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NCCN Guidelines Panel: Genetic/Familial High Risk Assessment: Breast and Ovarian

Specific Changes:

- 1) Expand the *BRCA1/2* testing criteria to include all patients with a personal diagnosis of pancreatic cancer.
- 2) Add the following footnote to the new “Personal history of pancreatic cancer” testing criteria
 - Due to the link between pancreatic cancer and multiple additional genes (i.e., *ATM*, *PALB2*, *CDKN2A*, *MLH1*, *MSH2*) implicated in hereditary cancer syndromes, testing with a multigene panel should be strongly considered as an alternative to *BRCA1/2* testing alone.

FDA Clearance: Not applicable.

Rationale: Multiple recent studies have demonstrated high positive rates for hereditary cancer genes (including *BRCA1/2*) in patients with a personal history of pancreatic cancer regardless of age and family history.

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.

Catts ZA, Baig MK, Milewski B, Keywan C, Guarino M, Petrelli N. Statewide Retrospective Review of Familial Pancreatic Cancer in Delaware, and Frequency of Genetic Mutations in Pancreatic Cancer Kindreds. *Ann Surg Oncol*. 2016 May;23(5):1729-35.

Flores K, Dinh K, Rouleau E, Whalen G, Wassef W, LaFemina J. Identification of genetic risk for pancreatic adenocarcinoma. *Cancer Genet*. 2015 Nov;208(11):559-63.

Grant RC, Selander I, Connor AA, Selvarajah S, Borgida A, Briollais L, Petersen GM, Lerner-Ellis J, Holter S, Gallinger S. Prevalence of germline mutations in cancer predisposition genes in patients with pancreatic cancer. *Gastroenterology*. 2015 Mar;148(3):556-64.

Holter S, Borgida A, Dodd A, Grant R, Semotiuk K, Hedley D, Dhani N, Narod S, Akbari M, Moore M, Gallinger S. Germline *BRCA* Mutations in a Large Clinic-Based Cohort of Patients With Pancreatic Adenocarcinoma. *J Clin Oncol*. 2015 Oct 1;33(28):3124-9.

Hu C, Hart SN, Bamlet WR, Moore RM, Nandakumar K, Eckloff BW, Lee YK, Petersen GM, McWilliams RR, Couch FJ. Prevalence of Pathogenic Mutations in Cancer Predisposition Genes among Pancreatic Cancer Patients. *Cancer Epidemiol Biomarkers Prev*. 2016 Jan;25(1):207-11.

Roberts NJ, Norris AL, Petersen GM, Bondy ML, Brand R, Gallinger S, Kurtz RC, Olson SH, Rustgi AK, Schwartz AG, Stoffel E, Syngal S, Zogopoulos G, Ali SZ, Axilbund J, Chaffee KG, Chen YC, Cote ML, Childs EJ, Douville C, Goes FS, Herman JM, Iacobuzio-Donahue C, Kramer M, Makohon-Moore A, McCombie RW, McMahon KW, Niknafs N, Parla J, Pirooznia M, Potash JB, Rhim AD, Smith AL, Wang Y, Wolfgang CL, Wood LD, Zandi PP, Goggins M, Karchin R, Eshleman JR, Papadopoulos N, Kinzler KW, Vogelstein B, Hruban RH, Klein AP. Whole Genome Sequencing Defines the Genetic Heterogeneity of Familial Pancreatic Cancer. *Cancer Discov*. 2016 Feb;6(2):166-75.

Salo-Mullen EE, O'Reilly EM, Kelsen DP, Ashraf AM, Lowery MA, Yu KH, Reidy DL, Epstein AS, Lincoln A, Saldia A, Jacobs LM, Rau-Murthy R, Zhang L, Kurtz RC, Saltz L, Offit K, Robson ME, Stadler ZK. Identification of germline genetic mutations in patients with pancreatic cancer. *Cancer*. 2015 Dec 15;121(24):4382-8.

Zhen DB, Rabe KG, Gallinger S, Syngal S, Schwartz AG, Goggins MG, Hruban RH, Cote ML, McWilliams RR, Roberts NJ, Cannon-Albright LA, Li D, Moyes K, Wenstrup RJ, Hartman AR, Seminara D, Klein AP, Petersen GM. BRCA1, BRCA2, PALB2, and CDKN2A mutations in familial pancreatic cancer: a PACGENE study. *Genet Med*. 2015 Jul;17(7):569-77.

Sincerely,

A handwritten signature in black ink, appearing to read 'Johnathan Lancaster', with a stylized, cursive script.

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Myriad Genetic Laboratories Inc.