Dear Dr. Sharpless:

The National Cancer Institute’s (NCI) patient and health professional Physician Data Queries (PDQ) about breast cancer prevention significantly underrepresent a key piece of breast cancer prevention: reducing breast cancer risk related to environmental exposures. For the purposes of this letter, environmental exposure refers specifically to cancer-causing chemicals.

We recognize that NCI is a leading and trusted source of information for all cancer-related considerations. It is because of this leadership role that we believe it is especially important for NCI to be a leader in educating health care providers, cancer patients and the general public about a significant body of evidence linking environmental exposures to breast cancer risk. The undersigned organizations and individuals therefore respectfully ask NCI to update its publicly available information about breast cancer risk and prevention to reflect current scientific understanding of these potential risks.

We understand that summarizing information about environmental risks isn’t easy. Breast cancer risk is complex and develops from interactions between genes, lifestyle and environmental exposures. The risk related to environmental exposures is even more complex as it may also be related to the timing of exposure in a woman’s life. Additionally, people are exposed to numerous chemicals simultaneously, rather than one chemical at a time, as is often the focus in research studies. Despite this complexity, research widely supports reducing environmental exposures when possible. Women want to reduce their breast cancer risk, and women and health care providers deserve the information to be able to take informed, preventative steps.

We are pleased that NCI is welcoming applications for research projects related to environmental exposures. We encourage you to expand this commitment beyond research to also include public information on the NCI website, which currently under-represents knowledge of this topic. The patient PDQ states that “it is not clear” whether the environment affects breast cancer, and also states “Studies have not proven that being exposed to certain substances in the environment, such as chemicals,
increases the risk of breast cancer.” The health professional PDQ states “Overall, the epidemiological and animal study evidence that supports an association between breast cancer and specific environmental exposures is generally weak.” These statements are unhelpful and misleading because they don’t communicate the large body of laboratory evidence showing that certain chemicals likely increase breast cancer risk, given that they increase mammary tumors in animal experiments. Challenges to studying environmental chemicals in humans mean that clear evidence of an association may not be obtainable, so the evidence we do have must be shared as an appropriate basis for action.

Numerous other federal agencies support our position that environmental exposures are part of the complex web of breast cancer risk factors that should be acknowledged, studied, and acted on. Examples include:

- **President’s Cancer Panel - Reducing Environmental Cancer Risk: What We Can Do Now** report concluded: “The burgeoning number and complexity of known or suspected environmental carcinogens compel us to act to protect public health, even though we may lack irrefutable proof of harm.... A precautionary, prevention-oriented approach should replace current reactionary approaches to environmental contaminants in which human harm must be proven before action is taken to reduce or eliminate exposure.... Public health messages should be developed and disseminated to raise awareness of environmental cancer risks and encourage people to reduce or eliminate exposures whenever possible.”

- **Institute of Medicine - Breast Cancer and the Environment: A Life Course Approach** report states: “... it may be prudent to avoid or minimize exposure because the available evidence suggests biological plausibility for exposure to be associated with an increased risk of breast cancer, or there is suggestive evidence from epidemiology, or both.”

- **Breast Cancer and the Environment Research Program (BCERP):** This National Institute of Environmental Health Sciences and NCI-funded program states that “Breast cancer is a complex disease. It is becoming clearer that the risk for developing breast cancer could be the result of numerous environmental exposures across the lifespan, acting in concert with an individual’s own genetics.” They also note that “While risk factors for breast cancer may occur at any time over the course of a woman’s life, there are certain periods of time during which her body may be particularly sensitive to some of these risks, which scientists refer to as windows of susceptibility. Exposures during these more susceptible times in a woman’s life can influence her chance of developing breast cancer later in life.”

- **The National Institute of Environmental Health Sciences** concluded that “Most experts agree that breast cancer is caused by a combination of genetic, hormonal, and environmental factors.”

- **Interagency Breast Cancer and Environmental Research Coordinating Committee** concluded that “Prevention is the key to reducing the burden of breast cancer,” and “By urgently pursuing research, research translation, and communication on the role of the environment in breast cancer, we have the potential to prevent a substantial number of new cases of this disease in the 21st century.”

By NCI’s own standards your agency is underrepresenting concerns about environmental links to breast cancer. The NCI website states that “While increased risk for some cancers is caused by inherited genetic factors (about 5%–10% of cancer cases), most cancers are caused by environmental and lifestyle factors.”

Additionally, NCI states that it looks to the National Toxicology Program (NTP) to identify carcinogens, but then does not acknowledge or address the identified chemicals of concern. For example, NTP lists
chemicals including ethylene oxide, benzene, 1,3-butadiene and others as having sufficient evidence to be considered mammary gland carcinogens and likely to be human carcinogens. Benzene and 1,3-butadiene exposures include gasoline and vehicle exhaust. Ethylene oxide is a sterilizing gas, and women have historically been exposed at work, for example, in healthcare). Yet these findings are not reflected in NCI’s PDQs. Importantly, the NTP has limited capacity to test for chemical safety and so its list should not be considered comprehensive.

The NCI site also states that it looks to the International Agency for Research on Cancer (IARC), the cancer agency of the World Health Organization, for lists of known or reasonably anticipated carcinogens. A 2011 review of human carcinogens by IARC lists ethylene oxide and tobacco smoking as “preventable exposures associated with human cancers, as identified by the International Agency for Research on Cancer,” specific to breast cancer. These two exposures are described as “agents with limited evidence in humans,” meaning “that a causal relationship was credible but that chance, bias, or confounding could not be ruled out with reasonable confidence.”

That IARC review goes on to note that “it is also likely that many human carcinogens remain to be identified” and that there are a “large number of probable and possible carcinogens identified by experimental studies.” The authors point to a separate review that “identified more than 200 chemicals that induce mammary gland tumors in experimental animals,” and explain that “most of these have been classified by IARC as carcinogenic, probably carcinogenic, or possibly carcinogenic to humans, but there were too few women in the epidemiological studies to permit conclusions about their potential to cause breast cancer.” The authors suggest that “better linkage between experimental results and human carcinogenicity should lead to the identification of human carcinogens on the basis of experimental results.” In other words, IARC’s limited list of breast carcinogens is attributable to weaknesses in the human research but does not provide reassurance that chemicals that cause mammary tumors are not also human breast carcinogens.

Beyond NTP’s and IARC’s lists, peer reviewed literature is another important source that providers could benefit from being aware of when making decisions concerning health. Examples include:

- A 2007 review of the science investigating environmental links to breast cancer found “216 chemicals were identified that have been associated with increases in mammary gland tumors...These include industrial chemicals, chlorinated solvents, products of combustion, pesticides, dyes, radiation, drinking water disinfection byproducts, pharmaceuticals and hormones, natural products, and research chemicals.” (Note: This is the review referenced in the IARC paragraph above).
- A 2014 review compiled methods for biomonitoring 100 potential breast carcinogens with expected human exposures. It also noted “Carcinogenicity in humans and rodents is generally consistent, although comparisons are limited because few agents have been studied in humans.”
- A 2015 report by an expert panel titled “Screening for Chemical Contributions to Breast Cancer Risk: A Case Study for Chemical Safety Evaluation” that identifies biological pathways to breast cancer as well as toxicology assays that can be used to screen chemicals for activity in these pathways.
- A 2019 review by the European Commission titled “Carcinogenicity assessment: Addressing the challenges of cancer and chemicals in the environment” notes that “while it is difficult to establish the contribution of chemical exposure to the societal burden of cancer, a number of measures can be taken to better assess the carcinogenic properties of chemicals and manage
their risks.” The paper summarizes how toxicological assessments and indications of public health status based on biomonitoring are “diverse evidence streams” that “have the potential to form the basis of an integrated and more effective approach to cancer prevention.”

In accordance with the numerous federal agencies, working groups and documents listed above, women and health care providers would benefit from NCI sharing information on the risk or potential risk of environmental exposures so that individuals, clinicians, and policymakers can take preventive actions. BCERP, for example, recommends that health care professionals educate people on the need to reduce environmental exposures when possible and provides specific examples of actions women can take to reduce their exposure to potentially harmful chemicals. While we believe their recommendations could be even more comprehensive, it demonstrates an important acknowledgement of the need to encourage preventive measures to protect people’s health.

We believe that NCI updating its information and approach to communicating about environmental exposures related to breast cancer risk would have a significant impact on the ability of women’s health organizations and health care providers to offer accurate information to women about their health risks. It would also allow individual women access to useful information to make decisions for their own health and the health of their families.

Based on the above, we ask NCI to implement a more complete approach to describing breast cancer risk linked to environmental exposures and to explain multidisciplinary scientific approaches for identifying risk factors for complex, multifactorial and long-latency diseases like breast cancer. We also request that this information be made available in the PDQs so that individuals, breast cancer/women’s health organizations, and health professionals can better understand the state of the evidence on environmental breast carcinogens. We respectfully ask NCI to do the following:

1. Diversify the Screening and Prevention Editorial Board to include toxicologists and environmental epidemiologists with expertise in breast carcinogenesis. We believe this would provide critical perspectives to help extend the content of both the patient and health professional PDQs. This board should regularly update the NCI breast cancer PDQs to reflect new research related to environmental links to the disease.

2. Update NCI’s overall approach to analyzing environmental risks for breast cancer that inform the development of patient and health professional PDQs. We suggest adding the following sample language to the breast cancer PDQs and to NCI’s descriptions of evaluating evidence:

   Studying the relationship between environmental chemicals and cancer is difficult, because it can take decades after an exposure before cancer is diagnosed, and the exposures often are invisible, so patients can’t tell us about them. That’s why scientists rely on a combination of evidence from studies in people and controlled experiments in laboratory animals and cells.

   Scientists do know that many chemicals are biologically active in ways that can influence breast cancer. For example, common chemicals cause mammary gland tumors in animals, interfere with the natural hormone estrogen (a known breast cancer risk factor), or disrupt other hormones. Exposure to certain chemicals early in life may disrupt development of the breast in ways that make it more susceptible to cancer later on.
Several panels of expert scientists and physicians recommend avoiding or reducing exposure when laboratory evidence links chemicals to breast cancer, rather than waiting for proof.

Avoiding exposure especially makes sense when an alternative is easy to choose. For example, people can avoid some hormone disruptors by reading product labels to avoid using products with parabens and some pesticides. In many cases, changes in government policies are needed to reduce exposure to chemicals that may increase breast cancer risk, since it can be impossible for individuals to know where these exposures occur or to influence them.

3. Make clear delineations in the patient breast cancer PDQ of breast cancer risk factors that are modifiable and not modifiable. The health professional PDQ presents risk factors in categories such as “Factors With Adequate Evidence of Increased Risk of Breast Cancer “and “Modifiable Factors With Adequate Evidence of Increased Risk of Breast Cancer.” We believe organizing the patient PDQ in a similar manner will help women better understand what is in their power to modify.

4. Broaden the sources of information on environmental links to breast cancer to include information from the following resources in the patient and health professional PDQs:
   
a. NTP\textsuperscript{15}
   b. IARC\textsuperscript{16}
   c. The Institute of Medicine’s *Breast Cancer and the Environment: A Life Course Approach* report.\textsuperscript{17}
   d. Peer-reviewed literature including, but not limited to:
      1. Recent review articles about breast cancer risks in women at higher genetic or family risk, in younger women, and in women during developmental periods of greater susceptibility, including:
Additionally, NCI should include language from other government efforts that suggest that taking precaution related to environmental exposures may accelerate prevention, even in the absence of absolute proof. Examples from these reports are quoted above.

5. Meet with some of the signatories of this letter, including advocates and researchers, to develop an action plan for implementing solutions to these requests.

We believe updating NCI’s approach to evaluating and sharing information about environmental links to breast cancer would provide helpful and actionable advice to the general public about opportunities to prevent risky exposures. It would also support health care providers in their ability to support patients and could serve as an important model for NCI’s overall approach to considering environmental links to other types of cancer.

Thank you for your consideration of these important issues. We look forward to hearing from you about next steps. Further communication on this important matter can be directed to Jayla Burton, Program Officer at Breast Cancer Action (jburton@bcaction.org).

Sincerely,

ORGANIZATIONS
1. Breast Cancer Action
2. Silent Spring Institute
3. Breast Cancer Prevention Partners
4. Sierra Club
5. Women’s Voices for the Earth
6. National Women’s Health Network
7. Zero Breast Cancer
8. Women's Health Institute
9. Science and Environmental Health Network
10. UCSF Program on Reproductive Health and the Environment
11. Fight For Zero, Inc
12. Lowell Center for Sustainable Production
13. Latinas Contra Cancer
14. Children’s Environmental Health Network
15. DES Action USA
16. MedShadow Foundation
17. Alaska Community Action on Toxics
18. Toxic Free NC
19. Dr. Yolanda Whyte Pediatrics
20. National Toxic Encephalopathy Foundation
21. Healthy Environment and Endocrine Disruptor Strategies, HEEDS.org
22. Cancer Resource Centers of Mendocino County
23. Friends of the Earth
24. Our Bodies Ourselves
25. Green Science Policy Institute
26. Social Science Environmental Health Research Institute
27. Clearya
28. Great Neck Breast Cancer Coalition
29. Breathe Project
30. Project Coffeehouse
31. Alliance of Nurses for Healthy Environments
32. Center for Biological Diversity
33. Alliance for Cancer Prevention UK
34. From Pink to Prevention
35. Berks Gas Truth
36. Bucks Environmental Action
37. San Francisco Bay Physicians for Social Responsibility
38. Worksafe
39. Better Path Coalition
40. Responsible Drilling Alliance (RDA)
41. Clean and Healthy New York
42. Maquiladora Health & Safety Support Network
43. Physicians for Social Responsibility-Arizona
44. Seventh Generation
45. Cancer Resource Center
46. American Sustainable Business Council
47. Grassroots Environmental Education
48. Woodland Coalition for Green Schools

INDIVIDUALS
1. Linda S. Birnbaum, PhD, DABT, ATS; Scientist Emeritus, NIEHS/NTP and Scholar-in-Residence, Duke University*
2. Margaret L Kripke, PhD; Professor Emerita at MD Anderson Cancer Center and former member of the President’s Cancer Panel*
3. Julia Brody, PhD; Executive Director and Senior Scientist, Silent Spring Institute*
4. Ruthann Rudel, MS; Director of Research, Silent Spring Institute*
5. Suzanne E. Fenton, PhD; Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC), author and adjunct graduate faculty at North Carolina State University, University of North Carolina-Chapel Hill, and Duke University*
6. Marion H. E. Kavanaugh-Lynch, MD, MPH; Director, California Breast Cancer Research Program*
7. Robert A. Hiatt, MD, PhD; Professor of Epidemiology & Biostatistics, Associate Director for Population Sciences, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco*
8. Marj Plumb, DrPH; Community-based breast cancer research consultant, Omaha, NE*
9. Karuna Jagger, MA; former Executive Director, Breast Cancer Action*
10. Jeanne Rizzo, RN: Breast Cancer Prevention Partners past President and former Co-chair of the Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC)*
11. Laura N. Vandenberg, PhD; Associate Professor, University of Massachusetts, Amherst*
12. Mary Beth Terry, PhD; Professor of Epidemiology (Environmental Health Sciences), Columbia University*
13. Gina M. Solomon, MD, MPH; Principal Investigator, Public Health Institute; Clinical Professor of Medicine, University of California San Francisco*
14. Jerrold J. Heindel, PhD; Co-director, HEEDS.org*
15. Sora Park Tanjasiri, DrPH, MPH; Professor, University of California, Irvine*
16. Rachel Morello-Frosch, PhD, MPH; Professor, University of California, Berkeley*
17. Barbara A. Cohn, MCP MPH PhD; Director and Senior Research Scientist, Child Health and Development Studies, Public Health Institute*
18. Ann Blake, PhD; Environmental & Public Health Consulting
19. Heather Sarantis, MS; Environmental Health Consultant and Lead Author of Paths to Prevention: The California Breast Cancer Primary Prevention Plan*
20. Janet Gray, PhD; Professor Emerita, Vassar College*
21. Alicia D. Justice, MPH; Chronic Disease Prevention Director, Association of State and Territorial Health Officials (ASTHO)*
22. Sarah Gehlert, MA, MSW, PhD; Dean and Professor, School of Social Work, The University of Southern California*
23. Janette Robinson Flint, Executive Director, Black Women for Wellness*
24. Scarlett Lin Gomez, MPH, PhD; Professor, Department of Epidemiology and Biostatistics, University of California, San Francisco*
25. Barbara Demeneix, PhD DSc; Professor Emeritus, CNRS Muséum Paris*
26. R. Thomas Zoeller, PhD; Professor Emeritus, University of Massachusetts Amherst*
27. Christopher J. Portier, PhD; Senior Contributing Scientist, Environmental Defense Fund*
28. Terrence Collins, PhD; Teresa Heinz Professor of Green Chemistry, Institute for Green Science, Carnegie Mellon University*
29. Susan F Wood, PhD; Research Professor of Health Policy and Management, Jacobs Institute of Women's Health, George Washington University*
30. Anna H. Wu, PhD; Professor of Preventive Medicine, University of Southern California*
31. Iona Cheng, PhD, MPH; Professor, University of California, San Francisco*
32. Bruce Blumberg, PhD; Professor, University of California, Irvine*
33. Susan Neuhausen, PhD; Professor, Beckman Research Institute of City of Hope*
34. Megan Schwarzman, MD, MPH; Research Scientist and Lecturer, University of California, Berkeley*
35. Adrian A. Franke, PhD; Professor, University of Hawaii*
36. Jennifer Kay, PhD; Research Scientist, Silent Spring Institute*
37. Kathryn Rodgers, MPH; Staff Scientist, Silent Spring Institute*
38. Richard Clapp, DSc, MPH; Professor Emeritus, Lowell Center for Sustainable Production*
39. Lauren C. Heberle, PhD; Associate Professor and Director, Center for Environmental Policy and Management, University of Louisville*
40. James Brophy, PhD; University of Windsor Canada*
41. Margaret Keith, PhD; University of Windsor Canada*
42. Jane McArthur, PhD Candidate, University of Windsor*
43. Leonard Wright, PhD; University of Auckland*
44. Peggy Reynolds, PhD; Professor, University of California, San Francisco*
45. Ana M. Soto, MD; Professor, Tufts University School of Medicine*
46. Michael Lerner, PhD; President and Co-Founder, Commonweal*
47. Eleni Tousimis, MD, MBA, FACS
48. Gina Werdel; Associate, Make It Toxic Free Campaign, U.S. Public Interest Research Group*
49. Roxana Amaya-Fuentes, MPH; Program Assistant, Children's Environmental Health Network*
50. Gail Kaufman
51. Lee Ann Slinkard
52. Peggy Huston, MBA
53. Julie Morgan, RN
54. Kristan J. Aronson, PhD; Breast Cancer Prevention Partners Scientific Advisory Board*
55. Elana Silver MS; Epidemiologist
56. Carmi Orenstein, MPH
57. Maricel V. Maffini, PhD; Independent Consultant*
58. Laura Fenster, PhD; Epidemiologist, Breast Cancer Prevention Partners Board and Scientific Advisory Panel and Retired California Department of Public Health*
59. John M. Essigmann, PhD; Professor, Massachusetts Institute of Technology*
60. Patrice Sutton, MPH; Research Scientist, University of California, San Francisco Program on Reproductive Health and the Environment; San Francisco Bay Physicians for Social Responsibility*
61. Robert M. Gould, MD; Associate Adjunct Professor, University of California, San Francisco Program on Reproductive Health and the Environment; Physicians for Social Responsibility*
62. Mary Martin Gant, MS
63. Joseph Su, PhD, MPH; Professor, University of Arkansas for Medical Sciences*
64. Dean P. Jones, PhD; Professor of Medicine and Director, Clinical Biomarkers Laboratory, Emory University*
65. Cheryl Osimo, Executive Director, Massachusetts Breast Cancer Coalition*
66. Ngina Lythcott, RN, MSW, DrPH; Intercultural Cancer Council (ICC)*
67. Caroline Farrell; Executive Director, Center on Race, Poverty and the Environment*
68. Susan Kutner, MD, Breast Surgeon, Breast Cancer Prevention Partners Science Advisory Panel*
69. Liza Grandia, PhD; Associate Professor, University of California Davis Department of Native American Studies*

* For identification purposes only.


