**FDA-NHI**

# BEST (Biomarkers, EndpointS, and other Tools) Resource : <https://www.ncbi.nlm.nih.gov/books/NBK326791/>

* Biomarker consortium: <https://fnih.org/what-we-do/biomarkers-consortium>
* Biomarker qualification guidelines (for development of markers)

<https://www.fda.gov/media/119271/download>

<https://fnih.org/sites/default/files/final/pdf/Evidentiary%20Criteria%20Framework%20Final%20Version%20Oct%2020%202016.pdf>

**other**

* Different classification of BM (type 0, 1, 2): <https://www.nature.com/articles/nrd1130#Sec9>
  + is it valuable ?
* National Comprehensive Cancer Network (NCCN) Biomarkers Compendium:

<https://www.nccn.org/professionals/biomarkers/Definitions.pdf>

* WHO disease classification : <https://www.who.int/classifications/icd/en/>

**Suggested minimal required information for biomarkers / disease-biomarker association**

|  |  |  |
| --- | --- | --- |
| **Attribute** | **Explanation** | **Examples** |
| Name | Name of biomarker | Molecular: name of gene/protein/metabolite/other molecule/variant/gene over- or under expression  Physiological: blood pressure, heart rate  Imaging: usually name of imagine technique (CT,PET,OCT) |
| Disease | Disease or condition related to the marker | Breast cancer |
| Usage | As defined by FDA-NIH | **diagnostic** – to detect or confirm presence of a disease or condition  **monitoring** – to assess the status of a disease (serially measured)  **prognostic** - identify likelihood of a clinical event, disease recurrence or progression of disease  **predictive** -  to identify individuals who are more likely to respond to exposure to a particular medical product or environmental agent  **pharmacodynamic**/**response** – to assess response to a treatment /medical product or an environmental agent  **susceptibility**/**risk -** indicates the potential for developing a disease or medical condition in an individual who does not currently have clinically apparent disease or the medical condition.  **safety -** measured before or after an exposure to a medical product or an environmental agent to indicate the likelihood, presence, or extent of toxicity as an adverse effect  [ + surrogate endpoint – used in clinical trials] |
| Type | Type of biomarker | Molecular: gene/protein/lipid/metabolite/genomic region\*  Imaging  physiological (digital?)  behavioral (digital?)  combinatorial – a combination of biomarkers |
| Source | Source of sample or the location in the body where the measurement is taken | Fluid: serum, whole blood, plasma, urine, CSF, saliva  Breath  Skin/tissue/organ |
| Assay | Experiment and technology used for measurement (=what is being measured and how) | Gene expression profiling with Microarray |
| Evidence | Evidence of the marker-disease association from literature | Sentence/reference/PMID |

(\*) molecular markers – sometime classified on a higher level (genomic/proteomic/metabolomic), for example: <http://www.cancerjournal.net/article.asp?issn=0973-1482;year=2016;volume=12;issue=2;spage=486;epage=492;aulast=Santosh>

Examples:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Name | disease | usage | type | source | Assay | evidence |
| Arterial stiffness | Cardiovascular Disease (CVD) | risk | physiological | finger | Aortic pulse wave velocity (Aortic PWV) | 16461838 |
| PDG-PET | Alzheimer | diagnostic | imaging | brain | Brain glucose metabolism | 31253185 |
| IL-6 | hepatocellular carcinoma (HCC) | diagnostic | protein | serum | Serum protein levels | 23082483 |
| Blood pressure | hypertension | pharmaco-dynamic(\*) | physiological | arm | Systolic and diastolic pressure | 24352797 |
| AKT  overexpression | Breast cancer | predictive (\*) | gene | tumor tissue | Gene expression profiling (GEP),Immunohistochemistry (IHC) on tissue microarrays (TMAs) | 22842582 |
| ER-PR-HER2 | Breast cancer | Prognostic/predictive(\*) | Combinatorial expression | tumor tissue | GEP,IHC,Microarray | 20107892 |

(\*) Predictive & pharmacodynamic/response markers will be related to a drug/treatment (antihypertensive agent or sodium restriction for hypertension ,trastuzumab & anti-HER2 therapy for breast cancer) – adding an attribute to this (sub)class?

Remarks:

* Sometimes an external ID (gene, variant, disease..) will be provided – is it not worth keeping?
* Some molecular markers like mutations/variants and protein are associated with a gene as well
* Combinatorial biomarkers will be associated with several markers (can also be of different types)
* Digital biomarkers <https://www.karger.com/Article/FullText/502000#ref2>