Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
PROSD-2 External request: Submission from Myriad Genetic Laboratories, Inc. 09/18/2020 Baseline evaluation, history and physical request: • Family cancer history. Please include the following footnote to provide guidance on the specific types of family cancer history to consider. o Family cancer history includes, but is not limited to, a first‐ or second‐degree relative with metastatic prostate cancer, ovarian cancer, male breast cancer, female breast cancer ≤45, colorectal or endometrial cancer ≤50, or pancreatic cancer or two or more first‐ or second degree relatives with breast, prostate, colorectal or endometrial cancer at any age. See NCCN Guidelines for Genetic/Familial High‐Risk Assessment: Breast, Ovarian and Pancreatic (CRIT‐1) and NCCN Guidelines for Genetic/Familial High‐Risk Assessment: Colorectal (LS‐1). For patients who meet hereditary risk assessment criteria established in these guidelines, germline genetic testing is recommended. • Replace footnote b as follows: o If there is a known or suspected cancer susceptibility gene mutation in the family, germline genetic testing is recommended and referral to a cancer genetics professional or urology professional should be considered. Certain germline mutations increase the risk for prostate cancer, earlier onset prostate cancer and/or more aggressive prostate cancer.	Based on a review of the data and discussion, the panel did not use the language proposed in the submission. However, the panel supported adding the following language: <u>Footnote a:</u> *Family or personal cancer history and/or family or personal history of high risk germline mutations can inform when to begin shared decision making regarding prostate cancer early detection. Family cancer history includes, but is not limited to, a first- or second-degree relative with metastatic prostate cancer, ovarian cancer, male breast cancer, female breast cancer ≤45 y, colorectal or endometrial cancer ≤50 y, or pancreatic cancer or two or more first- or second- degree relatives with breast, prostate (but not clinically localized Grade Group 1), colorectal or endometrial cancer at any age.* If there is a known or suspected cancer susceptibility gene, referral to a cancer genetics professional is recommended. BRCA1/2 pathogenic Mutation carriers have an increased risk of prostate cancer before age 65 years, and prostate cancer in men with germline BRCA2 *or HOXB13* mutations occurs earlier and is more likely to be associated with prostate cancer mortality. *For men with BRCA1, ATM, or mismatch repair (MLH1, MSH2, MSH6, PMS2) germline gene mutations timing of testing is less clear.* Consequently, *prostate cancer screening is recommended at age 40 for BRCA2 carriers, and* it is reasonable for men with *other* germline BRCA1/2 mutations to consider beginning shared decision making about PSA screening at age 40 years and to consider screening at annual intervals rather than every other year. See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic (CRIT-1) and *NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal (LS-1). Page EC, et al. Eur*	27	0	0	4

	Urol 2019;76:831-842. Giri VN, et al. J Clin Oncol 2020;38:2798-2811. See Submission.				
PROSD-2 External request: Submission from Myriad Genetic Laboratories, Inc. 09/18/2020 Risk assessment, age column request: • Revise the following in the flow chart to: o Age 40 – 75 y for African American men or those with germline mutations which increase the risk for prostate cancer[a,*] o Age 45 – 75 y o Age >75 y, in select patients • Add new Footnote (*): Men with *BRCA1/2* or *HOXB13* pathogenic mutations have a significantly increased risk for prostate cancer before age 65 years. Prostate cancer in men with *BRCA2* mutations occurs earlier and is more likely to be associated with prostate cancer mortality. Certain germline mutations increase the risk for prostate cancer, earlier onset prostate cancer and/or more aggressive prostate cancer. Consequently, for men with BRCA2 mutations it is reasonable to recommend shared decision – making about annual PSA screening beginning at age 40 years, or 10 years before the youngest prostate cancer diagnosis in the family. For men with *BRCA1, HOXB13, ATM, or mismatch repair (MLH1, MSH2, MSH6, PMS2)* germline gene mutations it is reasonable to consider shared decision – making beginning at age 40 years.	Based on a review of the data and discussion, the panel consensus supported revising the risk assessment column and footnotes a and b as follows: Risk assessment, changed: • Age 45–75 y, added *for average-risk patients* • Age 40–*75* y for those with: o *African ancestry* African-American men o Germline *BRCA1/2* mutations *that increase the risk for prostate cancer* o *Suspicious family history* Footnote a: Family or personal cancer history and/or family or personal history of high-risk germline mutations can inform when to begin shared decision-making regarding prostate cancer early detection. Family cancer history includes, but is not limited to, a first- or second-degree relative with metastatic prostate cancer, ovarian cancer, male breast cancer, female breast cancer ⩽45 y, colorectal or endometrial cancer ⩽50 y, or pancreatic cancer or two or more first- or second-degree relatives with breast, prostate (but not clinically localized Grade Group 1), colorectal or endometrial cancer at any age. If there is a known or suspected cancer susceptibility gene, referral to a cancer genetics professional is recommended. Mutation carriers have an increased risk of prostate cancer before age 65 years, and prostate cancer in men with germline BRCA2 or HOXB13 mutations occurs earlier and is more likely to be associated with prostate cancer mortality. For men with BRCA1, ATM, or mismatch repair (MLH1, MSH2, MSH6, PMS2) germline gene mutations timing of testing is less clear. Consequently, prostate cancer screening is recommended at age 40 for BRCA2 carriers, and it is reasonable for men with other germline mutations to consider beginning shared decision-making about PSA screening at age 40 years and to consider	27	0	0	4

	screening at annual intervals rather than every other year. See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic (CRIT-1) and NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal (LS-1). Page EC, Eur Urol 2019;76:831-842; Giri VN, et al. J Clin Oncol 2020;38:2798-2811.				
PROSD-3 External request: Submission from miR Scientific (09/29/20) Request footnote i, beginning with sentence 2: **"**However, there may be some patients who meet PSA standards for consideration of prostate biopsy, but for whom the patient and/or physician wish to further define risk. Free PSA may improve Cancer detection. **The miR Scientific Sentinel™ Prostate Cancer Test Platform provides significant accuracy in sensitivity and especially specificity to better inform decisions about the need for initial and/or repeat biopsy".** The probability of higher-grade cancer (Gleason Score > 3+4, Grade Group 2 or higher) may be further defined utilizing the **miR Scientific Sentinel™ Prostate Cancer Test Platform (preferred)** or the Prostate Health Index (PHI), SelectMDx. 4KScore, and EXODx Prostate Test" External request: Submission James McKiernan, MD – Columbia University Medical Center (09/23/20) Request Footnote i: For use as a molecular biomarker in the further evaluation of the indication for biopsy to determine cancer vs no cancer. As such, inclusion of the miR Scientific Sentinel Prostate Cancer Platform would be entirely appropriate in footnote i to be listed among the other molecular assays. If further validation studies confirm these performance characteristics demonstrated in the recent publication, the miR Scientific Test Platform might be considered "preferred".	Based on a review of the data and discussion, the panel consensus was not to make changes to the current recommendations [due to insufficient available data]. See Submission.	0	27	0	4

PROSD-3 and PROSD-4 External request: Submission from miR Scientific (09/29/20) Request footnote k: A negative MRI does not exclude the possibility of prostate cancer. Consider biomarkers **(e.g., miR Scientific Sentinel™ Prostate Cancer Test Platform as preferred**) and/or PSA density when deciding whether to avoid a biopsy in a man with a negative mpMRI result.	Based on a review of the data and discussion, the panel consensus was not to make changes to the current recommendations [due to insufficient available data]. See Submission.	0	27	0	4
PROSD-4 External request: Submission from miR Scientific (09/29/20) Request footnote p, beginning sentence 2: "Those patients with negative prostate biopsies should be followed with DRE and PSA. Tests that improve specificity in the post-biopsy setting including the **miR Scientific Sentinel™ Prostate Cancer Test Platform (preferred)** and percent free PSA, 4KScore, PHI, PCA3, and ConfirmMDx- should be considered in patients thought to be higher risk despite a negative prostate biopsy." External request: Submission James McKiernan, MD – Columbia University Medical Center (09/23/20) Request: Placement in footnotes I and p, along with the other identified molecular biomarker test assays to better define risk, including for monitoring individuals considered higher risk but with a negative first biopsy. Once again if the published sensitivity and specificity results are confirmed in future validation studies, it would suggest the miR Scientific Test Platform could be identified as the "preferred" biomarker in this area.	Based on a review of the data and discussion, the panel consensus was not to make changes to the current recommendations [due to insufficient available data]. See Submission.	0	27	0	4

NCCN Guidelines for Prostate Cancer Early Detection V.1.2021 – Annual on 10/19/2020