SUPPLEMENTAL DATA FILE 3a.

DEFINITIONS FOR VALUE DOMAIN TYPES AND SPECIFIC VALUES

Cause of Death Definitions

Due to or Related to Cancer	Cancer (1) is the underlying cause of death OR (2) appears elsewhere in the chain of morbid events leading directly to death For example, death due to cerebral herniation due to glioblastoma would be "due to or related to cancer."
Due to or Related to Cancer Treatment	Cancer treatment appears anywhere in the chain of morbid events leading directly to death. For example, death due to heart failure due to left ventricular dysfunction due to treatment with doxorubicin due to small cell lung cancer would be "due to or related to cancer treatment" (as well as "due to or related to cancer").
Neither Due to nor Related to Cancer or Cancer Treatment	Neither cancer nor cancer treatment appears in the chain of events leading directly to death

Ethnicity and Race Definitions from OMB Directive 15 (Revised)

Hispanic or Latino or Spanish Origin	A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.

American Indian or Alaska Native	A person having origins in any of the original peoples of North and South America (including Central America) and who maintain tribal affiliation or community attachment.
Asian	A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.
Black or African American	A person having origins in any of the black racial groups of Africa.
Native Hawaiian or Other Pacific Islander	A person having origins in any of the original peoples of Hawaii, Guan, Samoa, or other Pacific Islands.
White	A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Summary Stage Definitions

(Adapted From NCI SEER Training Modules)

Localized	A localized cancer is a malignancy limited to the organ of origin; it has spread no farther than the organ in which it started. There is infiltration past the basement membrane of the epithelium into the functional part of the organ, but there is no spread beyond the boundaries of the organ.
Regional	Regional stage refers to tumor extension beyond the limits of the organ of origin. Although the boundary between localized and regional tumor extension is usually well-identified, the boundary between regional and distant spread is not always clear. So, regional stage is perhaps the broadest category as well as the most difficult to properly identify
Metastatic	Distant metastases are tumor cells that have broken away from the primary tumor, have traveled to other parts of the body, and have begun to grow at the new location.

SUPPLEMENTAL DATA FILE 3b.

EXPANDED LIST OF CANCER SITES AND HISTOLOGY

The initial dropdown menu would have the 30 highest level options. Each of those highest level options would expand to the second level choices that would be the actual entries for the cancer site elements. Each of the second level choices corresponds to an ICD-O-3 Topographical Code. Each of the second level choices can further be expanded to select histologic/morphological type for elements that require that information (an example has been provided for "lip"). Each of the third level choices corresponds to an ICD-O-3 Morphological Code.

		ICD-O-3 Topographical Code	ICD-O-3 Morphological Code
1	**None**		
	None		
2	**Unknown**		
	Unknown		
3	**Oral Cavity & Pharynx**		
	Lip	**C00**	
	Neoplasm		800
	Carcinoma, NOS		801
	Carcinoma, Undifferentiated, NOS		802
	Giant & Spindle Cell Carcinoma		803
	Papillary Carcinoma, NOS		805
	Squamous Cell Carcinoma, NOS		807
	Lymphoepithelial Carcinoma		808
	Adenocarcinoma, NOS		814
	Adenoid Cystic & Cribriform Carcinoma		820
	Bronchio-Alveolar Adenocarcinoma		825
	Papillary Adenocarcinoma, NOS		826
	Mucoepidermoid Carcinoma		843
	Mucinous Adenocarcinoma		848
	Nevi & Melanomas		872
	Amelanotic Melanoma		873
	Malignant Melanoma in Junctional Nevus		874

	Epithelioid Cell Melanoma		877
	Mixed Tumor, Malignant, NOS		894
	Kaposi Sarcoma		914
	Follicular & Marginal Lymphoma, NOS		969
	Lymphoid Leukemia, NOS		982
	Base of Tongue	**C01**	
	Other and Unspecified Parts of Tongue	**C02**	
	Gum	**C03**	
	Floor of Mouth	**C04**	
	Palate	**C05**	
	Other and Unspecified Parts of Mouth	**C06**	
	Parotid Gland	**C07**	
	Other and Unspecified Major Salivary Glands	**C08**	
	Tonsil	**C09**	
	Oropharynx	**C10**	
	Nasopharynx	**C11**	
	Pyriform Sinus	**C12**	
	Hypopharynx	**C13**	
	Other and Ill-Defined Sites in Lip, Oral Cavity, and Pharynx	**C14**	
4	**Digestive System**		
	Esophagus	**C15**	
	Stomach	**C16**	
	Small Intestine	**C17**	
	Colon	**C18**	
	Rectosigmoid Junction	**C19**	
	Rectum	**C20**	
	Anus and Anal Canal	**C21**	
	Liver and Intrahepatic Bile Ducts	**C22**	
	Gallbladder	**C23**	
	Other and Unspecified Parts of Biliary Tract	**C24**	
	Pancreas	**C25**	
	Other and Ill-Defined Digestive Organs	**C26**	

5	**Respiratory System and Intrathoracic Organs**		
	Nasal Cavity and Middle Ear	**C30**	
	Accessory Sinuses	**C31**	
	Larynx	**C32**	
	Trachea	**C33**	
	Bronchus and Lung	**C34**	
	Thymus	**C37**	
	Heart, Mediastinum, and Pleura	**C38**	
	Other and Ill-Defined Sites Within Respiratory System and Intrathoracic Organs	**C39**	
6	**Bones, Joints, and Articular Cartilage**		
	Bones, Joints, and Articular Cartilage of Limbs	**C40**	
	Bones, Joints, and Articular Cartilage of Other and Unspecified Sites	**C41**	
7	**Hematopoietic and Reticuloendothelial Systems**		
	Hematopoietic and Reticuloendothelial Systems	**C42**	
8	**Skin**		
	Skin	**C44**	
9	**Retroperitoneum and Peritoneum**		
	Retroperitoneum and Peritoneum	**C48**	
10	**Connective, Subcutaneous, and Other Soft Tissues**		
	Connective, Subcutaneous, and Other Soft Tissues	**C49**	
11	**Breast**		
	Breast	**C50**	
12	**Female Genital Organs**		
	Vulva	**C51**	
	Vagina	**C52**	
	Cervix Uteri	**C53**	
	Corpus Uteri	**C54**	
	Uterus, NOS	**C55**	
	Ovary	**C56**	
	Other and Unspecified Female Genital Organs	**C57**	
13	**Placenta**		
	Placenta	**C58**	

14	**Male Genital Organs**		
	Penis	**C60**	
	Prostate	**C61**	
	Testis	**C62**	
	Other and Unspecified Male Genital Organs	**C63**	
15	**Urinary System**		
	Kidney	**C64**	
	Renal Pelvis	**C65**	
	Ureter	**C66**	
	Bladder	**C67**	
	Other and Unspecified Urinary Organs	**C68**	
16	**Eye and Adnexa**		
	Eye and Adnexa	**C69**	
17	**Peripheral Nerves and Autonomic Nervous System**		
	Peripheral Nerves and Autonomic Nervous System	**C47**	
18	**Brain and Spinal Cord**		
	Meninges	**C70**	
	Brain	**C71**	
	Spinal Cord, Cranial Nerves, and Other Parts of Central Nervous System	**C72**	
19	**Endocrine**		
	Thyroid Gland	**C73**	
	Adrenal Gland	**C74**	
	Other Endocrine Glands and Related Structures	**C75**	
20	**Other and Ill-Defined Sites**		
	Other and Ill-Defined Sites	**C76**	
21	**Lymph Nodes**		
	Lymph Nodes	**C77**	
22	**Unknown Primary Site**		
	Unknown Primary Site	**C80**	
Additional Choices When Identifying Fluid Sampling Sites			
23	**Blood/Serum/Plasma**		
	Hematopoietic and Reticuloendothelial Systems	**C42**	

24	**Urine**		
	Bladder	**C67**	
25	**Ascitic Fluid**		
	Retroperitoneum and Peritoneum	**C48**	
26	**CSF**		
	Spinal Cord, Cranial Nerves, and Other Parts of Central Nervous System	**C72**	
27	**Pleural Fluid**		
	Heart, Mediastinum, and Pleura	**C38**	
28	**Pericardial Fluid**		
	Heart, Mediastinum, and Pleura	**C38**	
29	**Sputum**		
	Other and Unspecified Parts of Mouth	**C06**	
30	**Bone Marrow**		
	Bones, Joints, and Articular Cartilage of Limbs	**C40**	
	Bones, Joints, and Articular Cartilage of Other and Unspecified Sites	**C41**	

SUPPLEMENTAL DATA FILE 3c.

PERFORMANCE STATUS CHOICES

Five first level choices, some of which expand.

1 **ECOG/Zubrod/WHO**
- ECOG/Zubrod/WHO: 0
- ECOG/Zubrod/WHO: 1
- ECOG/Zubrod/WHO: 2
- ECOG/Zubrod/WHO: 3
- ECOG/Zubrod/WHO: 4
- ECOG/Zubrod/WHO: 5

2 **Karnofsky**
- Karnofsky: 100%
- Karnofsky: 90%
- Karnofsky: 80%
- Karnofsky: 70%
- Karnofsky: 60%
- Karnofsky: 50%
- Karnofsky: 40%
- Karnofsky: 30%
- Karnofsky: 20%
- Karnofsky: 10%
- Karnofsky: 0

3 **Lansky**
- Lansky: 100%
- Lansky: 90%
- Lansky: 80%
- Lansky: 70%
- Lansky: 60%
- Lansky: 50%
- Lansky: 40%
- Lansky: 30%
- Lansky: 20%
- Lansky: 10%
- Lansky: 0

4 **Other**

5 **Unknown**

SUPPLEMENTAL DATA FILE 3d.

CANCER GRADING SCALES

Based on Cancer Protocol Templates from the College of American Pathologists

Breast

Breast DCIS

- Nuclear Grade I (low)
- Nuclear Grade II (intermediate)
- Nuclear Grade III (high)

Invasive Breast

- Nottingham Grade 1
- Nottingham Grade 2
- Nottingham Grade 3
- Only microinvasion present (not graded)
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy
- Score cannot be determined

Central Nervous System

Brain/Spinal Cord/Peripheral Nerve/Pituitary

- WHO Grade I
- WHO Grade II
- WHO Grade III
- WHO Grade IV
- Not Assigned

Endocrine

Adrenal

- Low (≤20 mitoses per 50 high-power fields)
- High (>20 mitoses per 50 high-power fields)

Appendix, Well-Differentiated Neuroendocrine Tumor

- Not applicable
- GX (cannot be assessed)
- G1 (low)
- G2 (intermediate)

Colon & Rectum, Well-Differentiated Neuroendocrine Tumor

- Not applicable
- GX (cannot be assessed)
- G1 (low)
- G2 (intermediate)

Pancreas, Well-Differentiated Neuroendocrine Tumor

- Not applicable
- GX (cannot be assessed)
- G1 (low)
- G2 (intermediate)

Small Bowel, Well-Differentiated Neuroendocrine Tumor

- Not applicable
- GX (cannot be assessed)
- G1 (low)
- G2 (intermediate)

Stomach, Well-Differentiated Neuroendocrine Tumor

- Not applicable
- GX (cannot be assessed)
- G1 (low)
- G2 (intermediate)

Thyroid, Carcinomas Only (Not Lymphomas, Sarcomas, or Metastases)

- Papillary Carcinoma
- Follicular Carcinoma
- Poorly Differentiated Thyroid Carcinoma
- Undifferentiated (Anaplastic) Carcinoma
- Medullary Carcinoma
- Carcinoma, Type Cannot be Determined
- Other

Gastrointestinal

Ampulla of Vater

- Not applicable (histologic type not usually graded)
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)
- Other

Anus

- Not applicable (histologic type not usually graded)
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)
- Other

Appendix

- Not applicable (histologic type not usually graded)
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)

Colon and Rectum

- Not applicable
- Cannot be determined
- Low grade (well-differentiated to moderately differentiated)
- High grade (poorly differentiated to undifferentiated)

Distal Extrahepatic Bile Ducts

- Not applicable (histologic type not usually graded)
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)

Esophagus

- Not applicable (histologic type not usually graded)
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)

Gallbladder

- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)
- Other

GIST

- GX (cannot be assessed)
- G1 (low grade; mitotic rate $\leq$ 5/5mm^2)
- G2 (high grade; mitotic rate >5/5mm^2)

Hepatocellular Carcinoma

- Not applicable
- GX (cannot be assessed)
- GI (well differentiated)
- GII (moderately differentiated)

GIII3 (poorly differentiated)
GIV (undifferentiated/anaplastic)
Other

Intrahepatic Bile Ducts

Not applicable
GX (cannot be assessed)
G1 (well differentiated)
G2 (moderately differentiated)
G3 (poorly differentiated)
G4 (undifferentiated)
Other

Pancreas (Exocrine)

Ductal Carcinoma

Not applicable
GX (cannot be assessed)
G1 (well differentiated)
G2 (moderately differentiated)
G3 (poorly differentiated)
G4 (undifferentiated)
Other

Adenocarcinoma

GX (cannot be assessed)
G1 (well differentiated; greater than 95% of tumor composed of glands)
G2 (moderately differentiated; 50% to 95% of tumor composed of glands)
G3 (poorly differentiated; (49% or less of tumor composed of glands)
G4 (undifferentiated)

Perihilar Bile Ducts

Not applicable
GX (cannot be assessed)
G1 (well differentiated) (adenocarcinomas: greater than 95% of tumor composed of glands)
G2 (moderately differentiated) (adenocarcinomas: 50% to 95% of tumor composed of glands)
G3 (poorly differentiated) (adenocarcinomas: 49% or less of tumor composed of glands)
G4 (undifferentiated)
Other

Small Intestine

Not applicable
GX (cannot be assessed)
G1 (well differentiated) (adenocarcinomas: greater than 95% of tumor composed of glands)
G2 (moderately differentiated) (adenocarcinomas: 50% to 95% of tumor composed of glands)
G3 (poorly differentiated) (adenocarcinomas: 49% or less of tumor composed of glands)
G4 (undifferentiated or small cell carcinoma)
Other

Stomach

Not applicable

GX (cannot be assessed)

G1 (well differentiated) (adenocarcinomas: greater than 95% of tumor composed of glands)

G2 (moderately differentiated) (adenocarcinomas: 50% to 95% of tumor composed of glands)

G3 (poorly differentiated or signet-ring cell carcinoma) (adenocarcinomas: 49% or less of tumor composed of glands)

G4 (undifferentiated)

Other

Genitourinary

Kidney (Fuhrman Grading System)

Not applicable

GX (cannot be assessed)

G1 (nuclei round, uniform, approximately 10 µm; nucleoli inconspicuous or absent)

G2 (nuclei slightly irregular, approximately 15 µm; nucleoli evident)

G3 (nuclei very irregular, approximately 20 µm; nucleoli large and prominent)

G4 (nuclei bizarre and multilobated, 20 µm or greater; nucleoli prominent, chromatin clumped)

Penis

Not applicable

GX (cannot be assessed)

G1 (well differentiated)

G2 (moderately differentiated)

G3 (poorly differentiated)

Prostate Gland (Gleason Score)

Gleason 1 (well differentiated)

Gleason 2 (well differentiated)

Gleason 3 (well differentiated)

Gleason 4 (well differentiated)

Gleason 5 (moderately differentiated)

Gleason 6 (moderately differentiated)

Gleason 7 (moderately differentiated)

Gleason 8 (poorly differentiated)

Gleason 9 (poorly differentiated)

Gleason 10 (poorly differentiated)

Testis

Not applicable

Ureter, Renal Pelvis

Not applicable

Cannot be determined

Urothelial carcinoma

Low-grade

High-grade

Other

Squamous cell carcinoma or adenocarcinoma

GX (cannot be assessed)

G1 (well differentiated)

G2 (moderately differentiated)

G3 (poorly differentiated)

Other

Other carcinoma

Low-grade

High-grade

Other

Urethra

Not applicable

Cannot be determined

Urothelial carcinoma

Low-grade

High-grade

Other

Squamous cell carcinoma or adenocarcinoma

GX (cannot be assessed)

G1 (well differentiated)

G2 (moderately differentiated)

G3 (poorly differentiated)

Other

Other carcinoma

Low-grade

High-grade

Other

Urinary Bladder

Not applicable

Cannot be determined

Urothelial carcinoma

Low-grade

High-grade

Other

Squamous cell carcinoma or adenocarcinoma

GX (cannot be assessed)
G1 (well differentiated)
G2 (moderately differentiated)
G3 (poorly differentiated)
Other

Other carcinoma

Low-grade
High-grade
Other

Gynecologic

Endometrium

Endometrioid and Mucinous Adenocarcinomas (FIGO Grading System)

FIGO Grade 1
FIGO Grade 2
FIGO Grade 3

For Other Carcinomas

G1 (well differentiated)
G2 (moderately differentiated)
G3 (poorly differentiated)
Not Applicable
Other

Ovary, Fallopian Tube

All Carcinomas (except Clear Cell Carcinoma, Low and High Grade Serous Carcinoma, and Sertoli-Leydig Cell Tumors)

GX (cannot be assessed)
G1 (well differentiated)
G2 (moderately differentiated)
G3 (poorly differentiated)

Clear Cell Carcinoma, Low and High Grade Serous Carcinoma, and Sertoli-Leydig Cell Tumors

Not applicable

Trophoblastic Tumors

Not applicable

Uterine Cervix

Not applicable
GX (cannot be assessed)
G1 (well differentiated)
G2 (moderately differentiated)
G3 (poorly differentiated)

Uterine Sarcoma

Leiomyosarcoma

Not applicable

Endometrial Stromal Sarcoma

- Low grade
- High grade
- Cannot be assessed

Adenosarcoma (select all that apply)

- Low grade
- High grade
- With sarcomatous overgrowth
- Cannot be assessed

Vagina

- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)
- Other

Vulva

- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- G4 (undifferentiated)
- Other

Head and Neck

Larynx

- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- Other

Lip and Oral Cavity

- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- Other

Major Salivary Glands
- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- Other

Nasal Cavity and Paranasal Sinuses
- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- Other

Pharynx
- Not applicable
- GX (cannot be assessed)
- G1 (well differentiated)
- G2 (moderately differentiated)
- G3 (poorly differentiated)
- Other

Hematologic

Bone Marrow
- Not applicable

Hodgkin Lymphoma
- Not applicable

Non-Hodgkin Lymphoma
- Not applicable

Ocular Adnexal Lymphoma
- Not applicable

Plasma Cell Neoplasms
- Not applicable

Ophthalmic

Retinoblastoma
- pGX (cannot be assessed)
- pG1 (well differentiated)
- pG2 (moderately differentiated)
- pG3 (poorly differentiated)
- pG4 (undifferentiated)

Uveal Melanoma
- Not applicable

Skin

Melanoma

Not applicable

Merkel Cell Carcinoma

Not applicable

Squamous Cell Carcinoma

GX (cannot be assessed)

G1 (well differentiated)

G2 (moderately differentiated)

G3 (poorly differentiated)

G4 (undifferentiated)

Thorax

Heart

Not applicable

Cannot be determined

Grade 1

Grade 2

Grade 3

Other

Lung (NSCLC, Small Cell, Carcinoid -- long list of histologic types)

Not applicable

GX: Cannot be assessed

G1: Well differentiated

G2: Moderately differentiated

G3: Poorly differentiated

G4: Undifferentiated

Other

Pleural Mesothelioma

Not applicable

Thymoma and Thymic Carcinoma

Not applicable

Bone

Grade 1 (low grade)

Grade 2 (intermediate grade)

Grade 3 (high grade)

Peritoneum

Not applicable (borderline neoplasms and mesotheliomas)

GX: Cannot be assessed

G1: Well differentiated

G2: Moderately differentiated
G3: Poorly differentiated
Other

Soft Tissue

Grade 1
Grade 2
Grade 3
Ungraded sarcoma
Cannot be determined

SUPPLEMENTAL DATA FILE 3e.

LIST OF BIOMARKERS

There are hundreds of thousands of different biomarkers in oncology. Biomarkers can include genes (genomics), transcription products (transcriptomics), protein synthesis products (proteomics), cellular metabolism products (metabolomics), inter and intra-cellular process products (epigenetics), immunologic products, etc. Biomarkers vary based on the type of alterations of the cellular process and the location(s) of the changes. Biomarkers identified by one testing methodology may not be found by a different method looking for the same alteration.

As a rule, any measured biomarker should be reported with as much detail as possible, which includes information such as biomarker (with specific gene, genetic region, specific alteration), results, and method of testing (with thorough if not exhaustive description and information).

Oncology biomarkers can be broken into several broad categories as designated below. It is expected that most genomic repositories should contain at minimum all the Category 1 and many of the Category 3 biomarkers for a given disease state. With the advent of tools such as next generation sequencing as well as broader payer coverage, most of the Category 2 and many Category 4 biomarkers will also be available and should be collected.

The following tables serve for illustrative purposes only and are not exhaustive.

Category 1: Biomarkers for which there is an FDA Approved Drug and FDA Approved Test (Companion Diagnostic) by disease state:

Disease State	Genetic Alteration (Biomarker)
Acute Myelogenous Leukemia (AML)	Internal tandem duplication (ITD) mutations and Tyrosine kinase domain mutations D835 and I836 in FLT3
Acute Myeloid Leukemia (AML)	IDH2 mutations
Aggressive Systemic Mastocytosis (ASM)	KIT D816V mutations
Breast Cancer	HER2 protein overexpression or amplification
Chronic Lymphocytic Leukemia (CLL)	Deletion of LSI TP53
Colorectal cancer (CRC)	RAS (panel) (KRAS and NRAS)
Colorectal cancer (CRC)	KRAS (7 somatic mutations in codons 12 and 13)
Colorectal cancer (CRC)	EGFR (HER1)
Gastric or gastroesophageal junction adenocarcinoma	HER2 protein overexpression
Gastrointestinal stromal tumors (GIST)	c-kit protein in CD117 antigen-expressing cells
Melanoma	BRAF (V600E and V600K mutations)
Myelodysplastic Syndrome/Myeloproliferative Disease (MDS/MPD)	PDGFRB
Non-Small Cell Lung Cancer (NSCLC)	BRAF (V600E)
Non-Small Cell Lung Cancer (NSCLC)	ROS1 (fusions)

Non-Small Cell Lung Cancer (NSCLC)	EGFR (L858R, Exon 19 deletions)
Non-Small Cell Lung Cancer (NSCLC)	PD-L1 protein expression
Non-Small Cell Lung Cancer (NSCLC)	EGFR (T790M)
Non-Small Cell Lung Cancer (NSCLC)	Rearrangements of Anaplastic Lymphoma Kinase (ALK)
Ovarian Cancer	BRCA1 and BRCA2 sequence alterations (deletions)

U.S. Food and Drug Administration. (2017). List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). [online] U S Food and Drug Administration. Available at https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm [Accessed 11 Oct. 2017]

Category 2: Example of biomarkers currently being studied in a clinical trial with targeted drugs

Targeted Biomarker
EGFR mut
MET amp
MET ex 14 sk
EGFR T790M
ALK transloc
ROS1 transloc
BRAF V600
mTOR mut
TSC1 or TSC2 mut
BRAF nonV600 or BRAF fusion
GNAQ/GNA11 mut
SMO/PTCH1 mut
NF2 loss
cKIT mut
DDR2 mut
CCND1,2,3 amp
CDK4 or CDK6 amp
NTRK fusions

National Cancer Institute. (2017). NCI-MATCH Trial (Molecular Analysis for Therapy Choice). [online] NCI-MATCH Precision Medicine Clinical Trial – National Cancer Institute. Available at: https://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match [Accessed on 11 Oct. 2017].

Category 3: Prognostic and/or treatment-aiding biomarkers

Disease State	Biomarker
Chronic Lymphocytic Leukemia (CLL)	ZAP70
Colorectal cancer (CRC)	Carcinoembryonic antigen (CEA)
Ovarian Cancer	Cancer Antigen 125 (CA125)
Pancreatic Cancer	Cancer Antigen 19.9 (CA19.9)
Prostate Cancer	Prostatic Specific Antigen (PSA)

Category 4: Research Biomarkers
Biomarkers that are not in any of the other categories but which are tested usually as part of a broad panel ranging from dozens to hundreds of biomarkers.

For example, the following is a representative panel of broad biomarkers in solid tumors from Washington University in St. Louis:

ABL1, AFF3, AKT1, AKT2, AKT3, ALK, APC, AR, ATM, ATRX, BAP1, BCL2L1, BRAF, BRCA1, BRCA2, BRIP1, CCND1, CDH1, CDK12, CDK6, CDKN1A, CDKN1B, CDKN2A, CHEK2, CREBBP, CSF1R, CTNNB1, DAXX, DDR2, EGFR, ERBB2, ERBB3, ERBB4, ERCC2, ESR1, ESR2, FANCA, FAT1, FBXW7, FGFR1, FGFR2, FGFR3, FGFR4, FLT1, FLT3, FLT4, FOXL2, GATA4, GNAS, H3F3A, HIST1H3B, HRAS, IDH1, IDH2, JAK1, JAK2, KDM5C, KDR, KEAP1, KIT, KLF4, KMT2C, KMT2D, KRAS, MAP2K1, MAP2K2, MAP3K3, MCL1, MED12, MET, MLH1, MN1, MTOR, MYB, MYBL1, MYC, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NRAS, NTRK1, NTRK2, PALB2, PBRM1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3R1, PIK3R2, POLD1, POLE, PPARG, PPP2R1A, PTEN, RAD54B, RAF1, RB1, RET, RIT1, ROS1, RXRA, SETD2, SHOC2, SMAD2, SMAD4, SMARCA4, SMARCB1, SOS1, SPRED1, STK11, TEK, TERT, TGFBR2, TP53, TRAF7, TSC1, TSC2, VHL and *WT1*

Washington University Physicians. (2017). Sequencing Tests: Cancer: Solid Tumor Gene Set. [online] Sequencing Tests – Genomics and Pathology Services | Genomics and Pathology Services. Available at: https://gps.wustl.edu/patient-care/sequencing-tests/ [Accessed on 11 Oct. 2017].

SUPPLEMENTAL DATA FILE 3f.

RESPONSE CRITERIA AND RESPONSE

The initial dropdown menu would contain the names of 30 sets of response criteria, beginning with criteria for solid tumors and ending with criteria for hematologic cancers. Each of the 30 sets would expand to a second level containing the range of responses enumerated under that set of criteria.

CRITERIA USED	RESPONSES
World Health Organization ("WHO")	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown
Response Evaluation Criteria in Solid Tumors ("RECIST") Version 1.0	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown
Response Evaluation Criteria in Solid Tumors ("RECIST") Version 1.1	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown
MD Anderson ("MDA") Criteria for Bone Metastasis	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown
Choi Criteria for Gastrointestinal Stromal Tumors	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown

Revised Assessment in Neuro-Oncology ("RANO") Criteria for High-Grade Gliomas	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown

European Association for the Study of the Liver ("EASL") Criteria for Hepatocellular Carcinoma	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown

Modified RECIST ("mRECIST") for Hepatocellular Carcinoma	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown

Response Evaluation Criteria in Cancer of the Liver ("RECICL") Criteria for Hepatocellular Carcinoma	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown

Positron Emission Tomography Response Criteria in Solid Tumors ("PERCIST")	Complete Metabolic Response (CMR)
	Partial Metabolic Response (PMR)
	Stable Metabolic Disease (SMD)
	Progressive Metabolic Disease (PMD)
	Unknown

European Organization for ReseS arch and Treatment of Cancer ("EORTC") Criteria for Positron Emission Tomography	Complete Metabolic Response (CMR)
	Partial Metabolic Response (PMR)
	Stable Metabolic Disease (SMD)
	Progressive Metabolic Disease (PMD)
	Unknown

Immune-Related Response Criteria ("irRC") for Immunotherapeutic Agents	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown

Choose All That Apply

National Comprehensive Cancer Network® Criteria for Acute Lymphoblastic Leukemia	Blood and Bone Marrow	Complete Remission (CR)
		Complete Remission with Incomplete Blood Count Recovery (CRi)
		Refractory Disease
		Progressive Disease (PD)
		Relapsed Disease (REL)
		Unknown
	Central Nervous System Disease	Complete Remission (CR)
		Primary Induction Failure (PIF)
		Relapsed Disease (REL)
		Unknown
	Mediastinal Disease	Complete Remission (CR)
		Partial Response (PR)
		No Response
		Progressive Disease (PD)
		Relapsed Disease (REL)
		Unknown
	Minimal Residual Disease Assessment	Molecular Complete Remission
		Minimal Residual Disease
		Unknown

International Working Group on Acute Myeloid Leukemia Criteria (2003)	Complete Remission (CR)
	Complete Remission with Incomplete Blood Count Recovery (CRi)
	Morphologic Leukemia-Free State
	Cytogenetic Complete Remission (CRc)
	Molecular Complete Remission (CRm)
	Partial Remission (PR)
	Treatment Failure
	Relapse
	Unknown

International Workshop on Chronic Lymphocytic Leukemia ("IWCLL") (2008)	Complete Remission (CR)
	Complete Remission with Incomplete Marrow Recovery (CRi)
	Partial Remission (PR)
	Stable Disease (SD)
	Progressive Disease (PD)
	Unknown

Lymphoma Research Foundation Workshop Revision of IWCLL for Immuno-Modulating Agents and Kinase Inhibitors (2012)	Complete Remission (CR)
	Complete Remission with Incomplete Marrow Recovery (CRi)
	Partial Remission (PR)
	Partial Remission with Lymphocytosis
	Progressive Disease (PD)
	Unknown

European LeukemiaNet Criteria for Chronic Myeloid Leukemia (2013)	Complete Hematologic Response (CHR)
	Complete Cytogenetic Response (CCyR)
	Partial Cytogenetic Response (PCyR)
	Molecularly Undetectable Leukemia
	Molecular Response$^{4.5}$
	Molecular Response$^{4.0}$
	Major Molecular Response (MMR)
	Unknown

National Comprehensive Cancer Network® Criteria for Chronic Myeloid Leukemia	Complete Hematologic Response
	Complete Cytogenetic Response (CCyR)
	Partial Cytogenetic Response (PCyR)
	Major Cytogenetic Response
	Minor Cytogenetic Response
	Complete Molecular Response (CMR)
	Major Molecular Response (MMR)
	Early Molecular Response (EMR)
	Relapse
	Unknown

National Comprehensive Cancer Network® Criteria for Hairy Cell Leukemia	Complete Response
	Less Than Complete Response

National Comprehensive Cancer Network® Criteria for Hodgkin Lymphoma (Deauville)	1
	2
	3
	4
	5
	X
	Unknown

Dynamic Visual Score for Hodgkin Lymphoma (Dann)	0
	1
	2
	3
	4
	Unknown

National Comprehensive Cancer Network® Criteria for B-cell Lymphomas (Lugano)	Metabolic Complete Response
	Metabolic Partial Response
	Metabolic No Response or Stable Disease
	Metabolic Progressive Disease
	Radiologic Complete Response
	Radiologic Partial Response
	Radiologic No Response or Stable Disease
	Radiologic Progressive Disease
	Unknown

National Comprehensive Cancer Network® Criteria for T-cell Lymphomas (Lugano)	Metabolic Complete Response
	Metabolic Partial Response
	Metabolic No Response or Stable Disease
	Metabolic Progressive Disease
	Radiologic Complete Response
	Radiologic Partial Response
	Radiologic No Response or Stable Disease
	Radiologic Progressive Disease
	Unknown

International Harmonization Project (IHP) Criteria for Malignant Lymphoma	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD) or Relapse
	Unknown

Qualitative Criteria for PET Response in Malignant Lymphoma (Hicks)	Complete Response (CR)
	Partial Response (PR)
	Stable Disease (SD)
	Progressive Disease (PD) or Relapse
	Unknown

National Comprehensive Cancer Network® Criteria for Multiple Myeloma (based on International Myeloma Working Group (IMWG) Criteria)	Sustained MRD-Negative
	Flow MRC-Negative
	Sequencing MRD-Negative
	Imaging Plus MRD-Negative
	Stringent Complete Response
	Complete Response
	Very Good Partial Response
	Partial Response
	Minimal Response
	Stable Disease
	Progressive Disease
	Clinical Relapse
	Relapse from Complete Response
	Relapse from MRD-Negative
	Unknown

Center for International Blood & Marrow Transplant Research ("CIBMTR") Criteria for Myelodysplastic Syndromes	Complete Remission (CR)
	Hematologic Improvement (HI)
	Hematologic Improvement -- Erythropoietic (HI-E)
	Hematologic Improvement -- Platelets (HI-P)
	Hematologic Improvement -- Neutrophils (HI-N)
	No Response (NR)/Stable Disease (SD)
	Progression from Hematologic Improvement (Prog from HI)
	Relapse from Complete Remission (Rel from CR)
	Progression to AML
	Unknown

Center for International Blood & Marrow Transplant Research ("CIBMTR") Criteria for Myeloproliferative Neoplasms	Complete Remission (CR)
	Hematologic Improvement (HI)
	No Response (NR)/Stable Disease (SD)
	Progression from Hematologic Improvement (Prog from HI)
	Relapse from Complete Remission (Rel from CR)
	Unknown

International Working Group ("IWG") -- 2006 Criteria for Myelodysplasia	Complete Remission (CR)
	Partial Remission (PR)
	Marrow CR
	Stable Disease
	Failure
	Relapse after CR or PR
	Cytogenetic Response
	Disease Progression
	Unknown

MDS/MPN International Working Group Criteria for Myelodysplastic/Myeloproli-ferative Neoplasms in Adults ("Overlap -- MDS/MPN Criteria") -- 2015	Complete Remission (CR)
	CR with Resolution of Symptoms
	Complete Cytogenetic Remission
	Partial Remission (PR)
	Marrow Response
	Clinical Benefit
	Stable Disease
	Failure
	Relapse after CR or PR
	Disease Progression
	Unknown