**CAC-MolDX: Molecular Testing for Detection of Upper Gastrointestinal Metaplasia, Dysplasia, Neoplasia Reconsideration Questions**

EGD-esophagogastroduodenoscopy
BE- Barrett's Esophagus
EAC- esophageal adenocarcinoma
GERD- gastroesophageal reflux disease

1. What presenting signs and symptoms would result in your referral for an EGD as part of BE evaluation (or other overlapping reason) in Medicare patients? Are all guidelines and clinical risk factors for BE considered equally? Is pathology required for the diagnosis?
2. Are all patients eligible for surveillance EGD referred for the procedure? What considerations are made for selecting eligible patients for EGD referral? How is risk/benefit evaluated?
3. What are the causes of lack of appropriate EGD referral? What are the causes of EGD non-compliance, if known or suspected?
4. What are the current limitations of traditional BE and EAC surveillance by EGD? What percentage of EGDs performed result in indeterminate results?
5. If a non-invasive or minimally-invasive test could reliably identify patients who are NOT likely to have BE or adenocarcinoma (i.e. "rule-out" test), how would such a test impact patient management? What evidence supports this? Would you still feel compelled to perform an EGD?
6. How accurate would such a test need to be to provide sufficient confidence in decision making to "rule-out" BE or adenocarcinoma? What is the harm of false positive results and the optimal balance between sensitivity and specificity?
7. If a non-invasive or minimally-invasive test could reliably identify patients who ARE likely to have BE or adenocarcinoma (i.e. "rule-in" test), how would such a test impact patient management? What evidence supports this?
8. How accurate would such a test need to be to provide sufficient confidence in decision making to "rule-in" BE or adenocarcinoma? What is the harm of false negative results and the optimal balance between sensitivity and specificity?
9. Have you used any such test? Please provide your experience and assessment of test performance and reliability.
10. Do you believe the current evidence supports the clinical use of existing tests? What evidence is the most compelling case to support their use? What evidence supports clinical utility and validity of these services?
11. Have these tests demonstrated the ability to identify more BE and EAC patients than traditional surveillance techniques? If not, how likely is this to be true? What is a reasonable expectation for improved early detection with such surveillance tools given that 50% of EAC patients do not present with GERD?
12. What are your concerns for the implementation of the use of these tests? What are the limitations in the existing data?
13. What are your concerns for using these tests for BE workup, given they do not evaluate other GEJ pathologies? Does it matter if the analytes measured in these tests are correlative to disease vs. causative or linked with pathogenesis?

14. Does the evidence support the accuracy of these tests in long segment disease, short segment disease, or both? Does this matter for test selection or clinical value?
15. Is the data generated in the BEST1-3 trials relevant to the US population? What are the differences between BE surveillance in the US and UK? What evidence and conclusions from BEST1-3 are NOT relevant to US decision-making practices?
16. What are the concerns around operator error in sample retrieval, given a highly variable sample failure rate in the literature?
17. Are there concerns about test accuracy in detecting low vs. high-grade dysplasia?