FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION & RESEARCH

BIOMARKER QUALIFICATION PROGRAM
EDUCATIONAL MODULE SERIES—MODULE 1

BIOMARKER TERMINOLOGY: SPEAKING THE SAME LANGUAGE

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BEST Resource: Harmonizing Terminology

- Created by the NIH-FDA Biomarker Working Group
- A glossary of terminology and uses of biomarkers and endpoints in basic biomedical research, medical product development, and clinical care

Available at: http://www.ncbi.nlm.nih.gov/books/NBK326791/

BIOMARKER TERMINOLOGY

- Definition of a Biomarker
- Types of Biomarkers
- Categories of Biomarkers
- Biomarker Validation
- Biomarker Qualification
- Context of Use

WHAT IS A BIOMARKER?

A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions.

Types: Molecular, histologic, radiographic, and physiologic characteristics are types of biomarkers.

Examples:

- Blood glucose (molecular)
- Tumor size (radiographic)
- Blood pressure (physiologic)

DIFFERENT CATEGORIES OF BIOMARKERS

PROGNOSTIC BIOMARKERS

Can be used to select patients with greater likelihood of having a disease-related endpoint event or a substantial worsening in condition in clinical trials.

For example: **Total kidney volume,** to select patients with autosomal dominant polycystic kidney disease at high risk for progressive decline in renal function for inclusion in interventional clinical trials.

SURROGATE ENDPOINT

An endpoint that is used in clinical trials as a substitute for a direct measure of how a patient feels, functions, or survives.

Validated Surrogate Endpoint

Supported by a clear mechanistic rationale and clinical data providing strong evidence that an effect on the surrogate predicts a clinical benefit; therefore, such endpoints can be used to support traditional approval without the need for additional efficacy information.

Example: Hemoglobin A1C reduction in diabetes clinical trials

Reasonably Likely Surrogate Endpoint

Supported by clear mechanistic and/or epidemiologic rationale but with insufficient clinical data to show that it is a validated surrogate endpoint; such endpoints can be used for accelerated approval for drugs or expedited access for medical devices.

Example: Radiographic evidence of tumor shrinkage in some cancer types

Candidate Surrogate Endpoint

A surrogate under evaluation for its ability to predict clinical benefit.

ANALYTICAL AND CLINICAL VALIDATION

Analytical Validation: Ensures specificity, accuracy, precision, and other characteristics of biomarker test or device

Establishing that the performance characteristics of a test, tool, or instrument are acceptable in terms of its sensitivity, specificity, accuracy, precision, and other relevant performance characteristics using a specified technical protocol (which may include specimen collection, handling, and storage procedures).

Clinical Validation: Ensures the test or device performs as intended

Establishing that the test, tool, or instrument acceptably identifies, measures, or predicts the concept of interest.

Concept: In a regulatory context, the concept is the aspect of an individual's experience or clinical, biological, physical, or functional state that the assessment is intended to capture (or reflect).

BIOMARKER QUALIFICATION

A conclusion, based on a formal regulatory process, that within the stated context of use, a biomarker can be relied upon to have a specific interpretation and application in medical product development and regulatory review.

A biomarker, once qualified for a particular context of use, will be publicly available and can be applied in any drug development program for the qualified context of use.

CONTEXT OF USE

A statement that fully and clearly describes the way the biomarker is to be used and the drug development-related purpose of the use.

BIOMARKER TERMINOLOGY

By speaking the same "biomarker language," we can enhance medical product development and may be able to get new treatments to patients sooner.

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LEARN MORE

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