

## **Proposal Abstract: Scientific Workshop on Mammary Gland Evaluation and Risk Assessment**

Identifying chemicals that increase the risk of breast cancer can lead to risk reduction through public health measures to reduce exposure. In human studies we see that conditions that affect the hormonal environment of the developing fetus may increase (having an older mother) or decrease (being a twin) breast cancer risk in adulthood, supporting the hypothesis that fetal exposure to endocrine disrupting chemicals (EDCs) – chemicals that affect hormone systems -- also affects breast cancer risk. However, the effects of fetal exposures to EDCs are difficult to study in humans because of the decades-long lag between fetal exposure and the age at which breast cancer is typically detected together with the inability to noninvasively observe the mammary tissue. Therefore, tests in animals are the primary way of predicting potential effects on breast cancer.

In a number of laboratories, researchers have shown that treatment of pregnant test animals with EDCs results in changes to the structure of the mammary gland in the offspring. These changes suggest that fetal exposure to EDCs may cause permanent changes to the breast that could lead to adverse health effects such as changes in the timing of puberty, problems with lactation, or increased susceptibility to carcinogens. However, this area of research is still emerging, and many questions remain about how to evaluate the changes in mammary gland structure and how to link these changes to problems such as potential effects on breast cancer. When regulators consider how much exposure to a chemical is likely to cause health effects, they have been concerned about these effects on mammary gland structure, but are reluctant to consider these changes as the basis for limiting exposures because of the lack of consistency in researchers' methods for reporting the structural changes and inadequate data linking those changes to adverse effects such as cancer.

In order to facilitate progress in these areas, we propose a scientific workshop to bring together biologists, toxicologists, and risk assessors to develop standard methods for describing changes in mammary gland structure and development, and to recommend changes to current tests used by regulatory agencies so that they include more thorough assessment of mammary glands. Another priority for the workshop will be to learn from regulatory agencies about the types of studies that would be more useful to them, so that biologists can design their studies appropriately and research funders have good information about how to prioritize their funding. Progress in these areas will ultimately lead to development of relatively inexpensive and quick chemical test methods that assess developmental effects on the mammary gland and can be interpreted as predictive of adverse effects, such as carcinogenicity, that currently have to be evaluated in expensive, long-term studies.

This proposed workshop is scheduled for November 17, 2009, in Oakland, CA, in conjunction with the annual meeting of the National Institutes of Environmental Health Sciences (NIEHS) Breast Cancer and Environment Research Centers (BCERC), because several BCERC researchers are working on this problem. Both NIEHS and the US Environmental Protection Agency are supporting this workshop, and this topic is a CBCRP priority issue, as identified in the program's Special Research Initiative targeting methods for evaluating chemicals' potential effects on breast cancer risk. We anticipate a group of about 65 invited scientists and will have space for members of the public to be included as observers.

The proposed workshop will facilitate progress in scientific research to understand how early life exposure to EDCs can influence mammary gland development and susceptibility to cancer, and in chemicals regulation that considers this mechanism by which chemical exposure can cause breast cancer. Progress in these areas will provide the basis for stronger regulations to limit chemical exposure and consequently limit associated risk of breast cancer. We anticipate several specific outcomes, including 1) improved study designs by mammary gland biologists working in the area of developmental chemical exposure, including published standards for consistent interpretation of effects on mammary gland structure and development; 2) better understanding among risk assessors and toxicologists of the implications of changes in mammary gland development patterns so that effects on the mammary gland will be evaluated more frequently and relied upon as a basis for chemical regulation. For example, information can be used to limit exposure to pesticides, restrict chemicals from consumer products, or set allowable exposure levels for workers; 3) clear direction for future research on this topic; 4) a scientific paper summarizing challenges and opportunities in this area; and 5) a follow-up public meeting for advocates and a written lay-summary of key outcomes from the workshop.