufacturers of BPA responded to concern about health risks by criticizing the evidence as controversial, limited and overblown. They called for more research. This all-too-familiar tactic has enabled many industries to continue

profiting from tobacco, lead, asbestos, DES and other toxic products while damaging public health.[124] When media reported early studies of BPA's estrogenic effects on the male reproductive system,[125] the chemical industry attacked, saying their scientists could not replicate the studies.[115,126] Laboratories hired by chemical companies quickly produced studies that found no harmful effects.[115,126]

A 2005 analysis of the BPA literature revealed a clear pattern of bias in reporting results: the funding source often determined the findings. Of 115 studies on health effects of BPA, 94 government-funded studies conducted in academic laboratories in Japan, Europe and the United States found adverse effects at low dose exposure. None of the studies funded by industry reported adverse effects.[115]

Leading scientists called for a new assessment of BPA based on mounting evidence of its DES-like effects. The NTP responded by appointing an advisory committee to assess the evidence and prepare a report. In March 2007, it was revealed that the advisory committee's report had been drafted by a private consulting firm with ties to the chemical industry. NTP fired the firm but accepted the report as unbiased.[127]

When the advisory committee reconvened in August 2007 to review the report, leading BPA researchers testified about errors in the report, failure to consider the full range of evidence and reliance on flawed data from industry.[128] The committee remained largely unconvinced, noting in their summary statement "some concern" only for pregnant women, fetuses, infants and children "that exposure to BPA causes neural and behavioral effects."

Neural and behavioral effects are a significant concern—particularly for women of childbearing age who are the first environment for infants. Four million children are born each year in the United States; most may be exposed to BPA in their mother's wombs.[129] One in every six children in the U.S. suffers from some type of learning or neurobehavioral disorder, ranging from attention-deficit hyperactivity disorder to autism.[130] This amounts to as many as 640,000 children who are harmed each year—an enormous public health issue and a lifelong problem for children and families.

In a parallel process, a collaboration of 38 internationally recognized scientific experts on BPA and other endocrine disruptors published an analysis of the research on BPA which included a consensus statement plus five peer-reviewed articles.[128] Unlike the NTP committee, the international collaboration concluded: "The wide range of adverse effects of low doses of BPA in laboratory animals exposed both during development and in adulthood is a great cause for concern with regard to the potential for similar adverse effects in humans. Recent trends in human diseases relate to adverse effects observed in experimental animals exposed to low doses of BPA."

Among the examples of trends they cited:

- Increase in breast and prostate cancer
- Uro-genital abnormalities in male babies
- Decline in semen quality in men
- Early onset of puberty in girls
- Metabolic disorders including insulin-resistant (type 2) diabetes
- Obesity in children and adults
- Neurobehavioral problems such as ADHD

The next step for NTP is to compile the data from the two reports, draft its own report and solicit public comment. Meanwhile, California may seek a Proposition 65 listing of BPA as a reproductive toxicant.[131]

One other country has taken action on BPA. Norway has advised the World Trade Organization of its intention to prohibit BPA and 17 other substances from consumer goods in that country. This prohibition will include clothing, bags, and toys but will not apply to food products or food packaging.[132] While this legislation applies only to Norway, it could become the new de facto standard for companies exporting to Europe since few companies will vary a product for one small market.

Regulation of the manufacture and use of BPA in the United States may be years away. Meanwhile, consumers can limit exposure to this chemical through the following measures recommended by the Environmental Working Group:

- Minimize the use of plastics, especially plastic wraps and containers, with the recycling label No. 7, which may contain BPA.
- Use glass baby bottles and dishes.
- Discard old, scratched plastic dishes and containers. Do not wash plastic dishes in the dishwasher using strong detergents, which can speed up wear and tear.
- Avoid canned foods and drinks.

TABLE 3 Plastics and Breast Cancer*

Plastic	Breast Cancer Fund Rating	Link to Breast Cancer: Carcinogen Byproduct of Manufacturing[a,b]	Link to Breast Cancer: Hormone Disruptors Can Leach Out[c]	Explanation	Source of Exposure in Consumer Products
#1 PET PETE Polyethylene terephthalate ethylene	OK				Soft drink, juice, water, detergent and cleaning product bottles
#2 HDPE High density polyethylene	OK				Opaque plastic milk and water jugs; bleach, detergent and shampoo bottles; some plastic bags
#3 PVC Polyvinyl chloride	Avoid	X	X	Vinyl chloride and dioxin, both known human carcinogens (NTP and IARC), are formed in manufacturing; dioxin is also a hormone disruptor; hormone disrupting phthalates can leach out of PVC.	Cling wrap; some plastic squeeze bottles; cooking oil, detergent and window cleaner bottles; toys; vinyl shower curtains; wall and floor coverings
#4 LDPE Low density polyethylene	OK				Grocery store bags, most plastic wraps, some bottles
#5 PP Polypropylene	OK				Most reusable food-storage containers; straws; syrup, yogurt and other clouded plastic containers; some baby bottles
#6 PS Polystyrene	Avoid	X		Styrene can leach from polystyrene, is an animal mammary carcinogen, and is possibly carcinogenic to humans (IARC).	Styrofoam food trays, egg cartons, disposable cups and bowls and carryout containers; opaque plastic cutlery
#7 Other Usually Polycarbonate	Avoid		X	Hormone-disrupting bisphenol A can leach from polycarbonate under heat and pressure or as plastic ages.	Many plastic baby bottles, 5-gallon water bottles, "sport" water bottles, metal food can liners, clear plastic "sippy" cups, dental sealants, some clear plastic cutlery

Portions of this table based on "Smart Plastics Guide: Healthier Food Uses of Plastics," Institute for Agriculture and Trade Policy, available at www.iatp.org/foodandhealth.

[a]Rudel RA, Attfield KA, Schifano JN, Brody JG. Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. Cancer. 2007;109(S12):2635-66.

[b]International Agency for Research on Cancer (IARC) carcinogenic risk classification is based on evaluation of potential tumor development at all sites, not only breast/mammary tissue. Categories include: known, probable, possible and others. The National Toxicology Program (NTP), within the National Institute of Environmental Health Sciences of the National Institute of Health, provides carcinogenicity ratings based on scientific evidence in both animals and humans. Categories include: known, reasonably anticipated, and others (Report on Carcinogens, 11th edition; US Department of Health and Human Services, Public Health Service, National Toxicology Program.) Not all chemicals have been rated by IARC or NTP.

[c] To date, neither the NTP nor IARC have classified most endocrine disruptors as carcinogens in humans. List of endocrine disruptors from: Brody JG, Rudel RA. Environmental pollutants and breast cancer. Environ Health Perspect. 2003;111:1007-19.

milk or, at minimum, require labeling of these additives so consumers can make informed purchases. In the absence of federal regulation, state governments should ban these substances or adopt strong labeling guidelines.

Research Required. Exposure studies are needed to measure the presence and levels of synthetic hormones in meat and dairy sold and consumed in the U.S. so the potential for negative health effects can be assessed.

Research that looks at red meat and dairy consumptions and their possible association with breast cancer should consider—and include in the methodology—the presence of synthetic hormones within these products. Without addressing these additives, it is not clear whether the research findings reflect the dietary nutritional composition of the food—e.g., vitamins, fat content and protein—or the presence of synthetic hormones.

Cosmetics and Personal Care Products

Because the U.S. lacks a premarket screening program, shampoo, deodorant, make-up, lotions and other products that consumers use every day contain chemicals linked to cancer, birth defects and other serious health problems. Words like "natural," "safe," and "pure" on labels have no definition in law and no relationship to the hazard inside the packaging. Major loopholes in federal law allow the $50 billion cosmetics industry to put unlimited amounts of chemicals into personal care products with no required testing, no monitoring of health effects and woefully inadequate labeling requirements.

The EU's 27-country, precedent-setting Cosmetics Directive (76/768/EEC) prohibits the sale of personal care products that contain any of the 1,100 carcinogens, mutagens or reproductive toxins (CMRs) classified as toxicants by the directive.[141] The United States restricts only 10 substances and there is no enforcement of those restrictions.[142,143] Taken alone, the chemicals in a single cosmetic product are unlikely to cause harm. But the average American woman uses 12 personal care products a day, resulting in exposure to 126 unique chemicals.[144] The combined exposure from personal care products adds to the personal chemical contamination from other consumer products, food, water, air and soil. As a result, more than 200 chemicals have been detected in people's body fluids and breast milk and in the cord blood of newborns.[145–148] The unregulated use of chemicals in personal care products is one aspect of the larger problem of chemicals in commerce without any functioning government framework to protect public health from harm.

A considerable amount of what consumers put on their skin ends up inside their bodies[149–151]—a huge concern for women of childbearing age. Finally, cosmetics are only one of many sources of daily toxic exposures. For example, the public is exposed to phthalates from many different personal care products, as well as from vinyl shower curtains, vinyl car seats, toys, medical devices and pharmaceuticals.

Federal Policy Recommendations. Federal legislation is needed that requires premarket health and safety testing of all cosmetics and personal care products, provides guidance to the cosmetic and personal care product industry on how to test their products for safety, restricts the use of ingredients that contain any toxic impurities or that may combine with other ingredients to form harmful impurities, and institutes mandatory recalls of cosmetics and personal care products containing ingredients that have not been proven safe through scientific testing and/or do not bear appropriate labels warning consumers that the product ingredients have not been tested for safety.

In addition, such legislation should require labeling of the constituent ingredients of fragrance and any nanomaterials in cosmetics and personal care products. Internet vendors should be required to display a conspicuous list of ingredients in cosmetic products sold on their web sites.

Cosmetic and personal care product manufacturers should be required to test products—especially those used by and on children—for their estrogenic activity. They should also be required to make all existing safety data available to government agencies and consumers. Finally, manufacturers should be required to invest in green chemistry solutions to replace toxic chemicals used in cosmetics and personal care products with safe alternatives.

Information on health hazards associated with specific chemicals used to formulate over 27,000 cosmetics and personal care products can be found by visiting the Environmental Working Group's "Skin Deep" database at www.cosmeticdatabase.org. Information on the Campaign for Safe Cosmetics, a market-based campaign developed to move the cosmetic industry toward safer production and secure stronger government oversight and regulation of the $50 billion cosmetic industry, can be found at www.safecosmetics.org.

State Policy Recommendations. States should require all companies selling cosmetic and personal care products in the state to

- provide certification that their formulations meet the standards of the EU Cosmetics Directive 76/768/EEC and are free of chemicals that are known or strongly suspected of causing cancer, mutation or birth defects.
- submit to their department of health a list of chemicals used in the manufacture of personal care products distributed in the state that authoritative scientific bodies have determined are associated with cancer, endocrine disruption, birth defects, or other health hazards, as well as persistence in the environment or bioaccumulation.
- file with the state department of health a timeline and plan for substituting chemicals of concern with safe alternatives.
- list fully all ingredients on the label, including components of fragrance and other mixtures and nanomaterials; and list fully all ingredients on the company's web site if internet sales of their products to that state are taking place.

TABLE 4 Household Cleaning Products and Human Health Concerns

Chemicals Found in Cleaning Products	Human Health Concern: Carcinogen	Central Nervous System	Reproductive Toxicant	Endocrine Disruptor	Source of Exposure
Diethanolamine		X			Cleaners, degreasers
Diethylene Glycol Monomethyl Ether			X		Floor finish, cleaner and polish
Diethylene Glycol Monoethyl Ether		X	X		Floor finish, tile and grout cleaner, microwave oven cleaner
Dibutyl Phthalate		X		X	Floor finish, floor shine and hardener
Nonylphenol Ethoxylate				X	Cleaners, degreasers, foaming cleaner, air freshener; spot and stain pretreater; metal polish
Octylphenol Ethoxylate				X	Cleaners, degreasers, surface deodorizer
n-Methyl Pyrolidinone			X		Floor finish, stripper, floor cleaner
Nitrilotriacetic Acid	X[a]				Carpet care products
Coconut Oil Diethanolamide (Cocamide DEA)		X			Cleaners, degreasers, floor cleaner; metal cleaner and polish
Coconut Oil Diethanolamine		X			Cleaners, degreasers
Triethanolamine		X			Cleaners, degreasers, bleach, floor bleach, floor cleaner, wood cleaner
Tetrachloroethylene	X[a,b]	X			Spray polish, spot remover

Adapted from "Carcinogens and Reproductive Toxins found in Cleaning Products." [Internet]. Western Sustainability and Pollution Prevention Network. Available from: http://wsppn.org/Janitorial/factsheets.cfm.
[a]Classified as a "reasonably anticipated" carcinogen by NTP.
[b]Classified as a "probable carcinogen" by IARC.

Research Required. Currently only 11% of the ingredients used in cosmetic products have been tested for safety. Research is needed to increase this number to 100%. Green chemistry solutions are needed to replace toxic chemicals used in cosmetics with safe alternatives. Finally, personal care products—especially those used by and on children—should be tested for their estrogenic activity.

Occupational Exposures

Although women make up nearly half the paid workforce in the United States, relatively few studies have been conducted to identify occupational exposures associated with breast cancer. Most occupational research on women reports risk by job type or title, rather than by specific exposures, making the findings difficult to interpret. Many women in the U.S. have two places of work: the home and the paid workplace. Each place has its unique set of exposures to chemicals and non-ionizing radiation, further complicating exposure assessment.

The evidence that does exist shows increased risk of breast cancer among two broad categories:

1. Those who work with toxic chemicals, such as chemists, dental hygienists, paper mill workers and microelectronics workers.[152–155]
2. Professionals in higher socioeconomic groups such as school teachers, social workers, physicians and journalists.[152–155]

There are other occupational groups with increased risk of breast cancer whose work involves chronic exposure to specific chemicals, higher than average levels of non-ionizing radiation, and in some cases, ionizing radiation as well.[152,156]

The U.S. Occupational Health and Safety Administration (OSHA) regulatory framework has reduced—but not eliminated—workers' exposures to industrial carcinogens. OSHA requires all chemical manufacturers and importers to develop material safety data sheets (MSDS) on each product they identify as hazardous. MSDS list acute and chronic health effects that might occur as a result of exposure. However, some studies of workers confirm that exposure to certain industrial agents, including ionizing radiation, asbestos, and benzene, can increase cancer risk even when the exposure level is at or below current regulatory limits.[156–159]

Federal Policy Recommendations. Federal occupational health policy should require that:

- workers be fully informed of the risks involved in performing their jobs, including chronic exposures

to chemicals and radiation linked to breast cancer and other adverse health effects; and
- workers receive maximum protection (personal protective equipment and culturally appropriate training in its use as well as environmental controls) to reduce or eliminate occupational exposures that can contribute to breast cancer.

State Policy Recommendations. States should fund community-based biomonitoring studies that include occupational groups as one of the early communities of focus. Understanding—and more accurately measuring—the exposures and resulting health outcomes of workers in occupations with increased risk of breast cancer is essential to protecting workers' health and could contribute significantly to our broader understanding of environmental exposures and breast cancer.

Research Required. Methodologies need to reflect real-world exposures. For example, chronic low-dose exposures to mixtures of chemicals must be considered as well as high-dose acute exposures. For women who have two workplaces, exposures at home and in the paid workplace to chemicals and non-ionizing radiation, for example, must be considered as well as their potential interaction with other risk factors.

Occupational exposure assessment needs to consider nontraditional occupations and work hours. Occupational health scientists need new methodologies to account for the fact that women may move in and out of jobs throughout their lives and work long hours one day and short shifts another.

Occupations Associated with Increased Risk of Breast Cancer

Aircraft and automotive workers[161,162]
Barbers and hairdressers[162,163]
Chemists and chemical industry workers[162,163]
Clinical laboratory technologists[162,164]
Computer and peripheral equipment operators[154,162,165]
Crop farmers and fruit and vegetable packers[162]
Dental hygienists[163]
Dentists[163]
Dry cleaning workers [162,163]
Flight attendants[153]
Food, clothing and transportation workers[162,163]
Furniture and woodworking industry workers[166]
Homemakers[167]
Journalists[167]
Librarians[154,164,165]
Nurses, particularly chemotherapy nurses[162,163,168]
Paper mill workers[162]
Physicians[153,162,163]
Publishing and printing industry workers[162]
Meat wrappers and cutters[163]
Microelectronics workers[169]
Radiologic technologists[170]
Rubber and plastics industry workers[163]
Social workers[165]
Telephone workers[163]

Nanotechnology

Nanotechnology has been called the "next industrial revolution." It involves the manipulation of materials and the creation of tiny structures and systems that exist at the scale of atoms and molecules. (To put things in perspective, a nanometer is one-billionth of a meter—to cover the width of a human hair you would have to line up 80,000 nanometers.) This manipulation changes the physical properties of materials. Opaque materials can become transparent, for example, and chemically stable materials can be made reactive.

These physical changes may lead to medical advances, more durable products, new ways to clean up pollution, increased fuel cell efficiency and, market research suggests, perhaps billions of dollars in profits.

Hundreds of consumer products, including cosmetics and personal care products, stain-resistant clothing, food storage containers and computers, now include nanomaterials, according to one academic report. A 2006 report by Friends of the Earth found that at least 116 personal care products containing nanoingredients—defined as smaller than 100 nanometers—are on the market.[160]

Scientists at Rice University's Center for Biological and Environmental Nanotechnology are using nanoparticles in new cancer detection and treatment, allowing them to target and destroy only cancerous cells. As news of nanotechnology's promise emerges, however, there are also concerns about health and environmental risks.

Nanomaterials can be extremely toxic. Due to their size and structure, they can be inhaled, ingested and absorbed into the body, enter the blood stream, penetrate cells and even interfere with critical DNA processes. According to the Natural Resources Defense Council, nanoparticles have caused inflammation and precancerous lesions, and have damaged brain cells in animal studies.[171]

Government is struggling to catch up with this new science. At the same time, consumers have a right to know if the cosmetics and personal care products they use contain untested nanomaterial ingredients. Manufacturers and retailers should take a precautionary approach to the use or sale of products with nanosized particles until these materials have been fully tested for their impact on the public, workers and environmental health.

Federal Policy Recommendations. To protect workers, consumers and the environment from the known and unknown consequences of nanomaterials, the FDA should require manufacturers to conduct comprehensive premarket testing of products formulated with

TABLE 5 Cosmetics and Breast Cancer

Chemical	Carcinogenic: Animal Mammary Gland Carcinogen[a]	Carcinogenic: Human Carcinogenic Risk Classification[b]	Disrupt Hormones: Disrupts Endocrine System/ Estrogenic[c]	Source of Exposure in Cosmetics
Benzene	X	IARC Known; NTP Known		Nail polish and nail polish remover
Bisphenol A			X	Cosmetic containers/packaging
1,3-Butadiene	X	IARC Probable; NTP Known		Rubber sponges for applying cosmetics
1,4-Dioxane*	X	IARC Possible; NTP Reasonably Anticipated		Petroleum-derived contaminant formed in manufacture of shampoos, body wash, children's bath products and other sudsing cosmetics
Ethylene Oxide	X	IARC Known; NTP Known		Fragrance
Musks, synthetic (xylene, ketone, ambrette, moskene, tibetene)			X	Fragrance
N-Nitrosamines* like n-nitrosodi-n-butylamine		IARC Possible; NTP Reasonably Anticipated		Chemical reactions occur over time in the product to produce nitrosamines, usually found in creams, lotions, shampoos and conditioners.
Nonylphenol			X	Lotions and a wide range of other products
Parabens (butyl-, ethyl-, methyl-, propyl-)			X	Antifungal agent, preservative and antimicrobial used in creams, lotions, ointments and other cosmetics
Petrolatum (polycyclic aromatic hydrocarbons (PAHs)* are common contaminants)	X	IARC Possible; NTP Reasonably Anticipated	X	PAHs are petrolatum contaminants; found in pretoleum jelly, lipsticks, baby lotions and oils; found in 1 of every 14 personal care products.
Phthalates (bi-n-butyl- (DBP), di (2-ethylhexyl)- (DEHP))			X	Nail polish, fragrance
Placental extract (progesterone main constituent)	X	NTP Reasonably Anticipated	X	Hair conditioners, shampoos and other grooming aids, particularly marketed to women of color
1,2-Propylene Oxide	X	IARC Possible; NTP Reasonably Anticipated		Fragrance
Titanium Dioxide (dioxin is a by-product of manufacturing and a contaminant)		IARC Known; NTP Known	X	Sunscreens and mineral make-up; use of titanium dioxide nanoparticles a possible threat to human health
Triclosan (dioxin is a by-product of manufacturing and a contaminant)	X	IARC Known; NTP Known	X	Antibacterial used in soaps, toothpate, mouthwash and other personal care products
Urethane (ethyl carbamate)		IARC Possible; NTP Reasonably Anticipated		Hair care products (mousses, gels, sprays), sunscreens, nail polish, mascara, foundation

*These chemicals do not appear on product labels because they are contaminants and formed in manufacturing through chemical reactions in the product.

[a]Rudel RA, Attfield KA, Schifano JN, Brody JG. Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. Cancer. 2007;109(S12):2635-66.

[b]International Agency for Research on Cancer (IARC) carcinogenic risk classification is based on evaluation of potential tumor development at all sites, not only breast/mammary tissue. Categories include: known, probable, possible and others. The National Toxicology Program (NTP), within the National Institute of Environmental Health Sciences of the National Institutes of Health, provides carcinogenicity ratings based on scientific evidence in both animals and humans. Categories include: known, reasonably anticipated, and others (Report on Carcinogens, 11th edition; US Department of Health and Human Services, Public Health Service, National Toxicology Program.) Not all chemicals have been rated by IARC or NTP.

[c]To date, neither the NTP nor IARC have classified most endocrine disruptors as carcinogens in humans. List of endocrine disruptors from: Brody JG, Rudel RA. Environmental pollutants and breast cancer. Environ Health Perspect. 2003;111:1007-19.

nanomaterial ingredients for their impact on public health, worker health and environmental health and prohibit the unsafe or untested use or sale of nanomaterial ingredients in consumer products. In addition, the FDA should create a publicly accessible database on the environmental, human health, and worker safety impacts of nanomaterial ingredients and require manufacturers to label all products they manufacture or sell that contain nanomaterial ingredients.

Research Required. Research on the health effects of nanomaterials should be conducted in unison with the research underway exploring its possible applications.

TOOLS AND RESEARCH NEEDED TO STRENGTHEN THE EVIDENCE AND REDUCE EXPOSURES

Statistics on Breast Cancer in All Populations

We need better statistics to help identify trends in breast cancer incidence and mortality, evaluate current programs, design new prevention and treatment plans, and measure our progress in eradicating the disease. There is general agreement that the incidence of breast cancer in the United States has risen in past decades; however, precise statistics on the actual incidence of breast cancer and the rate of change in various populations is difficult to establish due to our slow, fragmented and under-funded state cancer registries system and the absence of a single national cancer tracking system.

Both the National Cancer Institute (NCI) and the Centers for Disease Control and Prevention (CDC) separately fund cancer registries.[172,173] National estimates of incidence and mortality are projected from NCI's Surveillance, Epidemiology and End Results Program (SEER) data. According to the SEER web site, this population is "comparable to the general U.S. population with regard to measures of poverty and education" but "somewhat more urban and has a higher proportion of foreign-born persons."[174] SEER sites are concentrated on coastal cities, omitting much of the South and Midwest regions.

Cancer tracking has not kept pace with the increasing diversity of the U.S. population. In Asian Pacific Islanders (API), for example, collecting and reporting aggregate breast cancer rates tend to obscure those API groups with high incidence and/or mortality rates, perpetuating the myth that breast cancer incidence and mortality are low among all API women.[175,176] Disaggregating the data on California API women showed substantial increases in breast cancer incidence among Japanese, South Asian, Chinese and Korean women.[177]

Most research studies only look at women with invasive breast cancer. However, between 1980 and 2001, with increased use of mammography, diagnoses of ductal carcinoma in situ (DCIS) have increased sevenfold. Mainstream cancer organizations such as the American Cancer Society do not always include in situ breast cancer incidence rates in their breast cancer models and statistics. This presents a skewed picture of breast cancer in the U.S., especially as DCIS is usually treated the same as invasive breast cancer, with surgery and possibly radiation and/or chemotherapy.

Finally, under our current system, cancer reporting is a slow process subject to error due to delays. The 2003 cancer incidence and mortality statistics were reported in 2007.[178] According to the NCI, it takes "four to 16 years for 99 percent of the cancer cases to be reported."[179] There is much that needs to be done to mend our fragmented national and state breast cancer registries. Reliable statistics are essential to measuring progress toward our goal of eradicating breast cancer.

Federal and State Policy Recommendations. National standards should be created to strengthen states' public accountability and enforce their performance standards in cancer tracking. If the North American Association of Central Cancer Registries (NAACCR) and the CDC's National Program of Cancer Registries (NPCR) fail to provide leadership on these issues, Congress should mandate that NPCR set these standards for all registries receiving federal support.

Congress should direct the Institute of Medicine to conduct a study on the federal management of cancer registries and make recommendations that will guide development of a single cancer tracking system in the U.S.

Finally, state and federal registries should be adequately funded to achieve steady improvement in data quality and timeliness.

Biomonitoring

Biomonitoring, short for "biological monitoring," involves testing biological samples—such as urine or blood—for the presence of industrial compounds, pollutants and other chemicals in a person's body. Biomonitoring can generate data crucial to better understanding chemical exposures and their relationship to increasing rates of breast cancer, asthma, birth defects, autism and other diseases. Biomonitoring can also help identify communities disproportionately affected by chemical exposures, support efforts to improve environmental and health regulations, and help set priorities for legislative and regulatory action to protect public health.

Nationally, the Centers for Disease Control and Prevention (CDC) supports state and local public health information campaigns about blood lead levels in children.[180] The National Health and Nutrition Examination Survey (NHANES), an ongoing population-based survey carried out by the National Center for Health Statistics, also monitors chemical levels in blood and urine, which are published every two years in the

CDC's National Report on Human Exposure to Environmental Chemicals.[181] The most recent report, released in 2005, measured and analyzed 148 chemicals in the blood and urine of almost 8,000 individuals throughout the United States.[182] Aggregated nationally, the data does not tell states and local communities about their specific chemical body burdens. A third NHANES report is expected to be released in 2008.

Federal Policy Recommendations. The CDC should expand its biomonitoring grants program to support states that have existing programs with the goal of augmenting these programs in Fiscal Year 2009. For Fiscal Year 2010 and beyond, federal funds should be appropriated to support the creation of new state biomonitoring programs. Federal funds could be used to help states develop methods for identifying sources and routes of exposure for biomonitored chemicals; expand laboratory capacity; conduct subpopulation studies; conduct representative analyses of routinely collected blood, cord blood and other biospecimens; develop protocols for conducting biomonitoring of sensitive subpopulations such as children; and support biomonitoring field operations such as participant enrollment, sample collection, data analysis, report generation and results communications. This work should be coordinated with EPA's efforts to identify and monitor ambient air and other sources of toxic chemical releases.

Federal funding should support the creation of regional biomonitoring labs to share costs, resources and the development of analytical testing methods.

State Policy Recommendations. States should fund community-based studies that couple chemical monitoring data and biomonitoring of individuals within a geographic area, occupation, or disproportionately affected community (e.g., high disease rates and fenceline communities). Biomonitoring can then help assess effectiveness of chemical exposure reduction efforts within disproportionately affected communities.

Biomonitoring studies at the state level should include occupational groups. Understanding—and more accurately and directly measuring—the exposures and resulting health outcomes of workers in occupations with increased risk of breast cancer is essential to protecting workers' health and could contribute significantly to our broader understanding of environmental exposures and breast cancer.

To better understand early-life exposures and how they contribute to later-life disease, states should fund biomonitoring studies that examine cord blood, placenta, meconium, and other appropriate biospecimens.

Health Tracking

With funding from Congress in 2002, the CDC created the National Environmental Public Health Tracking Program.[183] The program defines health tracking as "the ongoing collection, integration, analysis, and interpretation of data about . . . environmental hazards, exposure to environmental hazards, and health effects potentially related to exposure to environmental hazards." Once analyzed, this information can be used by local, state and federal agencies to better prevent disease and protect health. Health tracking programs integrate multiple databases such as biomonitoring data, chemical release data, geographic distribution patterns of exposure and health outcome data.

The National Environmental Public Health Tracking Program has given grants to states to build their health tracking programs.[184] The CDC awarded planning grants to 27 states and implementation grants to 16 states.[184] Prior to these investments, however, most states had no tracking system to assess many of the exposures and health conditions that may be related to environmental hazards. Because health databases, registries and monitoring systems are not linked, and because some hazards and chronic diseases are not tracked at all, their utility is currently limited.[185] For example, for breast cancer, it is difficult to determine if there is an unusually high rate of the disease in a certain community or population. It is also difficult to determine which environmental hazards communities are exposed to and how they compare to other communities. Making the connections between environmental exposures and disease is an enormous challenge without comprehensive health tracking systems.

Federal Policy Recommendations. Congress should appropriate funds to build state infrastructure, which could include state laboratories capable of performing biomonitoring of human samples for an array of contaminants; initiating state Health and Nutrition Examination Surveys to provide data on a range of health indicators and environmental exposures; and State Human Exposure Assessment Surveys (HEXAS) to identify exposures in the indoor environment, where many pollutants concentrate.

The CDC should be directed to make funding available to state environmental health tracking programs to develop replicable models for disease, hazard and exposure data-sharing at the local, state and national levels that incorporate data confidentiality protections.

Advocates should continue to push for enactment of the Coordinated Environmental Public Health Network Act of 2007 (S 2082/HR 3643), introduced by House Speaker Nancy Pelosi and Senator Hillary Clinton, which expands and strengthens the nationwide health tracking network.[186]

The CDC should be further directed by Congress or through an executive order to include nongovernmental organizations representing health-affected constituencies and environmental health and environmental justice advocates in their advisory groups.

State Policy Recommendations. With CDC support, states should strengthen the coordination between health and environment agencies of health tracking programs.

Invest in New Science

Research is needed to address key emergent themes on environmental causes of breast cancer, including low dose exposures, multiple exposures, timing of exposures and later-life breast cancer, and early puberty and later-life breast cancer (see companion piece in this issue[18]). Federal and state policy makers can help advance needed research by providing funding and support.

Federal Policy Recommendations. The federal government should support large studies that follow girls from conception to adulthood, such as the National Children's Study (NCS) mandated by Congress in 2000, which will follow 100,000 children from conception to adulthood.[187] Securing congressional funding over the next five years of the NCS will be critical because during this time recruitment will be in full swing and prenatal and early life baseline measurements will take place.

In 2007–08 there were two active federal-level efforts to investigate the relationship between the environment and breast cancer: the NIEHS-funded Breast Cancer and Environment Research Centers (BCERC) exploring early puberty and connections to later-life breast cancer,[188] and the Breast Cancer and Environmental Research Act (BCERA), federal legislation which President Bush signed into law in October 2008. BCERA, as originally introduced, would have set up Centers of Excellence focused on researching environmental links to breast cancer. However, the bill was significantly amended prior to its adoption, and no longer mandates specific research on environmental causes of breast cancer. Instead, it sets up an Interagency Environmental Research Coordinating Committee to make recommendations and solicit proposals for breast cancer research more broadly.[189] Even when combined, both of these efforts represent a small portion of the federal funding needed to strengthen our understanding of the environmental links to breast cancer.

The EPA's Endocrine Disruptor Screening Program, mandated by Congress, is eight years behind schedule and not one chemical has been screened to date.[190,191] Advocates should keep the pressure on Congress and the EPA to ensure this important work is completed in a timely and fully transparent manner.

State Policy Recommendations. States should use the California Breast Cancer Research Program as a model of innovative state research programs. The CBCRP is a research program created by a ballot initiative and funded by a cigarette tax that created a special $18 million statewide initiative focused on the effects of the environment on breast cancer.[192] The program also stresses the applicability of research to policy solutions and emphasizes stakeholder involvement so that advocates, clinicians, researchers, policy makers and the general public can help direct research funding.

CONCLUSIONS

A substantial body of scientific evidence indicates that exposures to common chemicals and radiation, alone and in combination, are contributing to the increases in breast cancer incidence observed over the past several decades. In the first article in this two-part series, we document this evidence. Based on the evidence, we conclude that at this time the United States has neither the public health regulations in place nor the requisite research underway to eradicate the environmental causes of breast cancer. It is therefore imperative that we use this evidence to inform regulatory change and investment in key areas of research. This article is written with the goal of building bridges between scientists and the many important advocacy communities, including breast cancer advocates as well as members of the women's health, environmental justice and environmental health movements. By working together for these changes in research and legislation, we will decrease human exposures to toxic substances implicated in high rates of breast cancer, thereby decreasing the incidence of this disease.

References

1. Cutler SJ, Connelly, RR. Mammary cancer trends. Cancer 1969;23:767-71.
2. Jatoi I, Anderson WF, Rao SR, et al. Breast cancer trends among black and white women in the United States. J Clin Oncol. 2005;23:7836-41.
3. Howe HL, Wingo PA, Thun MJ, et al. Annual report to the nation on the status of cancer (1973-1998), featuring cancers with recent increasing trends. J Natl Cancer Inst. 2001;93:824-842.
4. Ries LAG, Melbert D, Krapcho M, et al. (eds). SEER Cancer statistics review, 1975-2004. [Internet]. Bethesda, MD: National Cancer Institute; 2007. Available from: http://seer.cancer.gov/csr/1975_2004/, based on November 2006 SEER data submission, posted to the SEER web site, 2007.
5. Hayat MJ, Howlader N, Reichman ME, et al.. Cancer statistics, trends and multiple primary cancer analyses from the Surveillance, Epidemiology, and End Result (SEER) Program. Oncologist. 2007;12:20-37.
6. Ravdin PM, Cronin KA, Howlader N, et al. The decrease in incidence in breast cancer incidence in 2003 in the United States. N Engl J Med. 2007;356:1670-4.
7. Glass AG, Lacey JV, Carreon JD, et al. Breast cancer incidence, 1980–2006: Combined roles of menopausal hormone therapy, screening mammography, and estrogen receptor status. J Natl Cancer Inst. 2007;99:1152-61.
8. Centers for Disease Control and Prevention. Decline in breast cancer incidence: United States, 1999–2003. Morbidity and Mortality Weekly Report. 2007;56:549-53.
9. Jemal A, Siegel E, Ward E, et al. Cancer statistics: 2006. CA: Cancer J Clin. 2006;56:106-30.
10. U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics. Overview: Office of Pollution Prevention and Toxics Programs [Internet]. 2007 Oct 8. Available from: http://www.epa.gov/oppt/pubs/oppt101c2.pdf
11. U.S. Environmental Protection Agency Office of Pollution Prevention and Toxics. Chemical hazard data availability study:

What do we really know about the safety of high production volume chemicals? [Internet]. 2008. Available from: http://www.epa.gov/HPV/pubs/general/hazchem.pdf
12. Rudel RA, Camann DE, Spengler JD, et al. Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in air and dust. Environ Sci Technol. 2003;37:4543-53.
13. Siddiqui MK, Anand M, Mehrotra PK, et al. Biomonitoring of organochlorines in women with benign and malignant breast disease. Environ Res. 2004;98:250-7.
14. Nickerson K. Environmental contaminants in breast milk. J Midwifery Womens Health. 2006;51:26-34.
15. Rudel RA, Attfield KA, Schifano JN, et al. Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. Cancer. 2007;109(S12):2635-66.
16. Birnbaum LS, Fenton SE. Cancer and developmental exposure to endocrine disruptors. Environ Health Persp. 2003;111:389-94.
17. Fenton SE. Endocrine-disrupting compounds and mammary gland development: early exposure and later life consequences. Endocrinology. 2006;147:S18-S24.
18. Gray J, Evans N, Taylor B, et al. State of the evidence: The connection between breast cancer and the environment. 2008;Int J Occup Environ Health. 15:
19. Lux MP, Fasching PA, Beckmann MW. Hereditary breast and ovarian cancer: review and future perspectives. J Mol Med. 2006;84:16-28.
20. Hankinson SE, Colditz GA, Willett WC. Towards an integrated model for breast cancer etiology: the lifelong interplay of genes, lifestyle, and hormones. Breast Cancer Res. 2004;6:213-18.
21. Michels KB, Mohllajee AP, Roset-Bahmanyar ER, et al. Diet and breast cancer. Cancer. 2007;109(S12):2712-2749.
22. Zheng SM, Lee I-M, Manson JE, et al. Alcohol consumption and breast cancer risk in the Women's Health Study. Am J Epidemiol. 2007;165:667-76.
23. Visvanathan K, Crum RM, Strickland PT, et al. Alcohol dehydrogenase genetic polymorphisms, low-to-moderate alcohol consumption, and risk of breast cancer. Alcohol Clin Exp Res. 2007;31:467-76.
24. Monninkhof EM, Elias SG, Vlems FA, et al. Physical activity and breast cancer: a systematic review. Epidemiology. 2007;18:137-57.
25. Kruk J, Aboul-Enein HY. Environmental exposure, and other behavioral risk factors in breast cancer. Curr Cancer Ther Rev. 2006;2:3-21.
26. Russo J, Hu YF, Silva IDCG, et al. Cancer risk related to mammary gland structure and development. Microsc Res Tech. 2001;52:204-23.
27. National Toxicology Program (2005). Eleventh Report on Carcinogens. National Institute of Environmental Health Sciences. National Institutes of Health.
28. National Research Council (2005). Biologic effects of ionizing radiation VII: Health risks from exposure to low levels of ionizing radiation. National Academy of Science, Washington DC
29. Calaf GM, Hei TK. Establishment of a radiation- and estrogen-induced breast cancer model. Carcinogenesis 2000;21:769-776.
30. American Society of Radiologic Technologists. Does your state regulate medical imaging and therapy technologists? [Internet]. 2007 Nov 15. Available from https://www.asrt.org/media/pdf/govrel/doesyourstateregulate.pdf
31. NIEHS Working Group Report. Assessment of health effects from exposure to power-line frequency electric and magnetic fields. Research Park Triangle:National Institute of Environmental Health Sciences of the National Institutes of Health. 1998.
32. Ahlbom A, Cardis E, Green A, et al. Review of the epidemiological literature on EMF and health. Environ Health Persp. 2001;109 (Suppl 6):911-33.
33. German Federal Office for Radiation Protection. [Internet]. Berlin, Germany. 2007 Sept. Available from: http://www.bfs.de/en/bfs.
34. European Environmental Agency. Radiation risks from everyday devices assessed [Internet]. 2007 Nov 15. Available from: www.eea.europa.eu/highlights/radiation-risk-from-everyday-devices-assessed
35. Carpenter D, Sage C, Davanipour Z, et al. The BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF). [Internet]. 2007 August. Available from: http://www.bioinitiative.org/report/index.htm.
36. Federal Communications Commission. Code of Federal Regulations. [Internet]. 2007 October. Available from: http://wireless.fcc.gov/index.htm?job=rules_and_regulations.
37. Electromagnetic Radiation Policy Institute. Frequently asked questions [Internet]. 2007 Nov 15. Available from: www.emrpolicy.org/faq/index.htm
38. U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics. Overview: Office of Pollution Prevention and Toxics Programs [Internet]. 2007 Oct 8. Available from: www.epa.gov/oppt/pubs/oppt101c2.pdf , October 8, 2007.
39. Bennett M, Davis BJ. The identification of mammary carcinogens in rodent bioassays. Environ Mol Mut. 2002;39(2-3):150-7.
40. U.S. Environmental Protection Agency. Summary of the Toxic Substances Control Act. [Internet] Available from: http://www.epa.gov/lawsregs/laws/tsca.html
41. Wilson MP, Chia DA, Ehlers BC. Green chemistry in California: a framework for leadership in chemicals policy and innovation. 2006.Berkeley: California Policy Research Center, University of California.
42. National Academy of Sciences. Commission on Life Sciences. Toxicology Testing: Strategies to Determine Needs and Priorities. 1984. Washington, D.C.: National Academy of Sciences Press.
43. U.S. General Accounting Office. Toxic Substances Control Act: Legislative Changes Could Make the Act More Effective (GAO/RCED-94-103) [Internet]. Washington, D.C.: U.S. Government Printing Office (1994). Available from: http://archive.gao.gov/t2pbat2/152799.pdf)
44. U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics. Chemical Hazard Data Availability Study: What Do We Really Know About the Safety of High Production Volume Chemicals? [Internet]]Washington, D.C.: Environmental Protection Agency (1998). Available at: http://www.epa.gov/hpv/pubs/general/hazchem.pdf
45. 110th Congress of the United States of America. S3040: Kids' Safe Chemicals Act of 2008. [Internet]. Available from: http://www.govtrack.us/congress/bill.xpd?bill=s110-3040
46. 110th Congress of the United States of America. HR.4040: Consumer Product Safety Improvement Act. [Internet] Available from: http://thomas.loc.gov/cgi-bin/query/z?c110:H.R.4040
47. California Environmental ProtectionAgency Office of Environmental Health Hazard Assessment (OEHHA). The Safe Drinking Water and Toxic Enforcement Act of 1986. [Internet]. Available from: http://www.oehha.ca.gov/prop65/law/P65law72003.html.
48. Safer States. [Internet]. Available from: http://saferstates.com/
49. Thorpe B, Rossi M, Easthope T, et al. . Louisville Charter for Safer Chemicals: A platform for creating a safe and healthy environment through innovation. [Internet]. Available from: http://www.louisvillecharter.org/home.shtml
50. Wingspread Statement on the Precautionary Principle. [Internet]. Available from: http://www.who.int/ifcs/documents/forums/forum5/precaution/wingspread/en/index.html
51. U.S. Environmental Protection Agency. 1996 Food Quality Protection Act: Implementation Plan. [Internet]. March 1997, Washington DC. Available from: http://www.epa.gov/pesticides/regulating/laws/fqpa/fqpa_implementation.htm.
52. Brody JG, Moysich KB, Humblet O, Attfield KR, Beehler GP, Rudel RA. Environmental pollutants and breast cancer: epidemiologic studies. Cancer 2007;109(S12):2667-711.
53. Labreche, FP, Goldberg, MS. Exposure to organic solvents and breast cancer in women: a hypothesis. Am J Ind Med. 1997; 32(1):1-14.
54. Warner MB, Eskenazi B, Mocarelli P, et al. Serum dioxin concentrations and breast cancer risk in the Seveso Women's Health Study. Environ Health Persp. 2002;110:625-8.
55. Betts KS. Secondhand Suspicions: Breast Cancer and Passive Smoking. Environ Health Persp. 2007;115(3):A136-143
56. State of California Air Resources Board. Appendix III: Proposed identification of Environmental Tobacco Smoke as a Toxic Air Contaminant. [Internet]. 2005 June. p. 7-119. California Environmental Protection Agency. Office of Environmental Health Hazard Assessment. Available from: ftp://ftp.arb.ca.gov/carbis/regact/ets2006/app3part%20b.pdf

57. American Non-smokers Rights Foundation. Overview list—how many smokefree laws? [Internet]. 2007 Nov 15. Available from: www.no-smoke.org/pdf/mediaordlist.pdf
58. State of California. Air Resources Board. Risk Reduction Plan to Reduce Particulate Matter Emissions from Diesel-Fueled Engines and Vehicles. [Internet]. California Environmental Protection Agency. Stationary Source Division. Mobile Source Control Division. Available from: http://www.arb.ca.gov/diesel/documents/rrpFinal.pdf
59. American Lung Association. [Internet]. Available from: http://www.lungusa.org/site/c.dvLUK9O0E/b.33691/
60. Environmental Defense Fund. [Internet]. Available from: http://www.edf.org/page.cfm?tagID=97
61. Natural Resources Defense Council. [Internet]. Available from: http://www.nrdc.org/air/default.asp
62. US Environmental Protection Agency. Six Common Air Pollutants. [Internet]. Available from: http://www.epa.gov/air/urbanair/
63. Alexander BH, Mandel JS, Baker BA, et al. Biomonitoring of 2,4-dichlorophenoxyaceetic acid exposure and dose in farm families. Environ Health Persp. 2007;115:370-6.
64. Cohn BA, Wolff MA, Cirillo PM, et al. DDT and breast cancer in young women: new data on the significance of age at exposure. Environ Health Persp. 2007;115:1406-14.
65. Fenton SE. Endocrine-disrupting compounds and mammary gland development: early exposure and later life consequences. Endocrinology.2006;147(Suppl):S18-S24.
66. Raynor JL, Enoch RR, Fenton SE. Adverse effects of prenatal exposure to atrazine during a critical period of mammary gland growth. Toxicol Sci. 2005;87:255-66.
67. US Environmental Protection Agency. Endocrine Disruptor Screening Program (EDSP). [Internet]. Available from: http://www.epa.gov/endo/.
68. Canada News Wire. Canadian Cancer Society Applauds Pesticide Ban. [Internet]. 2008 November. Available from: http://www.newswire.ca/en/releases/archive/November2008/13/c8287.html.
69. Éditeur officiel du Québec. Pesticides Management Code. [Internet]. Available from: http://www2.publicationsduquebec.gouv.qc.ca/dynamicSearch/telecharge.php?type=3&file=/P_9_3/P9_3R0_01_A.htm
70. San Francisco Administrative Code, Chapter 39 San Francisco Integrated Pest Management Program. [Internet]. Available from: http://www.sfgov.org/site/uploadedfiles/bdsupvrs/ordinances00/o0002-00.pdf
71. Integrated Pest Management Program Report Reduced Risk Pesticide List 2000, San Francisco Integrated Pest Management Program. [Internet]. Available from: http://www.ci.sf.ca.us/ipm/list2000/coverhtm#list2000.
72. Oakland City Council. Resolution adopting integrated pest management policies for the City of Oakland. [Internet]. 1997 December. Available from: http://www.oaklandpw.com/AssetFactory.aspx?did=2001
73. European Commission. Commission Decision of 10 March 2004 concerning the non-inclusion of atrazine in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing this active substance, 2004/248/EC. Off J Eur Union 2004;L78:53-5.
74. US Environmental Protection Agency. Decision Documents for Atrazine. [Internet]. 2006 April. Available from: http://www.epa.gov/oppsrrd1/reregistration/REDs/atrazine_combined_docs.pdf.
75. Cooper RL, Stoker TE, Tyrey L et al. Atrazine disrupts the hypothalamic control of pituitary-ovarian function. Toxicol Sci. 2000;53:297-307.
76. O'Connor JC, Plowchalk DR, Van Pelt CS, et al. Role of prolactin in chloro-S-triazine rat mammary tumorigenesis. Drug Chem Toxicol. 2000;23:575-601.
77. Sanderson JT, Letcher RJ, Heneweer M, et al.. Effects of chloro-S-triazine herbicides and metabolites on aromatase activity in various human cell lines and on vitellogenin production in male carp hepatocytes. Environ Health Persp. 2001;109:1027-31
78. Fan WQ, Yanase T, Morinaga H, et al. Atrazine-induced aromatase expression in SF-1 dependent: implications for endocrine disruption in wildlife and reproductive cancers in humans. Environ Health Rep. 2007;115:720-7.
79. Nabholtz JM. Aromatase inhibitors in the management of early breast cancer. EurJournal of Surg Oncol. 2008;34(11):1199-207.
80. Cepa M, Correia-da-Silva G, da Silva EJ, et al. New steroidal aromatase inhibitors: suppression of estrogen-dependent breast cancer cell proliferation and induction of cell death. BMC Cell Biology. 2008;9:41.
81. Hayes TB, Stuart AA, Mendoza M, et al. Characterization of atrazine-induced gonadal malformations in African clawed frogs (Xenopus laevis) and comparisons with effects of an androgen antagonist (cyproterone acetate) and exogenous estrogen (17b-estradiol): Support for the demasculinaza-tion/feminization hypothesis. Environ Health Persp. 2006:114(S1):134-141.
82. U.S. Securities & Exchange Commission. Form 20-F 2000: Novartis, innovative medicines—improved lives. As filed with the Securities and Exchange Commission on April 11, 2001 [Internet]. 2007 Aug 10. Available from: www.novartis.com/downloads/investors/Novartis-20F-2000.pdf
83. Gitlitz J, Franklin P. Water, Water Everywhere: The Growth of Non-Carbonated Beverages in the United States. 2007: Container Recycling Institute. Available at: http://www.container-recycling.org/assets/pdfs/reports/2007-waterwater.pdf.
84. Moore CJ. Synthetic polymers in the marine environment: A rapidly increasing long-term threat. Environ Res 2008:108(2):131-139.
85. Institute for Agriculture and Trade Policy. Smart plastics guide [Internet]. 2007 Oct 15. Available from: http://www.healthobservatory.org/library.cfm?refID=77083
86. Maffini MV, Rubin BS, Sonnenschein C, et al. Endocrine disruptors and reproductive health: the case of bisphenol-A. Mol Cell Endocrinol. 2006;254-255:179-86.
87. Markey CM, Luque EH, Munoz-de-Toro MM, et al. In utero exposure to bisphenol A alters the development and tissue organization of the mouse mammary gland. Biol Reprod. 2001;65:1215-23.
88. Wadia PR, Vandenberg LN, Schaeberle CM, et al. Perinatal bisphenol A exposure increases estrogen sensitivity of the mammary gland in diverse mouse species. Environ Health Persp. 2007;115:80-6.
89. Swann SH, Main KM, Liu F, et al.(2005). Decrease in anogenital distance among male infants with prenatal phthalate exposure. Environ Health Persp.2005;113:1056-1061.
90. Jobling S, Reynolds T, White R, et al. A variety of environmentally persistent chemicals, including some phthalate plasticizers, are weakly estrogenic. Environ Health Persp 1995;113: 1056-1061.
91. Ohlson CG. Hardell L. Testicular cancer and occupational exposures with a focus on xenoestrogens in polyvinyl chloride plastics. Chemosphere. 2000:40(9-11):1277-82.
92. Den Hond E. Schoeters G. Endocrine disrupters and human puberty. Int J Androl. 2006;29(1):264-71.
93. 110th Congress of the United States of America. HR 6228: Ban Poisonous Additives Act of 2008. [Internet]. Available from: http://thomas.loc.gov/cgi-bin/query/D?c110:1:./temp/~c110fR0Sst
94. State of California. Assembly Bill 1879. [Internet]. Available from: http://www.leginfo.ca.gov/pub/07-08/bill/asm/ab_1851-1900/ab_1879_bill_20080929_chaptered.pdf
95. State of California. Senate Bill 1713. [Internet]. Available at: http://www.leginfo.ca.gov/pub/07-08/bill/sen/sb_1701-1750/sb_1713_bill_20080822_amended_asm_v94.pdf
96. Schonfelder G, Wittfoht W, Hopp H, et al. Parent bisphenol A accumulation in the human maternal-fetal-placental unit. Environ Health Persp. 2002;110:A703-7.
97. Burridge E. Bisphenol A: surging polycarbonate in Asia has boosted bisphenol A's fortunes. Eur Chem News. 2004;81:17.
98. Dodds EC, Lawson W. Nature. 1936;137:996.
99. Dodds EC, Goldberg L, Lawson W, Robinson R. Oestrogenic activity of certain synthetic compounds. Nature. 1938;141:247-8.
100. Dieckmann WJ, Davis ME, Rynkiewicz LM, Pottinger RE. Does the administration of diethylstilbestrol during pregnancy have therapeutic value? Am J Obstet Gynecol. 1953;66:1062-75.
101. Sugiura-Ogasawara M, Ozaki Y, Sonta S, Makino T, Suzumori K. Exposure to bisphenol A is associated with recurrent miscarriage. Hum Reprod. 2006;20:2325-9.
102. National Toxicology Program. Diethylstilbesterol, CAS No. 56-53-1. [Internet]. Report on Carcinogens, 11th Edition. Avail-

able from: http://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s071diet.pdf.
103. Raun AP, Preston RL. History of dietheylstilbesterol use in cattle. [Internet]. American Society of Animal Science. Available from: http://www.asas.org/Bios/Raunhist.pdf
104. Hammes B, Laiman CJ. Diethylstilbestrol for the identification and management of DES-exposed individuals. J Midwifery Womens Health 2003:48(1):19-29.
105. Guisti RM, Iwamoto K, Hatch EE. Diethystilbestrol revisited: a review of the long-term health effects. Ann Intern Med. 1995; 122:778-88.
106. Herbst AL, Scully RE. Adenocarcinoma of the vagina in adolescence: a report of seven cases including six clear cell carcinomas (so-called mesonephromas). Cancer. 1970;25:745-57.
107. Herbst AL, Ulfelder H, Poskanzer DC. Adenocarcinoma of the vagina: Association of maternal stilbestrol therapy with tumor appearance in young women. N Engl J Med. 1971;284:878-81.
108. Bibbo M, Gill WB, Azizi F, et al. Follow-up study of male and female offspring of DES-exposed mothers. Obstet Gynecol J. 1977;49:1-8.
109. Colton T, Greenberg ER, Noller K, et al. Breast cancer in mothers prescribed diethylstilbestrol in pregnancy: further follow-up. J Am Med Assoc. 1993;269:2096-2100.
110. Titus-Ernstoff L, Hatch EE, Hoover RN, et al. Long-term cancer risk in women given diethylstilbestrol (DES) during pregnancy. Brit J Cancer 2001; 84: 126-133.
111. Palmer JR, Wise LA, Hatch EE, et al. Prenatal diethylstilbestrol exposure and risk of breast cancer. Cancer Epidemiol Biomarkers Prev. 2006;15:1509-14.
112. Troisi R, Hatch EE, Titus-Ernstoff L, et al. Cancer risk in women prenatally exposed to diethylstilbestrol. Int J Cancer. 2007;121:356-60.
113. Houlihan J, Lunder S, Jacob A. Timeline: BPA: from invention to phase out. Environmental Working Group Research Report. 2008. [Internet] Available at: http://www.ewg.org/reports/bpatimeline
114. Grandjean P, Bellinger D, Bergman A, et al. The Faroes statement: human health effects of developmental exposure to chemicals in our environment. Basic Clin Pharmacol Toxicol. 2007;102:73-75.
115. vom Saal FS, Hughes C. An extensive new literature concerning low-dose effects of bisphenol A shows the need for a new risk assessment. Environ Health Persp. 2005;113:926-33.
116. Lang IA, Galloway TS, Scarlett A, et al. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. J Am Med Assoc. 2008;300(11): 1303-10.
117. vom Saal FS, Myers JP. Bisphenol A and risk of metabolic disorders.[comment]. J Am Med Assoc.2008;300(11):1353-5.
118. Ropero AB, Alonso-Magdalena P, Garcia-Garcia E, et al. Bisphenol-A disruption of the endocrine pancreas and blood glucose homeostasis. Int J Androl.2008;31(2):194-200.
119. Newbold RR, Jefferson WN, Banks EP (2007). Long-term adverse effects of neonatal exposure to bisphenol A on the murine female reproductive tract. Reprod Toxicol. 2007; 24:253-258.
120. Richter CA, Birnbaum LS, Farabollini F, et al. In vivo effects of bisphenol A in laboratory rodent studies. Reprod Toxicol 2007;24:199-224.
121. US Environmental Protection Agency. Integrated Risk Information System. Bisphenol A (CASRN 80-05-7). [Internet]. 1988. Available from: http://www.epa.gov/iris/subst/0356.htm.
122. Calafat, AM,Ye X,Wong L-Y, et al.. Exposure of the US population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. Environ Health Persp. 2008; 116:39-44.
123. Vandenberg LN, Hauser R, Marcus M, et al. Human exposure to bisphenol A (BPA). Reprod Toxicol. 2007;24:139-177.
124. Michaels D, Monforton C. Manufacturing Uncertainty: Contested science and the protection of the public's health and environment. Am J Pub Health 2005:95(S1):S39-S47.
125. Gross L. The toxic origins of disease. PLoS Biol. 2007;5:1392-1398.
126. vom Saal, F and W Welshons. Large effects from small exposures. II. The importance of positive controls in low-dose research on bisphenol A. Environ Res. 2006;100:50-76.
127. Environmental Working Group. Letter to Center for the Evaluation of Risks to Human Reproduction: Interim Draft Report on Bisphenol A. [Internet]. June 2007. Available from: http://www.ewg.org/node/21835.
128. vom Saal FS, Akingbemi BT, Belcher SM, et al. Chapel Hill bisphenol A expert panel consensus statement: Integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. Reprod Toxico. 2007; 24:131-138.
129. Schonfelder G, Wittfoht W, Hopp H, et al.. Parent bisphenol A accumulation in the human maternal-fetal-placental unit. Environ Health Persp.2002;110(11):A703-707.
130.. Boyle CA, Decoufle P, Yeargin-Allsopp M. Prevalence and health impact of developmental disabilities in U.S. children. Pediatrics. 1994;93:399-403.
131. California Office of Environmental Health Hazard Assessment. Announcement of Chemicals Selected by OEHHA for Consideration for Listing by the Developmental and Reproductive Toxicant Identification Committee and Request for Relevant Information on the Developmental and Reproductive Toxicity of These Chemicals EXTENSION OF PUBLIC COMMENT PERIOD: Bisphenol A. [Internet]. [03/21/08] posted 03/11/08. Available at: http://www.oehha.ca.gov/prop65/CRNR_notices/state_listing/data_callin/extend031108.html.
132. Norwegian RoHS, 18 substances banned. Reported July 23, 2007. [Inernet] 2007 Pct 15. Available from www.evertig.com/news/read_news.do?news=8237–&cat=7
133. Horrigan L, Lawrence RS, Walker P. How sustainable sgriculture can address the environmental and human health harms of industrial agriculture. Environ Health Persp 2002;110(5): 445-456.
134. Schecter A, Papke O, Harris TR,t al. Polybrominated Diphenyl Ether (PBDE) Levels in an Expanded Market Basket Survey of U.S. Food and Estimated PBDE Dietary Intake by Age and Sex. Environ Health Persp 2006;114(10):1515-1520.
135. Hankinson S, Willett WC, Colditz GA, et al. Circulating concentrations of insulin-like growth factor 1 and risk of breast cancer. Lancet. 1998;351:1393-6.
136. Daxenberger, A, Bernhard BH, Sauerwein H. Increased milk levels of insulin-like growth factor 1 (IGF-1) for the identification of bovine somatotropin (bST) treated cows. Analyst. 1998;123:2429-35.
137. Allen NE, Roddam AW, Allen DS, et al. A prospective study of serum insulin-like growth factor-I (IGF-1), IGF-II, IGF-binding protein-3 and breast cancer risk. Brit J Cancer. 2005;92: 1283-7.
138. Schernhammer ES, Holly JM, Pollak MN et al.. Circulating levels of insulin-like growth factors, their binding proteins, and breast cancer risk. Cancer Epidemiol Biomarkers Prev. 2005;14:699-704.
139. Ciftci K, Su J, Trovitch PB. Growth factors and chemotherapeutic modulation of breast cancer cells. J Pharm Pharmacol. 2003;55:1135-41.
140. Furstenberger G, Morant R, Senn HJ. Insulin-like growth factors and breast cancer. Onkologie. 2003;26:290-4.
141. European Commission. Enterprise and Industry Directorate General. Consumer goods—Cosmetics. Consolidated Version of Cosmetics Directive 76/768/EEC. [Internet]. Updated 3/10/2008. Available from: http://ec.europa.eu/enterprise/cosmetics/html/consolidated_dir.htm
142. US Food and Drug Administration. Cosmetic Ingredients: Understanding the Puffery. [Internet]. FDA Consumer Magazine 1992 May. Available from: http://www.fda.gov/fdac/reprints/puffery.html
143. CIR (Cosmetics Ingredient Review). Cosmetic ingredients banned by FDA (11 total, through June, 2008). [Internet]. 2008 June. Available from: http://www.cir-safety.org/staff_files/banned.pdf
144. Environmental Working Group (2004). Exposures Add Up—Survey Results. [Internet]. Available from: http://www.cosmeticsdatabase.com/research/exposures/php.
145. Commonweal Biomonitoring Resource Center (2005). Taking It All In: Documenting Chemical Pollution in Californians through Biomonitoring. [Internet]. Available from: http://www.commonweal.org/programs/download/TIAI_1205.pdf
146. Environmental Working Group (2006). Across Generations: Industrial Chemicals in Mothers and Daughters: The pollution

we share and inherit. [Internet]. Available from: http://www.ewg.org/reports/generations/
147. Environmental Working Group (2005). Body Burden: The Pollution in Newborns. [Internet]. Available from: http://www.ewg.org/node/17686.
148. Environmental Working Group.). Body Burden: The Pollution in People. [Internet]. 2003. Available from: http://archive.ewg.org/reports/bodyburden1/.
149. Bronaugh RL, Collier SW, Macpherson SE, et al. Influence of metabolism in skin on dosimetry after topical exposure. Environ Health Persp 1994:102(S11): 71-74.
150. Schettler T. Human exposure to phthalates via consumer products. Int J Androl 2006; 29:134-139.
151. Janjua NR, Frederiksen H, Skakkebæk NE, et al.. Urinary excretion of phthalates and paraben after repeated whole-body topical application in humans. Int J Androl.2008; 30:1–11.
152. Cantor KP, Stewart, PA, Brinton LA, et al. Occupational exposures and female breast cancer mortality in the United States. J Occup Environ Med. 1995;37(3):336-48.
153. Weiderpass E, Pukkala E, Kauppinen T, et al. Breast cancer and occupational exposures in women in Finland. Am J Ind Med. 1999;36:48-53.
154. Petralia SA, Vena JE, Freudenheim JL, et al. Breast cancer risk and lifetime occupational history: Employment in professional and managerial occupations. Occup Environ Med 1998;55:43-48.
155. Habel LA, Standford JL, Vaughan TL et al. Occupation and Breast Cancer Risk in Middle-Aged Women. J Occup Environ Med 1995;37(3): 349-356.
156. Cardis E, Vrijheid M, Blettner M, et al. Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries. Brit Med J 2005;331:77-80.
157. Jacobs M, Clapp R. Industrial Carcinogens: A Need for Action.[Internet] 2008. Available from: http://www.healthandenvironment.org
158. Stayner L, Smith R, Bailer J, et al. Exposure-Response analysis of risk of respiratory disease associated with occupational exposure to asbestos. Occup Environ Med.1997; 54:646–652.
159. Hayes RB, Songnian Y, Dosmeci M, et al. Benzene and lymphohematopoietic malignancies in humans. Am J Indust Med. 2001; 40:117–126.
160. Friends of the Earth. Nanomaterials, sunscreens and cosmetics: Small ingredients, big risks [Internet]. 2007 Nov 15. Available from: www.foe.org/camps/comm/nanotech/nanocosmetics.pdf.
161. Thompson D, Kriebel D, Quinn MM, et al. Occupational exposure to metalworking fluids and risk of breast cancer among female autoworkers. Am J Ind Med. 2005;47:153-60.
162. Band PR, Le ND, Fang R, et al. Identification of occupational cancer risks in British Columbia: a population-based case-control study of 995 incident breast cancer cases by menopausal status, controlling for confounding factors. J Occup Environ Med. 2000;42:284-310.
163. Goldberg MS, Labreche F. Occupational risk factors for female breast cancer: A review. Occup Environ Med. 1996;53(3):145-56.
164. Zheng T, Holford TR, Taylor Mayne S, et al. A case-control study of occupation and breast-cancer risk in Connecticut. J Cancer Epidemiol Prev. 2002;7:3-11.
165. Teitelbaum SL, Britton JA, Gammon MD, et al. Occupation and breast cancer in women 20–44 years of age. Cancer Causes Control. 2003;14:627-37.
166. Hansen J. Breast cancer risk among relatively young women employed in solvent-using industries. Am J Indust Med. 1999; 36:43-47.
167. Morton WE. Major differences in breast cancer risks among occupations. J Occup Environ Med. 1995;37:328-335.
168. Coyle B, Polovich M. Handling hazardous drugs: how safe are you? Am J Nurs. 2004;104(2):104.
169. Watterson A, LaDou J. Health and safety executive inspection of UK semiconductor manufacturers. Health and Safety Executive Inspection; 2003;9:392-395.
170. Sigurdson AJ, Morin Doody M, Rao RS, et al. Cancer incidence in the U.S. Radiologic Technologists Health Study, 1983–1998. Cancer. 2003;97:3080-3089.
171. Natural Resources Defense Council. Nanotechnology's invisible threat: Small science, big consequences [Internet]. 2007 Nov 15. Available from: www.nrdc.org/health/science/nano/fnano.pdf
172. National Cancer Institute. Surveillance Epidemiology and End Results. Available at: http://seer.cancer.gov/
173. Centers for Disease Control and Prevention. National Program of Cancer Registries (NPCR). [Internet]. Available from: http://www.cdc.gov/CANCER/npcr/
174. National Cancer Institute. Surveillance Epidemiology and End Results: Population Characteristics. [Internet]. Available from: http://seer.cancer.gov/registries/characteristics.html
175. National Cancer Institute. Surveillance Epidemiology and End Results: Number of Persons by Race and Hispanic Ethnicity for SEER participants (2000 Census Data). [Internet]. Available from: http://seer.cancer.gov/registries/data.html#a3
176. Miller BA, Chu KC, Hankey BF, et al. Cancer incidence and mortality patterns among specific Asian and Pacific Islander populations in the U.S. Cancer Causes Control. 2008; 19:227–256.
177. Miller BA, Kolonel LN, Bernstein L, et al. Racial/ethnic patterns of cancer in the United States 1988–1992. Bethesda, MD: National Cancer Institute, 199658.
178. Centers for Disease Control and Prevention. National Program of Cancer Registries (NPCR). United States Cancer Statistics: 2004 Incidence and Mortality. 2007. [Internet]. Available from: http://www.cdc.gov/cancer/npcr/npcrpdfs/US_Cancer_Statistics_2004_Incidence_and_Mortality.pdf
179. Clegg LX, Feuer EJ, Midthune DN, Fay MP, Hankey BF. Impact of reporting delay and reporting error on cancer incidence rates and trends. J Natl Cancer Inst. 2002;94:1537-45.
180. Centers for Disease Control and Prevention. Managing Elevated Blood Lead Levels Among Young Children: Recommendations from the Advisory Committee on Childhood Lead Poisoning Prevention. [Internet]. March 2002. Available from: http://www.cdc.gov/nceh/lead/CaseManagement/caseManage_main.htm .
181. Centers for Disease Control and Prevention. National Report on Human Exposure to Environmental Chemicals. [Internet]. Available from: http://www.cdc.gov/exposurereport/.
182. Centers for Disease Control and Prevention. Press Release: CDC Releases Extensive Survey of Americans' Exposure to Environmental Chemicals. [Internet]. July 21, 2005. Available from: http://www.cdc.gov/od/oc/media/pressrel/r050721.htm.
183. Centers for Disease Control and Prevention. National Environmental Public Health Tracking Program. [Internet]. Available from: http://www.cdc.gov/nceh/tracking/default.htm.
184. Centers for Disease Control and Prevention. National Environmental Public Health Tracking Funded Programs. [Internet]. Available from: http://www.cdc.gov/nceh/tracking/projects/home.htm
185. California Environmental Health Tracking Program. Overview of environmental health tracking [Internet]. 2007 Nov 15. Available from: www.catracking.com/sub/eht.htm
186. 110th Congress of the United States of America. S. 2082: Coordinated Environmental Public Health Network Act of 2007. [Internet]. Available from: http://www.thomas.gov/cgi-bin/query/D?c110:2:./temp/~mdbsIUt6LC::
187. The National Children's Study. Funding and Legislation. [Internet]. Available from: http://www.nationalchildrensstudy.gov/about/Pages/funding.aspx
188. National Institute of Environmental Health Sciences and National Cancer Institute. Breast Cancer and the Environment Research Centers (BCERC). [Internet]. Available from: http://www.bcerc.org/home.htm
189. 110th Congress of the United States of America. HR 1157: Breast Cancer and Environmental Research Act of 2008 (Enrolled as Agreed to or Passed by Both House and Senate) [Internet]. Available from: http://www.govtrack.us/congress/bill.xpd?bill=h110-1157
190. U.S. Environmental Protection Agency. Endocrine Disruptor Screening Program. [Internet]. Available from: http://www.epa.gov/endo/
191. Erickson BE. Tests of endocrine disruptors delayed. Chem Engr News.2008;86:60-62.
192. California Breast Cancer Research Program. [Internet]. Available from: http://www.cbcrp.org/.