Prepared Comments for Molecular and Clinical Genetics Panel of the Medical Devices Advisory Committee Docket No. FDA–2023–N–4720

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HCA Healthcare Overview

182 Hospitals

2K+ sites of care

20 states and the **United Kingdom**

41.7M Patient Encounters	**2.1M** Admissions	**1.6M** Surgeries	**8.4M** ER Visits
1.6M Cancer Patient Encounters	**130K** New Cancer Patients	**>25K** MCED Trial Participants	**~294K** Colleagues*

All volumes are estimated one-year volumes except MCED trial participants which represent aggregate participation in MCED studies since 2017.
*As of Dec. 31, 2022

Escalating Urgency To Address the Unmet Need

- Overall, 70% of cancer deaths are attributable to cancers without an effective screening strategy[1]
- Traditional cancer by cancer screening strategies cannot effectively address this need
- Multi-Cancer Early Detection (MCED) tests, well-suited to detect highly lethal cancers, should be recognized as distinct from and complementary to traditional breast, colon and cervical cancer screenings
- Community health systems, integral to any population-level screening strategy, are increasingly able to identify and engage individuals at risk for multiple cancers but lack comprehensive screening tools
- Current modeling suggests the potential to save 100,000 additional lives annually when complementing existing cancer screening studies[2]

1. SEER Stat Database: Incidence - SEER 18 Regs Research Data, Nov 2017 Sub. Includes persons aged 50+ diagnosed 2006-2015
2. Clarke CA, Hubbell E, Kurian AW, Colditz GA, Hartman AR, Gomez SL. Projected Reductions in Absolute Cancer-Related Deaths from Diagnosing Cancers Before Metastasis, 2006-2015. Cancer Epidemiol Biomarkers Prev. 2020 May;29(5):895-902. doi: 10.1158/1055-9965.EPI-19-1366. Epub 2020 Mar 30. PMID: 32229577.

MCED Study Design and Endpoint Considerations

- MCED testing is fundamentally different from existing “one test, one cancer” screening strategies, and study endpoints should be tailored to the distinct advantages of a shared cancer signal and aggregate cancer detection
- Head-to-head comparisons between MCED detection of a single cancer type versus performance of an established single cancer screening modality would not be clinically meaningful
- Given rapid improvements in technology, we would argue against mandates for mortality endpoints as the timeframe for study results would provide insight on out-of-date technology
- Recognizing AJCC Stage Groups define populations with similar prognoses, the conversion of a significant percentage of patients from advanced stage (III/IV) to early stage (I/II) would represent a clinically meaningful endpoint
- FDA should consider surrogate and patient-centric endpoints for population cancer screening that have been suggested in the literature, such as stage shift[1], stage-specific incidence, quality-of-life outcomes, the proportion of patients treated with curative intent intervention (eg, surgery[2]) and/or modeled cancer-specific mortality[3]

1. Hubbell E, Clarke CA, Aravanis AM, Berg CD. Modeled Reductions in Late-stage Cancer with a Multi-Cancer Early Detection Test. Cancer Epidemiol Biomarkers Prev. 2021 Mar;30(3):460-468. doi: 10.1158/1055-9965.EPI-20-1134. Epub 2020 Dec 16. PMID: 33328254.
2. Shaib Y, Davila J, Naumann C, El-Serag H. The impact of curative intent surgery on the survival of pancreatic cancer patients: a U.S. Population-based study. Am J Gastroenterol. 2007 Jul;102(7):1377-82. doi: 10.1111/j.1572-0241.2007.01202.x. Epub 2007 Mar 31. PMID: 17403071.
3. Clarke CA, Hubbell E, Kurian AW, Colditz GA, Hartman AR, Gomez SL. Projected Reductions in Absolute Cancer-Related Deaths from Diagnosing Cancers Before Metastasis, 2006-2015. Cancer Epidemiol Biomarkers Prev. 2020 May;29(5):895-902. doi: 10.1158/1055-9965.EPI-19-1366. Epub 2020 Mar 30. PMID: 32229577.

Accelerating Insights for MCED in the Community Setting

- Robust clinical validation of MCED performance currently exists in peer-reviewed literature and demonstrates remarkable consistency across retrospective and prospective studies with a compelling positive predictive value and high specificity
- Sarah Cannon has pioneered a national support infrastructure, including a broad retrospective protocol, to support community providers and patients while accelerating knowledge generation
- Our experience has demonstrated the feasibility of primary-care based MCED offerings:
  - Across a sample size of more than 1,600 patients tested, 14 individuals had a cancer signal detected; of those, 11 persons have completed diagnostic evaluation to date
  - Among the 6 confirmed cancers, 3 were early stage one cancers including Stage 1 Oropharyngeal cancer, Stage 1B pancreatic adenocarcinoma, Stage IB breast cancer – all three have received curative intent treatment
  - Amongst the 6 confirmed cancer diagnoses, the average time to confirmation/resolution was 44.17 days (median = 43.5 days)
  - Among 5 false positives, only one patient required an invasive procedure that was well tolerated

Conclusions

- MCED platforms represent a promising new paradigm to address a critical unmet need related to detection of highly lethal cancers

- Study endpoints should recognize the unique nature of MCED testing versus traditional “one test, one cancer” screening and should embrace appropriate surrogate endpoints for cancer-specific mortality that allow for timely and actionable insights

- Community health systems, likely to be critical to the success or failure of any population level screening programs, should be key participants in study design efforts and well represented in clinical trials

Thank You!