Chemicals and Breast Cancer
Better Ways to Detect Toxic Chemicals and Improve Breast Cancer Prevention
Breast cancer is the most common invasive cancer in American women, and the leading cause of death in women in their late thirties to mid-sixties. Advanced breast cancer is increasingly found in women in their twenties and thirties. Yet studies estimate that inherited risk factors account for less than a third of all breast cancer cases. What accounts for the other two thirds? Most likely a combination of factors. A growing body of research shows links between breast cancer and chemicals that we are exposed to in our environment and in consumer products, especially when those exposures occur during vulnerable periods, such as fetal development and puberty. Understanding how some chemicals may contribute to breast cancer could ultimately help prevent new cases of this disease.

Unfortunately, there is little safety information available for tens of thousands of chemicals that are currently in use. Hundreds of new chemicals are introduced each year, and most of those aren’t tested for how they affect human health. Even the small number of chemicals that undergo safety testing are not routinely evaluated for their impacts on breast tissue. Without that data, it’s impossible to determine which chemicals are hazardous or to identify safer alternatives.

Changes in the regulation of toxic substances offer new opportunities to find out which chemicals may pose a risk. This booklet highlights some of the key findings and recommendations of the report, Pathways to Breast Cancer: A Case Study for Innovation in Chemical Safety Evaluation, written by the members of the Breast Cancer and Chemicals Policy (BCCP) project, and funded by the California Breast Cancer Research Program. That project was designed to find ways to address the gap in information about chemicals and breast cancer. A panel of experts met to develop an approach for identifying chemicals that raise the risk of developing breast cancer, using the best existing scientific methods. This approach could also be useful in identifying chemicals that contribute to other diseases. Further, the panel identified testing methods that should be improved and areas in need of more research.

These are practical, comprehensive ways scientists can identify potentially hazardous chemicals, so that chemical manufacturers, consumers, and federal and state programs can find safer alternatives. Advocates can use this information to insist on the implementation of these tests by chemical manufacturers, researchers, and the companies who sell products.
Manufactured chemicals are in the air we breathe, the water we drink, and many of the household cleaners and personal care products we use in our homes and on our bodies. We might hear rumors about chemicals that could be dangerous to our health, but do we really know which ones are likely to raise our risk of developing breast cancer? Do manufacturers know? Does the government know? In many cases, the answer is no.

It doesn’t need to be that way. Researchers estimate that one out of every eight women born today will be diagnosed with breast cancer in her lifetime. In 2009, the year for which the most recent statistics are available, over 200,000 women in the U.S. were diagnosed with breast cancer and over 40,000 women died of the disease. These facts highlight why we need to find out which chemicals increase a person’s chance of developing breast cancer.

One reason we know so little about which chemicals pose health risks is because U.S. laws, for the most part, do not require chemical producers to test their products for safety before they are sold. Aside from pesticides and pharmaceuticals, most chemicals in the United States are regulated under the Toxic Substances Control Act, or TSCA. For the tens of thousands of industrial chemicals found in our environment and in consumer products, TSCA places the burden on the Environmental Protection Agency (EPA) to prove that a chemical presents an unreasonable health or environmental risk before it can regulate that chemical. But the law puts the EPA in a bind by not giving it the power to properly regulate chemicals or even require testing. Only five chemicals have been partially restricted for use under TSCA since the law was enacted in 1976. The law is so weak and ineffective, EPA has been unable to ban all uses of asbestos, a well known cancer-causing chemical. For the hundreds of new chemicals produced each year, companies need to submit to the government only the information they have already gathered; no additional testing is required. Typically, only a fraction of that information is made available to the public.

### Established Environmental Causes of Breast Cancer

We already know that some environmental exposures can lead to breast cancer. Estrogenic compounds such as those in hormone replacement therapy (HRT) and diethylstilbestrol (DES), a hormone once prescribed to pregnant women to reduce their risk of miscarriage, can raise a woman’s risk of developing breast cancer. Substances that affect hormones, such as alcohol, can also raise breast cancer risk. High-frequency radiation (like x-rays) can cause direct DNA damage that can lead to breast cancer, as can some chemicals such as the medical disinfectant, ethylene oxide, and the gasoline component, benzene.

More than two hundred compounds have been found to cause mammary (breast) tumors in animals. These include vinyl chloride, used to make polyvinyl chloride (PVC) products such as vinyl flooring and packaging; 1,3-butadiene, used in the production of synthetic rubber and latex; and acrylamide, used in making papers, dyes and plastics, and present in caulking, food, and adhesives. Many more compounds have never been researched for their toxicity. The next step is to look beyond these known causes and investigate a much broader list of environmental factors, including chemicals that have never been tested or are just being introduced into commerce as replacements for chemicals being phased out.
Even when companies test chemicals, they do not routinely evaluate them for their potential to cause breast cancer.

Breast tissue responds differently than other parts of the body when it is exposed to chemicals. In some cases, breast tissue is more sensitive to chemicals. There is a need for toxicity tests that look specifically at the effects of chemicals on breast tissue.

A combination of weak laws and inadequate tests leaves the government without the information required to protect public health, and it leaves us without the information we need to make safer chemical choices. In recent years there have been encouraging new developments in regulating toxic chemicals and bringing more information about chemicals to the public. Advocates, chemical manufacturers, and government agencies have all called for updating TSCA. Legislation to reform TSCA has been introduced in Congress. (Visit www.saferchemicals.org for more information). On a local level, several states have taken initiative to reduce the public's exposure to toxic chemicals. California, Maine, Washington, and Minnesota have passed a variety of laws focused on chemicals of concern in consumer products. In 2013, 28 states introduced legislation targeting individual chemicals and many other states introduced more comprehensive chemicals policy legislation. However, none of these state initiatives is focused on better testing methods, and none requires companies to submit data on chemical toxicity.

One of the many urgent questions about breast cancer in the U.S. is why different population groups develop breast cancer and die of the disease at widely differing rates. For example, African American women under age forty have a higher risk of breast cancer than Caucasian women, but this trend reverses after age forty. Yet African American women over forty are nearly two times as likely to die from breast cancer compared with white women.11

We are still struggling to understand the root causes of these disparities in order to design effective interventions. We know that there are differences—depending on race and socioeconomic status—in women's exposure to environmental contaminants in their homes and workplaces. It is important to note in this context that immigrants to the U.S. often have a higher risk of breast cancer compared to their foreign-born counterparts. For example, U.S.-born Chinese women have a higher risk of breast cancer compared to Chinese women born in China, suggesting environment’s role in cancer. With more information about toxic chemicals and safer alternatives, we should be able to reduce the incidence of breast cancer in all women.

“The true burden of environmentally induced cancers has been grossly underestimated.”

— President’s Cancer Panel report, 201013
Women in the United States are more likely to develop breast cancer than any other type of cancer. Why are breasts so susceptible to cancer? Scientists believe one reason is that breasts grow and change throughout a woman's life, including during fetal development, puberty, pregnancy and menopause. Various hormones, including placental, ovarian, and pituitary, play a part in these changes. Anything that interferes with the normal functioning of these hormones at each developmental stage can potentially alter breast tissue. Scientists believe, based on evidence from animals and humans, that during these critical windows, chemical exposure can change breast tissue development in ways that increase breast cancer risk.

### Critical Periods of Mammary Gland Development

Mammary gland development in rodents shares features with human breast development, and many research scientists rely on rodent models when investigating a chemical's toxicity. This timeline highlights critical periods of mammary gland development in rodents and the potential health impacts of chemical exposure during these periods.¹²

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<th>Exposure Period</th>
<th>Potential health impacts of chemical exposure at this stage</th>
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| **Gestational and Newborn**     | • Early or delayed development of the mammary gland  
• Early or delayed puberty  
• Inappropriate gender-specific characteristics; for example, male rodents with nipples |
| birth  
*Mammary buds are formed*     |                                                                                                                          |
| **Before and During Puberty**   | • Earlier than expected development of mammary glands  
• Delayed development of mammary glands  
• Altered sensitivity to chemical compounds and/or cancer-causing substances (carcinogens) |
| Ducts for lactation (milk secretion) develop, and structures at the tips of ducts, called terminal end buds, expand |                                                                                                                          |
| **Pregnancy**                   | • Changes in lactation (ability to lactate, content of milk, length of time lactating)  
• Death of offspring  
• Reduction in how well pregnancy protects against breast cancer |
| Development of milk-producing (lobuloalveolar) glands and milk production |                                                                                                                          |
The public, and our leaders, have made it clear that we need to do more to prevent breast cancer. Protecting everyone from chemicals that may raise breast cancer risk is one significant way of addressing this problem.

As more chemicals are tested for toxicity, we will need a practical and cost-effective approach to identifying those chemicals that contribute to breast cancer risk.

The Breast Cancer and Chemicals Policy (BCCP) project developed a Hazard Identification Approach for identifying those chemicals using the best existing scientific methods. The panel identified the categories of chemicals that should be prioritized for testing.

The group also identified the currently available toxicity tests that should be used to determine whether a chemical raises breast cancer risk. The panel identified changes in biological processes that occur early or “upstream” from the development of tumors, and recommend that chemicals be tested for their ability to raise breast cancer risk by causing the following upstream events:

- DNA damage
- Changes to how cells grow and divide
- Changes to hormones
- Changes in breast development

One shortfall of most current approaches to toxicity testing is that they look for the final signs of disease, such as a tumor, to determine whether a chemical causes cancer. This method is inefficient, and it is also likely to miss many potential carcinogens. Moving toward early indicators of harm, such as these upstream events, is also more time-and resource-efficient, enabling the testing of many more chemicals. For chemicals such as pesticides that are required to undergo premarket testing, it currently costs $5-$10 million and years of work to perform standard toxicity tests for one chemical. This cost could be lower with testing that focuses on early indicators of harm.

Currently, most toxicity tests study what happens when you expose adult animals to chemicals. Toxicity tests should be designed and conducted so they account for the difference in susceptibility to chemicals within different life stages, particularly, in the case of breast cancer, during critical periods when mammary glands are developing or changing. Testing should also account for factors such as genetic differences or underlying disease that might make a person more susceptible to a chemical. Future research should investigate additional biological pathways associated with breast cancer, and find new ways of detecting those early events that are likely to alter breast cancer risk.
# Hazard Identification Approach

The Hazard Identification Approach is a method for testing and detecting chemicals that may raise the risk of cancer. It can serve as a resource for chemical manufacturers, consumers, and federal and state programs wishing to identify both hazardous chemicals and safer alternatives.

## Chemical Prioritization:
The following categories of chemicals should be given first priority when testing chemicals for their ability to raise the risk of cancer.

### Chemicals with High Hazard Potential:
Chemicals with qualities that suggest they are most likely to increase the risk of breast cancer, including:
- Chemicals that are structurally similar to those known to cause breast cancer
- Chemicals with indicators showing that they or their possible metabolites are active in the body’s endocrine system
- Chemicals that may alter breast development
- Chemicals that may alter genes

### Chemicals with High Exposure Potential:
Chemicals to which people are most likely to be exposed, particularly during vulnerable life stages. Potential for exposure should be assessed across the life cycle of the product from manufacturing through disposal. These include:
- Chemicals that have the potential to accumulate in the body, persist in the environment, or contact breast tissue
- Chemicals produced in large quantities, or used widely in consumer products or workplaces

## Testing Priorities:
Toxicity testing should look for the following changes in biological processes that are associated with the development or progression of breast cancer.

### Rapid screening (in vitro): Tests that look for:
- Genotoxicity: a chemical’s ability to change a cell’s genetic material (DNA)
- Cell cycle changes: a chemical’s ability to change normal cycles of cell growth
- Endocrine disruption: a chemical’s ability to mimic or alter hormones in the body’s endocrine (hormone) system

### Animal Studies (in vivo): Tests that look for:
- Genotoxicity in breast epithelial cells: a chemical’s ability to change the genetic material in the cells that line the milk duct (epithelial cells) of the mammary gland
- Cell cycle changes: a chemical’s ability to change normal cycles of cell growth specifically in mammary epithelial cells
- Precursor changes, biomarkers, and induction of mammary gland tumors: a chemical’s ability to alter the development and maturation of the mammary gland
- Endocrine disruption at different stages of development: a chemical’s ability to mimic or block hormones in animal reproductive structures at specific developmental stages

Results of cell-based (in vitro) testing will sometimes provide enough information to raise concern that a chemical increases the risk of breast cancer. When more information is required, whole animal (in vivo) testing may be necessary. In particular, animal models enable us to test chemicals for their potential effects on breast tissue during critical windows of development. Currently, altered mammary gland development can only be assessed by whole animal (in vivo) studies.
What’s Next?

A committee of the National Academy of Sciences in 2007 reviewed both established and newly emerging methods of testing chemicals for toxicity and found the need for “a transformative paradigm shift” in toxicity testing.\(^\text{14}\)

To inform such a paradigm shift, scientists must continue studying the ways breast cancer can develop. Further research should be conducted to do the following:

- Better understand the biological pathways associated with breast cancer.
- Adapt current testing methods to specifically address mechanisms of disease development that are relevant to breast cancer.
- Develop new toxicity test methods—for example, hormone activity and DNA enzyme repair mechanisms—to detect events likely to alter breast cancer risk and to replace current test methods that are inadequate.
- Adapt methods of rapidly testing many chemicals—called “high-throughput screening”—so that these new rapid tests are also relevant to how breast cancer occurs.

While new science is developed, we must continue moving forward to help protect the millions of people now at risk for developing breast cancer. Chemical toxicity testing, and the public policies that require it, can be critical tools in the work of preventing breast cancer. The Hazard Identification Approach is a starting point to address the backlog of untested chemicals.

The toxicity information it can provide will help consumers, workers, product manufacturers, chemical producers, and policy makers make safer choices.

### What You Can Do

- **Tell companies and policy makers you want more chemical testing, and specifically testing for the effects of a chemical on mammary tissue.**
- **Learn more about how to support policy changes and hold companies accountable at the Breast Cancer Fund:** [breastcancerfund.org](http://breastcancerfund.org), the Breast Cancer Action: [bcaction.org](http://bcaction.org), and the Safer Chemicals, Healthy Families Coalition: [saferchemicals.org](http://saferchemicals.org)
- **Avoid unnecessary exposure to hazardous chemicals.** To learn more about how to limit these exposures see the suggestions at the University of California, San Francisco Program on Reproductive Health and the Environment: [http://prhe.ucsf.edu/prhe/toxicmatters.html](http://prhe.ucsf.edu/prhe/toxicmatters.html)
- **When practical, avoid unnecessary exposure to radiation in the form of x-rays and other medical imaging.**
Other Recent Reports On Reducing Breast Cancer Risk

The President’s Cancer Panel Report of 2010:

The report makes clear that the current federal cancer research agenda has been limited by inadequate funding to study the role of chemicals in causing cancer. The report criticizes federal government agencies for “not fulfilling their responsibilities to protect public health” through regulation that would limit the public’s exposure to known or suspected carcinogens, such as asbestos, formaldehyde, and trichloroethylene. It highlights the need for reform of federal chemicals policy and stronger regulation of chemicals by shifting the burden of proof from the government to manufacturers.

http://deainfo.nci.nih.gov/advisory/pcp/annualReports/pcp08-09rpt/PCP_Report_08-09_508.pdf

The Institute of Medicine (IOM) of the National Academies’ Breast Cancer and the Environment: A Life Course Approach, 2011:

A 360-page report in which the IOM reviewed current evidence on breast cancer and the environment and made thirteen research recommendations for better identifying and characterizing environmental links to breast cancer. In the report, the IOM urges a life-course approach to studying the disease, highlighting evidence that women and girls might be more susceptible to some risk factors during certain life stages, such as fetal development and puberty. The report also identifies several chemicals linked to breast cancer, such as benzene and 1,3 butadiene, both found in cigarette smoke, and others such as pesticides, BPA, and phthalates that have “biological plausibility” to raise breast cancer risk.


Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC) Report, February 2013:

Emphasizes that prevention is the key to reducing the burden of breast cancer. One of the committee’s main recommendations is to intensify the study of chemical and physical factors that potentially influence the risk of developing—and the likelihood of surviving—breast cancer.

http://www.niehs.nih.gov/about/boards/ibcercc/
**About Us**

This booklet is based on the report *Pathways to Breast Cancer*, written by Meg Schwarzman, MD, MPH Center for Occupational and Environmental Health, UC Berkeley and Clinical Instructor, Family and Community Medicine, UC San Francisco; and Sarah Janssen, MD, PhD, MPH, former Senior Scientist, Health Program, Natural Resources Defense Council and Assistant Clinical Professor, Division of Occupational and Environmental Medicine, UC San Francisco.

The Hazard Identification Approach was created with a multidisciplinary expert panel assembled from the fields of cancer biology, toxicology, medicine, epidemiology, public health, environmental justice, and public policy. A list of panel members is included in the document *Pathways to Breast Cancer*.

**Acknowledgements**

This work was funded by the California Breast Cancer Research Program. Thanks to Maria Dolan and Julie Van Scoy for their work on the writing, design and layout of this booklet.

**References**

12. Adapted from S.E. Fenton, 2006 Endocrinology. 147 (Supplement): S18-34.