# Regulatory Matters

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## Biomarkers on my mind

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Early in my regulatory medical writing career, I wrote several protocols in the cardiology therapeutic area. I was introduced to the cardiac biomarkers troponin I and N-terminal prohormone brain natriuretic peptide (NT-proBNP), which are indicators of cardiac injury and cardiac dysfunction, respectively. Before that, I had done a lot of work in oncology, and I was accustomed to biomarkers such as HER2 that can be used to define a patient population for a given treatment. It was at that point that I began to comprehend the diverse roles biomarkers play in drug development.

A biomarker is *a defined characteristic that is measured as an indicator of normal biological processes, pathological processes, or responses to an exposure or intervention.*[1] This definition is rather broad, and thus it is helpful to break this definition into more manageable pieces. The International Council for Harmonisation (ICH) E16 guidance on biomarkers describes their several purposes:[2]

- Selecting an eligible patient population for an indication or participation in a clinical study. These types of biomarkers can be used to identify individuals with a subtype of disease of interest. HER2 resides in this space: therapies such as trastuzumab are indicated for individuals who have HER2-positive breast cancer. This type of biomarker is of particular interest for precision medicine because it can predict response to therapy.
- Assessing disease state or prognosis. My good friends troponin I and NT-proBNP are in this category.
- Assessing the mechanism of action, including the mechanism of pharmacological mode of action, therapeutic effect, or toxicity.
- Optimising the dose.
- Monitoring drug response, both drug safety and drug efficacy.
- Maximising efficacy.
- Minimising toxicity.

As you can see, biomarkers can be used in a variety of contexts: predicting an individual's risk of developing a disease, diagnosing a disease state, identifying a disease subtype, predicting a response to a therapy, detecting the effect of a therapy on an individual, monitoring the status of the disease, and monitoring safety.

Biomarkers come in many forms, including molecular, histologic, radiographic, or physiologic.[1] A lot of recent research has been devoted to genomic biomarkers, which can measure the expression, function, or regulation of a gene and serve as indicators of normal biologic processes, pathogenic processes and/or responses to therapeutics or other interventions.[3] Genomic biomarkers include pharmacogenomic biomarkers, which are variations of DNA or RNA characteristics related to drug response. Because drug response includes the processes of drug absorption and disposition (pharmacokinetics) and drug effects (pharmacodynamics, drug efficacy, and drug adverse effects), pharmacogenomic biomarkers are becomingly increasingly important for drug discovery, drug development, and clinical practice.[3]

Biomarkers can be used to predict clinical outcomes and accelerate the drug development process. Traditionally, clinical outcome assessments are used to support regulatory approval of therapies; however, a validated biomarker can also be used for regulatory approval for therapies. ICH E16 lays out general principles for qualifying biomarkers for submissions – that is, demonstrating that a biomarker reliably reflects a biological process, response, or event.[2] The submission for biomarker qualification is organised along the same lines as the Common Technical Document, with sections for regional administrative information, summaries, quality reports, nonclinical reports, and clinical reports.

Our hopes for personalised medicine rely on having sensitive (able to correctly detect true positives) and specific (able to correctly detect true negatives) biomarkers to tailor therapies to individuals. The biomarker space is continuously evolving, and I am gratified every time I encounter a new biomarker in my writing. The diverse potential of biomarkers is why I have biomarkers on my mind.

### References

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