Testimony of H. Kim Lyerly, M.D.
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House Energy and Commerce Committee
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Chairman Pallone, Ranking Member Deal and Members of the Committee, thank you for holding this hearing on such important legislation, the Breast Cancer and Environmental Research Act. I am Dr. H. Kim Lyerly, Director of the Duke Comprehensive Cancer Center. I am a breast cancer surgeon, researcher and a member and former Chair of the Department of Defense peer-reviewed Breast Cancer Research Program Integration Panel. I am grateful for the opportunity to testify today.

We all know how serious the problem of breast cancer is. Unfortunately, it is difficult to find a person who has not been touched in some way by breast cancer – either themselves or through friends or family members. A woman's chances of developing breast cancer have increased over the years. It is estimated that more than 250,000 women and nearly 2,000 men will be diagnosed with breast cancer in 2008. Sadly, more than 40,000 women and 450 men will die of the disease this year. Despite some progress, we still do not know what causes most breast cancers, how to prevent them or how to cure breast cancer for any individual woman.

Finding the cause or causes of breast cancer could be the key to unlocking this and other diseases – finding ways to prevent the disease from occurring in the first place, and also helping to better treat the disease and eventually cure it. While it is clear that traditional genetic studies can help us understand the etiology of a small fraction of cancers, it was demonstrated in this decade that identical twins, those who are essential genetic duplicates of each other, have only a 10-15

percent chance of having breast cancer if their twin had breast cancer. Clearly, something other than your inherited genes, as we know them, is leading to breast cancer in the majority of women. It is important to focus significant resources on these issues and doing so will have ramifications beyond breast cancer.

Breast Cancer and the Environment

Breast cancer is a complex and heterogeneous disease. Research into the causes of breast cancer is a difficult area to study, particularly when examining environmental links. To date, any efforts in this arena have been fragmented. Laboratory and epidemiologic research may give some clues to the possible carcinogenicity of chemicals and other environmental exposures. Some resources have been put into genetics programs at the National Institutes of Health (NIH) to look at genetic variation in groups of patients with specific illnesses. Some resources have been put into the National Institute of Environmental Health Sciences (NIEHS) to develop environmental technology to validate exposures. These are nascent areas of research that are necessary. While this research is ongoing, we are far from determining the clinical utility of these relationships.

Some resources have gone to analyze clusters of cancer cases to generate hypotheses about potential risk factors. Unfortunately, the identification of a cluster does not necessarily reveal the exposure, or whether an individual exposure is responsible for the elevated rate of disease. An added challenge is the measurement of exposures over a lifetime, as exposures are intertwined and may be confounded by socioeconomic, occupational and reproductive factors. Studies such as the Sisters' Study at NIEHS look into these areas. In addition, recent data has demonstrated the maternal exposure can influence risk. For example, dietary supplements in experimental

animal models can cause "epigenetic" changes, or changes in the ability of genes to be expressed. Theses epigenetic changes can then be passed on from generation to generation and increase cancer susceptibility in offspring. Clearly, new knowledge, and new concepts of what constitutes environmental exposure, are being brought to light at an ever increasing pace.

While biomarker, other genetic research and cohort studies are important, these are only a few aspects of the needed research into this area. We need to fund scientific freedom to determine different approaches to this problem and a cohesive, strategic program. Supporting different approaches is a hallmark of great research. We cannot presuppose which discipline or which approach has the answers. We must support collaboration among all with the expertise to address a health problem, especially one that poses such a complex scientific dilemma.

The DOD Breast Cancer Model

The examples I discuss above are just a few examples of how trying to determine what in our environment causes breast cancer is so challenging. It requires an innovative and strategic approach, with many different scientific disciplines working together. I have carefully reviewed the approach that H.R. 1157 describes and I can say it is the right and the best approach in this context. And it should be done through NIH because of the complexity of the problem and the collaborations contemplated. This legislation moves beyond fragmented approaches to a broad, innovative approach that fosters scientific freedom and public input to work in collaboration on a compelling national public health problem. I have seen the framework suggested by this bill work so well. The design of the program in this legislation is based on the model at the

Department of Defense peer-reviewed Breast Cancer Research Program. As a scientist and past Chair of the Integration Panel, I can tell you firsthand why this model has been so successful.

The Department of Defense (DOD) peer-reviewed Breast Cancer Research Program has established itself as a model medical research program, respected by the military and throughout the cancer and broader medical community for its innovative and accountable approach. The DOD Breast Cancer Research Program is meant to challenge the research community to work together to design innovative research that will foster new directions in breast cancer research.

The Institute of Medicine recommended the existing structure that includes scientific peer review and programmatic review by an Integration Panel (IP). The IP of the Department of Defense peer-reviewed Breast Cancer Research Program is made up of scientists and breast cancer advocates, including experts in basic, transitional, clinical, psychosocial and public health research. The Integration Panel recommends a research investment strategy; reviews the results of the peer review panels' deliberations and comparison of scorings across panels; recommends the applications to be funded; and assists in overall program evaluation.

The IP's overarching role is to ensure the Program remains focused on its mission: eradicating breast cancer. The Panel is there to guarantee scientific freedom and minimize duplication. Once the scientific and technical peer review has been completed, the Integration Panel reviews the proposals with the mission and the strategic investment strategy in mind – looking at not only what proposals are scientifically meritorious, but also at which are the most meaningful. This step is critical. It is extremely important to note that, unlike most traditional funding programs,

the DOD Program – and the structure proposed by the pending Breast Cancer and Environmental Research Act – does not tell the scientific community what to do, or what specific study to perform. The scientists are free to use their best judgment to decide what questions they will ask and what areas their proposals will address. And they do so with input from the consumer advocate community.

Another aspect of the proposed legislation has been validated by the DOD Program. It is extremely important that the program require grantees to be multi-disciplinary, multi-institutional and to collaborate with community-based organizations. As I said earlier, environmental research is complex and difficult. It requires the best minds working together. We cannot stay within the silos of science if we want to unravel the secrets of how our environment is related to breast cancer.

The DOD Breast Cancer Research Program has been a model in this area. It has spearheaded concepts such as team science that proposed combining expertise to address significant issues, by promoting funding mechanisms that require disparate disciplines and/or investigators to communicate, cooperate and jointly address problems. These collaborative grants encourage not just individual scientists but also institutions to work together. I have seen the results of promoting team science and interactions through the multi-disciplinary and multi-institutional model, and I fully support inclusion of this model in the Breast Cancer and Environmental Research Act. Team-oriented science can work, it is especially critical for complex environmental research, and it requires novel funding mechanisms to ensure that teams are both recognized for their successes, and accountable for their shortcomings.

Specific Application to the Proposed Legislation

The Panel in the Breast Cancer and Environmental Research Act would act much like the Integration Panel at the DOD Breast Cancer Research Program. The Panel would determine the mechanisms necessary to address the overarching goal of the legislation. Those mechanisms would be released to the scientific community with a request for proposals in response. The plan ensures that we do not restrict but rather foster scientific freedom, creativity, and innovation. The idea is not to predetermine for the scientific community what specific research areas are to be addressed. The idea is to create a framework for scientists and consumers to fund scientifically meritorious research related to the environment and causes of breast cancer – research that is meaningful and will get us closer to finding the answers we need, in a strategic, collaborative way.

The Importance of Consumer Involvement

Breast cancer is not just a problem of science, but it is a problem of people. The inclusion of trained consumers at every level is critical to the success of the DOD Breast Cancer Research Program. The Program is a collaboration of the critical stakeholders – scientists, clinicians, the military and trained consumers with a connection to breast cancer.

The consumers play a key role in ensuring that the research that is funded is responsive to needs of both the scientific and patient communities. Their perspective is necessary to ensure that the grants funded are meaningful and will have impact. Consumer advocates bring a vitally important perspective to scientific research. And they keep the scientists on task. Together, they

can look at the current state of knowledge, and then design appropriate and necessary mechanisms to allow scientists, in collaboration with advocates, to develop proposals to research the most important questions.

I have quotes from several of my colleagues in the scientific community who have worked on the Integration Panel or in other capacities in the DOD Breast Cancer Research Program. Many of the scientists who have participated in the Program have said that the Program – and working with the advocates – has changed the way they do research. This has a profound impact on the way scientists approach their work.

For example, Dr. George Sledge of Indiana University said, "Of the many advances in breast cancer research over the past decade, among the most important is the role of advocates in furthering and focusing the research agenda."

Dr. Regina Resta of New York said, "I served as a scientist on a DOD breast cancer study section [peer review panel]… The idea of the 'consumer reviewer' frankly, struck me as somewhat forced and potentially unhelpful in the review process. I was WRONG…these women added immeasurably to the process."

Finally, Dr. Michael Diefenbach of Mount Sinai School of Medicine wrote, "I have served as a reviewer for the Department of Defense's Breast and Prostate Cancer Review programs and I am a member of the behavioral study section for the National Cancer Institute… I find survivors or advocate reviewers as they are sometimes called bring a sense of realism to the review process

that is very important to the selection and ultimately funding process of important research…Both sides bring important aspects to the review process and the selected projects are ultimately those that can fulfill scientific rigor and translatability from the research arena to clinical practice. I urge that future review panels include advocate reviewers in the review process."

In addition to these scientists, and many others who have praised the DOD Breast Cancer Research Program, the IOM has reviewed the Program twice and has praised the design of the Program. In its 1997 review of the Program, the IOM stated,

> *The program fills a unique niche among public and private funding sources for cancer research… Among the most outstanding features of the program are the flexible approaches for setting priorities annually [and] the involvement of breast cancer advocates (consumers) in the peer review process…*

The report goes on to state, "The Integration Panel, along with the USAMRMC, is responsible for a breast cancer program viewed as successful by this committee." In 2004 a report by the IOM reiterated these remarks.

Finally, I would just like to talk a bit about how this approach has affected my research in my own institution. As you may know, Duke University has one of the most outstanding schools of environmental research in the United States, as well as an outstanding medical center. Policies of required cross-disciplinary research promoted by the DOD, led a number of investigators in the Cancer Center to actively meet and engage in collaborations with the Nicholas School of the Environment, an event that had not taken place previously. Environmental scientists, molecular

epidemiologists, and basic scientists work together with breast cancer specialists to explore how environmental exposures can increase a woman's risk of breast cancer, and possibly inhibit current strategies to prevent cancer. In addition, we have seen rapid increases in breast cancer in parts of the world undergoing rapid economic growth, which must be explored. Traditional forms of support could not, and did not support interactions reflecting these collaborations in the past. It is imperative that mechanisms that will enable these types of interactions be supported

In conclusion, the approach used by the DOD peer-reviewed Breast Cancer Research Program has changed the world of breast cancer research. We now need to apply the same model to investigate the causes of breast cancer. And it is our hope that this research model might inspire new approaches in other areas of scientific inquiry. As I said earlier, if we know what causes the disease, we can learn how to prevent it, how to better treat it and even to cure it. It is time that we take a fresh look at the environment and breast cancer. This proven approach will bring innovation and new thinking to the problem, will best use our resources and will complement ongoing work at NIH and elsewhere.