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

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

- Safety
- Diagnostic
- Susceptibility/Risk
- Predictive
- Prognostic
- Monitoring
- Response

Biomarker Categories
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.

<table>
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<tr>
<th>Validated Surrogate Endpoint</th>
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<tbody>
<tr>
<td>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.</td>
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<th>Reasonably Likely Surrogate Endpoint</th>
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<td>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.</td>
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<th>Candidate Surrogate Endpoint</th>
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<td>A surrogate under evaluation for its ability to predict clinical benefit.</td>
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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).
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.
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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