Biomarker Qualification Program Educational Module Series—Module 1: Biomarker Terminology: Speaking the Same Language

Hi. I'm Dr. Shashi Amur with the FDA's Center for Drug Evaluation and Research, also known as CDER.

In this module, I'll introduce some important concepts and terminology relevant to biomarkers.

Unclear terminology and definitions impede progress. In an effort to harmonize the terminology related to biomarkers, the Joint Leadership Council of FDA and NIH published the BEST Resource in 2016, which is a glossary of terms that could serve as a point of consensus for all stakeholders.

In this module, I'll go through some of the key terms that pertain to biomarkers and their application in medical product development. The definitions I'll be introducing are all listed in the BEST Resource glossary.

Specifically, I will cover the definition of a biomarker, types of biomarkers, categories of biomarkers, the difference between biomarker validation and biomarker qualification, and, finally, context of use.

So, let's start with the term "biomarker." What is a biomarker?

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

Molecular, histologic, radiographic, and physiologic characteristics are types of biomarkers. Some examples are blood glucose, tumor size, and blood pressure.

Biomarkers are divided into seven categories. Each of these categories lends itself to different uses.

For example…

A prognostic biomarker is defined as a biomarker used to identify likelihood of a clinical event, disease recurrence, or progression.

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.

These can be used for patient stratification or enrichment in clinical trials. An example of the use of prognostic biomarkers, utilized for enrichment, is total kidney volume that may be employed to select patients with autosomal dominant polycystic kidney disease at high risk for progressive decline in renal function for inclusion in interventional clinical trials.

Some of these biomarkers can be used as surrogate endpoints in clinical trials, based on available evidence.

Surrogate endpoint can be defined as an endpoint that's used in clinical trials as a substitute for a direct measure of how a patient feels, functions, or survives.

An example of a validated surrogate endpoint is hemoglobin A1C reduction, used as a surrogate endpoint in diabetes clinical trials.

An example of a reasonably likely surrogate endpoint is radiographic evidence of tumor shrinkage and progression-free survival in certain cancer types to predict an improvement in overall survival.

In relevance to biomarkers, analytical and clinical validation refer to the biomarker test or device and help ensure that the test or device performs as intended.

Validation of a biomarker test or device is a critical step to ensure that the biomarker data are accurate and reproducible.

CDER's Biomarker Qualification Program is a way to establish a biomarker's value for a particular context of use in drug development and for regulatory review.

A biomarker used in a typical drug-approval process would have to undergo additional regulatory review before it could be used in another program.

Here's the advantage of qualification: 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.

What do we mean by "context of use"?

The context of use is a statement that fully and clearly describes the way the biomarker is to be used in drug development.

The context of use drives the level of evidence, which in turn drives the qualification process, and thus, it's very important to consider the context of use early in biomarker qualification considerations.

We'll be covering the context of use in depth in a separate module.

By speaking the same "biomarker language," we can enhance medical product development, and that means we can get new treatments to the patients who need them sooner.

In this module, I introduced some key concepts and terminologies related to biomarkers, including the definition of a biomarker, types and categories of biomarkers, biomarker validation and qualification, and context of use.

Please consult CDER's website and the BEST Resource to learn more about biomarker terminology and access additional information about biomarker qualification.