Comments to the Food and Drug Administration Molecular and Clinical Genetics Panel of the Medical Devices Advisory Committee Open Hearing on Multi-Cancer Detection Tests (MCEDs), November 29, 2023

Robert A. Smith, PhD
Senior Vice President, Cancer Screening
Director, ACS Center for Cancer Screening and Early Cancer Detection Research
American Cancer Society
Atlanta GA

American Cancer Society®

The Burden of Cancer in the U.S. is High

- The ACS estimates that there will be ~ 1.9 million new cases of cancer and ~ 610,000 deaths in the U.S. in 2023
  - Cancer is the leading cause of death from all causes before the age of 85
  - Cancer is the leading cause premature mortality from all causes of death
  - Death from cancer accounted for 9.3 million person-years of life-lost in 2018, and an average of 15.5 years of life lost per person

- **Approximately 60% of the cancer deaths in men and 55% of the cancer deaths in women are from cancers without a screening strategy**

Source: American Cancer Facts & Figures 2023

American Cancer Society®

In this group of 18 common cancers, each one has more favorable prognosis if it is found at an earlier stage (local & regional) vs. a distant stage. *This is true for the 13 cancers for which there is no recommended screening strategy*

Table 8. Five-year Relative Survival Rates* (%) by Stage at Diagnosis, US, 2012-2018

	All stages	Local	Regional	Distant		All stages	Local	Regional	Distant
Breast (female)	91	99	86	30	Non-Hodgkin lymphoma	74	86	77	67
Colon & rectum†	65	91	73	14	Oral cavity & pharynx	68	86	69	40
Colon	63	91	72	13	Ovary	50	93	74	31
Rectum	68	90	74	17	Pancreas	12	44	15	3
Esophagus	21	47	26	6	Prostate	97	>99	>99	32
Kidney & renal pelvis	77	93	72	15	Stomach	33	72	33	6
Larynx	61	78	46	34	Thyroid	98	>99	98	53
Liver‡	21	36	13	3	Urinary bladder§	77	70	39	8
Lung & bronchus	23	61	34	7	Uterine cervix	67	92	59	17
Melanoma of the skin	94	>99	71	32	Uterine corpus	81	95	70	18

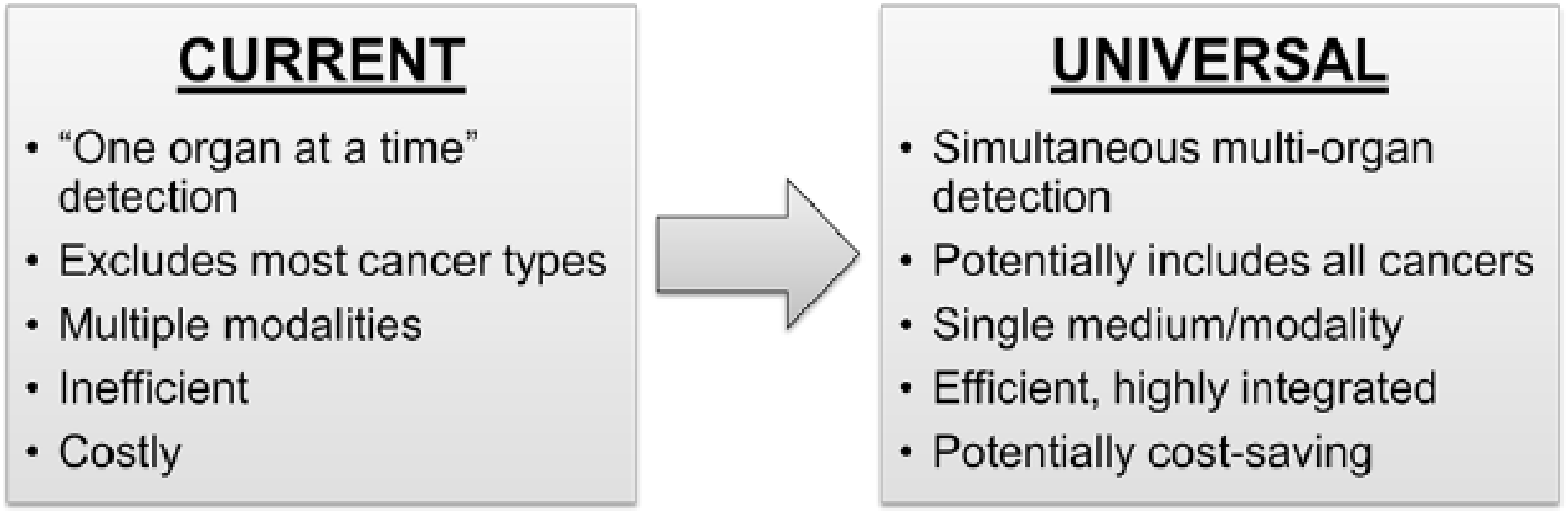
*Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 17 areas from 2012-2018, all followed through 2019. Rates by stage reflect Combined Summary Stage (2004+). †Excludes appendix. ‡Includes intrahepatic bile duct. §Rate for in situ cases is 96%.

Local: an invasive malignant cancer confined entirely to the organ of origin. **Regional:** a malignant cancer that 1) has extended beyond the limits of the organ of origin directly into surrounding organs or tissues; 2) involves regional lymph nodes; or 3) has both regional extension and involvement of regional lymph nodes. **Distant:** a malignant cancer that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis to distant organs, tissues, or via the lymphatic system to distant lymph nodes.

Source: SEER*Explorer, National Cancer Institute, 2022. Available from https://seer.cancer.gov/explorer/. Colon & rectal cancer – SEER*Stat software (version 8.4.0.1), National Cancer Institute, 2022.

American Cancer Society®

Current single-organ and future universal cancer screening approaches: a conceptual comparison of features



The potential for significant progress in adding new single cancer screening tests to those that exist is very low. MCEDs represent a *potential* "game changer" in the control of cancer.

Precision Oncology (2018) 2:23 ; doi:10.1038/s41698-018-0066-x

American Cancer Society®

Key Considerations for the Evaluation of MCEDs--Benefits

- **The goal of cancer screening, for single cancers or multiple cancers, is to reduce the incidence of advanced disease**
- **Thus, the primary endpoints in MCEDs should be:**
  - **The aggregate incidence rate of advanced cancer for cancers included in a MCED**
  - **The aggregate death rate for cancers included in a MCED**
- **Based on experience to date, a reduction in the incidence of advanced disease would be expected to be followed by a reduction in morbidity and mortality**
- **From an evaluation design standpoint, a focus on individual cancers would require impossible sample sizes, and is at odds with the design of an MCED**
- Although there is interest in how MCEDs perform at the level of the individual cancers, ***these are secondary endpoints*** to better understand test performance, the natural history of the disease, and for R&D purposes

American Cancer Society®

Key Considerations for the Evaluation of MCEDs—Safety and harms

- **Cancer screening tests should be regarded as a process of information gathering to determine if the patient has cancer**
- We should measure conventional screening outcome measures (sensitivity, specificity, PPV, etc.), as well as features of the process of evaluation of positive findings. *Care pathways exist….are they being followed?*
- Concerns about anxiety associated with recall have not shown lasting effect in single cancer screening, and anxiety is measurably reduced with clear communication from providers.
- Although the possibility for some overdiagnosis must be considered, it is very difficult to measure with confidence, and it does not appear to be a serious issue in the intended use of these tests.
- Concerns that individuals will forego conventional screening tests should be regarded as a cautionary reminder for clear communication to providers and the public that MCEDs are not intended to replace conventional screening tests.

American Cancer Society®

On behalf of the American Cancer Society, we thank the Committee for the opportunity to provide testimony on the important issue of evaluation of MCED tests