The following articles are submitted in support of this proposed change:


**FDA Clearance:** FDA clearance is not required for this assay because the assay is performed in the central laboratory at Genomic Health that is regulated and certified under the Clinical Laboratory Improvement Amendments (CLIA) and the College of American Pathologists (CAP).

**Rationale:** The reporting of prospective outcomes from multiple datasets, including the RS <11 arm of TAILORx, the WSG PlanB trial (RS <12), the Israeli Clalit registry (RS <18), and the SEER/NCI analysis (RS <18) that include >38K ER+, EBC patients treated based on the RS result, is definitive evidence that the 21-gene RT-PCR assay identifies patients who should not be treated with and do not benefit from CT. In addition, based on these four studies, the 8th edition of the AJCC is now exclusively utilizing the 21-gene RT-PCR assay to downstage patients with T1/T2, N0, M0, ER+, HER2-negative EBC as high as IIIA down to IA, if they have RS <11. This underscores the importance of having the 21-gene RT-PCR assay RS information on every appropriate patient as part of the standard diagnostic and staging work-up prior to treating with systemic therapy.

The following articles are submitted in support of this proposed change:


Sincerely,

[Signature]

Christy Russell, MD
Senior Director, Medical Affairs
Genomic Health, Inc.