On behalf of HaloDx, I respectfully request the NCCN Colon Cancer Panel to review the enclosed data for inclusion of the Imunoscore® Colon testing as part of the standard of care management of patients with localized colon cancer as an adjunct to the TNM staging in the postsurgical pathologic review.

Specific Changes: Recommend the Imunoscore® Colon assay as an additional routine component of the Pathologic Staging (COL-3) and Pathologic Review (COL-B) indicating that Imunoscore® Colon is the unique standardized and validated test allowing an accurate measure of the immune cell infiltrate in tumors for improving the risk of recurrence assessment of patients with localized colon cancer.

FDA Clearance: FDA clearance is not required for the Imunoscore® assay as it is performed in the central laboratory which is regulated and certified under the Clinical Laboratory Improvement Amendments (CLIA).

Rationale: An international multicentre study (including over 3500 stage I-III patients from 13 countries) led by the Society for Immunotherapy of Cancer (SITC, US) further validated the prognostic value of Imunoscore® and demonstrated its superiority to that of existing tumor parameters including the T-stage, the N-stage, the grade of differentiation, the venous emboli, the lymphatic invasion, the perineural invasion, and the MSI/MMR status, thereby supporting the implementation of Imunoscore® as a new component for a TNM-Immune (TNM-I) classification of cancer to improve prognostication. In support of the proposed change, the SITC indicated the characterization of tumor immunity with Imunoscore® as a valid prognostic indicator. It was also shown that Imunoscore® provided significant prognostic information in low- (T1-3N1) and high-risk (T4 or N2) subsets of stage III colon cancer from a phase III clinical trial.

Altogether, the data support that Imunoscore® is a critical addition to clinical care of patients with localized colon cancer to provide a more accurate prognosis, thereby helping with treatment decision.
The following articles are submitted in support of this proposed change:

1) Galon J, et al. Type, density, and location of immune cells within human colorectal tumors predict clinical outcome. *Science* 2006; 313:1960-4 (*IF: 33.6*) [*T cell infiltrates have a prognostic value superior to and independent of the TNM classification and histological prognostic factors suggesting that recurrence and survival are governed in large part by the state of the local adaptive immune response*]


5) Pages F et al. International validation of the consensus Immunoscore for the classification of colon cancer: a prognostic and accuracy study. *Lancet*. 2018 May 26;391(10135):2128-2139. (*IF: 47.8*) [*Largest international consortium validating a standardized immune parameter to stratify patients with colon cancer. Immunoscore had a prognostic value superior to that of existing tumor parameters*]

6) Sinicrope F et al. Immunoscore to provide prognostic information in low- (T1-3N1) and high-risk (T4 or N2) subsets of stage III colon carcinoma patients treated with adjuvant FOLFOX in a phase III trial (NCCTG N0147; Alliance). *J Clin Oncol* 36, 2018 (suppl 4S; abstr 614) - *Presented at ASCO GI 2018* [*Clinical validation in stage III patients from a phase III clinical trial. The data underscored the limitation of T and N staging*]

Thank you for your review of this submission.

Sincerely,

![Signature]

Fabienne Hermitte, PhD
VP Medical Affairs
HalioDx