



Submitted by: Chief Medical Officer
Name: Johnathan Lancaster, MD, PhD
Company/Organization: Myriad Genetic Laboratories, Inc.
Address: 320 Wakara Way, Salt Lake City, UT 84108
Phone: 801-505-5090
Email: jlancaster@myriad.com
Date of request: February 5, 2016
NCCN Guidelines Panel: Breast Cancer Screening and Diagnosis

Specific Changes: Add a list of commonly qualifying family history examples as sub-bullets or a footnote under the “Screening or Symptom Category” for “Women who have a lifetime risk >20% as defined by models that are largely dependent on family history” on page BSCR-2. Examples of breast cancer family histories that meet the 20% threshold include the following:

- Women with two first degree relatives with breast cancer at any age
- Women with three relatives with breast cancer at any age
- Women with one first degree relative who had breast cancer under age 60

FDA Clearance: Not applicable.

Rationale: Current guidelines from this NCCN panel, as well as those from the Genetic/Familial High-Risk Assessment: Breast and Ovarian panel (page ADDIT-2), support enhanced screening considerations when a patient meets >20% lifetime risk based on genetic test results (*BRCA1/2*, *CHEK2*, *ATM*, *PALB2*, etc.) and/or familial risk models (Claus, Tyrer-Cuzick, etc.). Although these risk models are broadly available, many physicians in a position to identify women for screening may not routinely run risk models as part of their screening evaluation. It may therefore be helpful to highlight common family history examples that would put women in a high risk category.

NCCN Guidelines for Colorectal Cancer Screening, page CSCR-6, provides similar guidance for specific colorectal cancer family history management.

The following articles are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

Metcalf KA¹, Finch A, Poll A, Horsman D, Kim-Sing C, Scott J, Royer R, Sun P, Narod SA. Breast cancer risks in women with a family history of breast or ovarian cancer who have tested negative for a BRCA1 or BRCA2 mutation. *Br J Cancer*. 2009 Jan 27;100(2):421-5.

Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet*. 2001 Oct 27;358(9291):1389-99.

Pharoah PD1, Day NE, Duffy S, Easton DF, Ponder BA. Family history and the risk of breast cancer: a systematic review and meta-analysis. *Int J Cancer*. 1997 May 29;71(5):800-9.

Rawal R1, Bertelsen L, Olsen JH. Cancer incidence in first-degree relatives of a population-based set of cases of early-onset breast cancer. *Eur J Cancer*. 2006 Nov;42(17):3034-40. Epub 2006 Sep 22.

Olsen JH1, Seersholm N, Boice JD Jr, Krüger Kjaer S, Fraumeni JF Jr. Cancer risk in close relatives of women with early-onset breast cancer--a population-based incidence study. *Br J Cancer*. 1999 Feb;79(3-4):673-9.

Sincerely,

A handwritten signature in black ink, appearing to be 'JL', written in a cursive style.

Johnathan Lancaster, MD, PhD
Chief Medical Officer
Myriad Genetic Laboratories Inc.