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December 7, 2020

Submitted electronically to: <https://www.regulations.gov>

Richard Pazdur, MD
Director, Oncology Center for Excellent
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705

**Re: FDA-2020-D-1553: Premenopausal Women With
Breast Cancer: Developing Drugs for Treatment; Draft
Guidance for Industry**

Dear Dr. Pazdur,

The Society for Women's Health Research (SWHR) is pleased to offer comments in response to the U.S. Food and Drug Administration (FDA) draft industry guidance regarding the inclusion of premenopausal women with breast cancer within clinical treatment trials. We write specifically in response to Docket No. FDA-2020-D-1553, "Premenopausal Women With Breast Cancer: Developing Drugs for Treatment; Draft Guidance for Industry."

SWHR is a 30-year-old national organization dedicated to promoting research on biological sex differences in disease and improving women's health through science, policy, and education. SWHR championed the framework for the scientific discipline of sex-based biology, which encourages the inclusion of female subjects in clinical trials and analyzes the differences between women and men in relation to disease.

Given our history of advocating for increased inclusion of women in clinical trials, SWHR is pleased to see this guidance calls for improved inclusion rates of premenopausal women within breast cancer trials. Premenopausal women with hormone-receptor positive (HR+) breast cancer are often underrepresented in cancer treatment studies.¹

While breast cancer broadly is seen most often in older, postmenopausal women, approximately one-fifth of breast cancer cases are diagnosed in women under the age of 50. Further, prevalence rates of breast cancer in younger women are increasing: incidence of metastasized breast cancer

¹ Azim HA Jr., Partridge AH. Biology of breast cancer in young women. Breast Cancer Res 2014;16:427.



increased 2% annually between 1978 and 2008.² In addition, younger women diagnosed with breast cancer — especially those with endocrine-sensitive disease — often show poorer prognosis compared to older women. Younger women also face unique concerns during cancer treatment, such as poorer perceived quality of life and difficulty adhering to ongoing treatment.³ Because these patients are particularly at risk for negative outcomes, they are also in particular need of effective, reliable therapies.

Because of the poor inclusion rates for younger women in breast cancer clinical trials, treatment in this population is frequently based on studies conducted on postmenopausal patients. This is true despite the fact that cancer pathophysiology may be different in premenopausal versus postmenopausal women.⁴ Therefore, SWHR strongly supports this draft guidance, which warns against the use of menopausal status as exclusion criteria and stipulates that “[p]remenopausal women with adequate estrogen suppression and postmenopausal women should be equally eligible and included in clinical trials for drugs or combinations manipulating the hormonal axis.” Given the significance of long-term side effects within a younger patient population, we are also pleased to see directed collection of data surrounding the long-term health impacts of treatment.

We understand that the issues of fertility and fertility preservation are outside the scope of current guidance. However, treatment-related infertility is a crucial issue when considering cancer survivorship within the premenopausal population. For those with HR⁺ breast cancer, the need to postpone conception during long-term adjuvant endocrine therapy exacerbates this concern. Fertility concerns are associated with reduced quality of life, in addition to distress and symptoms of depression.⁵ SWHR encourages the continued consideration of fertility and fertility preservation within future clinical trials guidance, especially as research in this area continues to evolve. Issues such as infertility, which directly impact quality of life and mental health, must be prioritized in conjunction with physical care and treatment.

SWHR is grateful for the opportunity to provide feedback to the FDA on this draft guidance. If you have any questions, please do not hesitate to contact SWHR's Director of Public Policy and Government Affairs, Melissa Laitner, PhD, MPH, at melissa@swhr.org.

Sincerely,

Kathryn G. Schubert, MPP
President and Chief Executive Officer
Society for Women's Health Research

² Johnson RH, Chien FL, Bleyer A. Incidence of breast cancer with distant involvement among women in the United States, 1976 to 2009. *JAMA* 2013;309:800–5

³ Azim Jr. HR, Davidson NE, Ruddy KJ. Challenges in treating premenopausal women with endocrine-sensitive breast Cancer. *American Society of Clinical Oncology Educational Book*. 2016;36, 23-32.

⁴ Bardia A, Hurvitz S. Targeted therapy for premenopausal women with HR⁺ HER2- advanced breast cancer: Focus on special considerations and latest advance. *Clin Cancer Res*; 2018,24(21) 5206-5218.

⁵ *Ibid.*