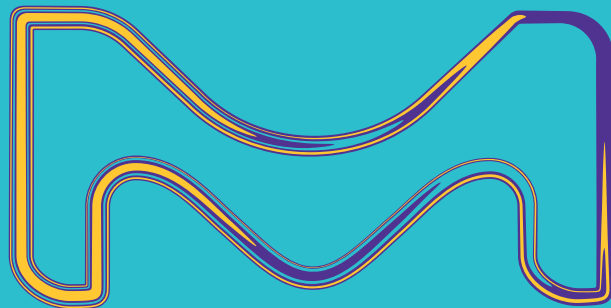


# Impact of clinical trial design on potential IVD regulatory claims

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# Disclaimer

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# Overview

- IVDs systems assess biomarkers
- Biomarkers are an integral part of drug development
- Biomarkers can have many different roles in drug development
- There are many ways to deploy biomarkers in clinical trial designs, resulting in different claims

# Biomarker Definitions

- A **biological marker** or **biomarker** is a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathologic processes, or biological responses to a therapeutic intervention. A biomarker can be a physiologic, pathologic, or anatomic characteristic or measurement that is thought to relate to some aspect of normal or abnormal biologic function or process. Biomarkers measured in patients before treatment can be used to select patients for inclusion in a clinical trial. Changes in biomarkers following treatment may predict or identify safety problems related to a candidate drug, or reveal a pharmacological activity expected to predict an eventual benefit from treatment. Biomarkers can help reduce uncertainty in drug development and evaluation by providing quantifiable predictions about drug performance and they can contribute to dose selection.
- A **composite biomarker** consists of several individual biomarkers that are combined in a stated algorithm to reach a single interpretive readout.



# Biomarker Definitions

- A *diagnostic* biomarker is a disease characteristic that categorizes a person by the presence or absence of a specific physiological or pathophysiological state or disease.
- A *prognostic* biomarker is a baseline characteristic that categorizes patients by degree of risk for disease occurrence or progression of a specific aspect of a disease. A prognostic biomarker informs about the natural history of the disorder in that particular patient in the absence of a therapeutic intervention. It can be used as an *enrichment strategy* to select patients likely to have clinical events of interest or to progress rapidly.



# Biomarker Definitions

- A *predictive* biomarker is a baseline characteristic that categorizes patients by their likelihood of response to a particular treatment relative to no treatment. A predictive biomarker can be used as an enrichment strategy to identify a subpopulation likely to respond to a treatment intervention in a particular way. It may predict a favorable response or an unfavorable response (i.e., adverse event).
- A *pharmacodynamic* (or activity) biomarker is one for which a change in the biomarker shows that a biological response has occurred in a patient who has received a therapeutic intervention and for which the magnitude of the change is considered pertinent to the response. A pharmacodynamic biomarker may be treatment-specific or more broadly informative of disease response.

Examples include:

- Blood pressure
- Cholesterol
- HemoglobinA1c (HbA1C)
- Intraocular pressure
- Radiographic measures



# Types of Biomarkers

## **Prognostic biomarker:**

Biomarker that informs about the likely disease course in an *untreated* subject

## **Predictive biomarker:**

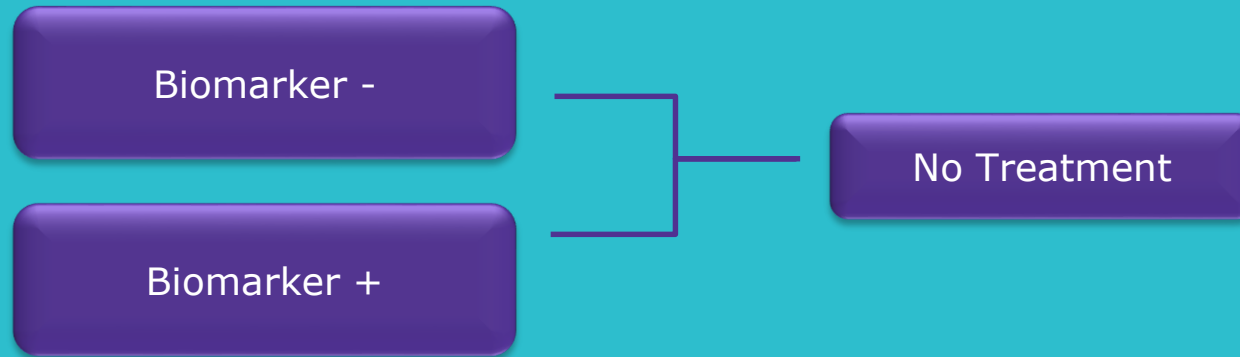
Identification of subject likely to *respond to a given treatment*

## **Selective biomarker:**

*Selection of patient for treatment*



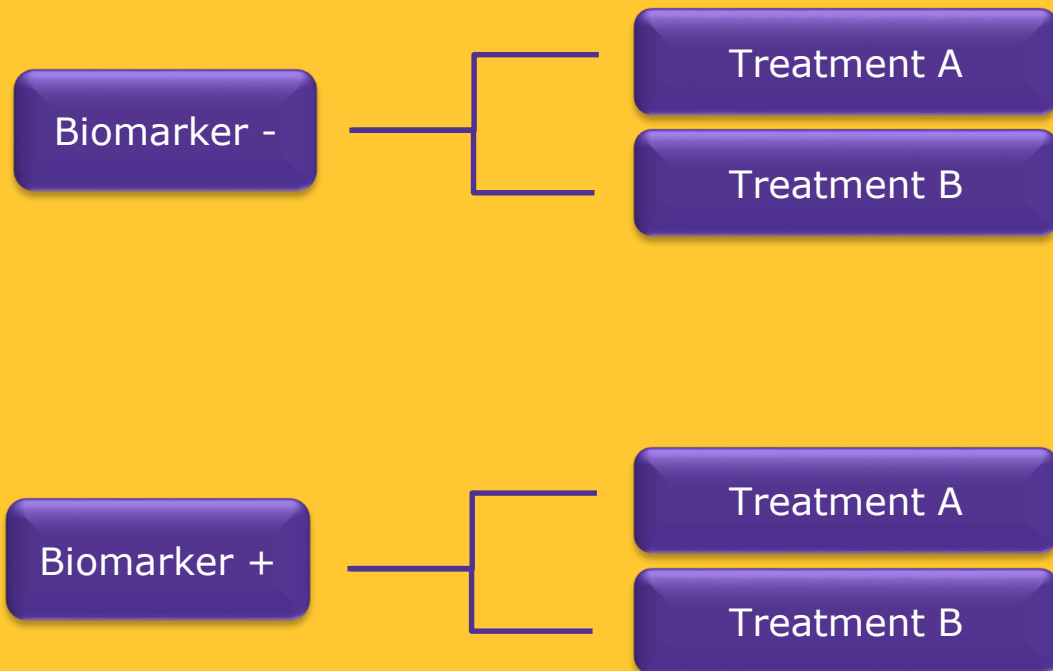
# Prognostic Claim



- Neither biomarker positive nor biomarker negative patients receive treatment
- It can be used as an *enrichment strategy* to select patients likely to have clinical events of interest or to progress rapidly (e.g. Fibrinogen / COPD Exacerbation)



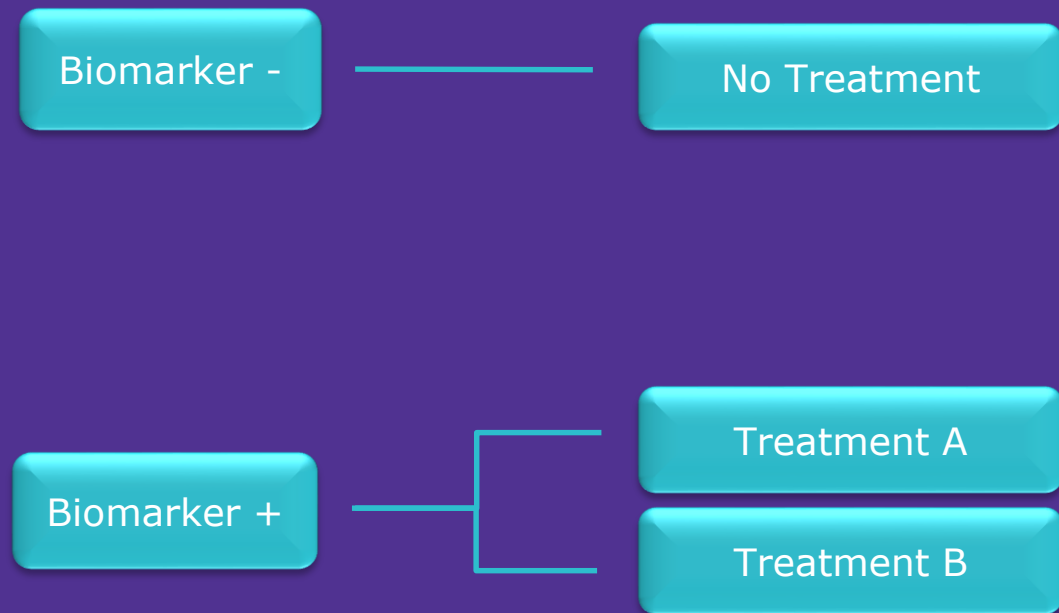
# Prognostic and Predictive Claim



- Prognostic and predictive biomarker
- Important if the impact of the biomarker on the disease course is not well understood, historical data is not available



# Selective Biomarker Claim



- No treatment outcome for the biomarker unselected population
- Biomarker is *selective*



# Companion Diagnostic (CDx)

A companion diagnostic is a medical device, often an in vitro device, which provides information that is essential for the safe and effective use of a corresponding drug or biological product. The test helps a health care professional determine whether a particular therapeutic product's benefits to patients will outweigh any potential serious side effects or risks.

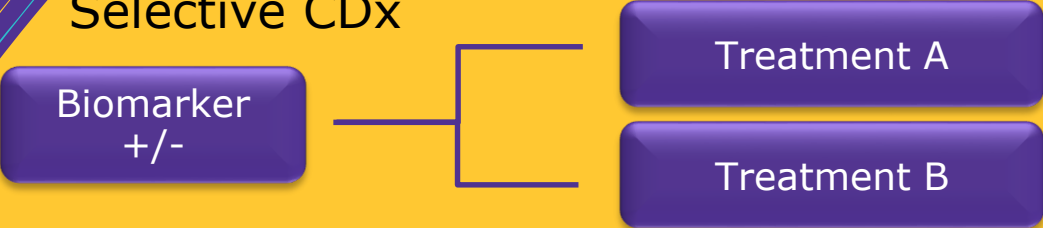
## Companion diagnostics can:

- Identify patients who are most likely to benefit from a particular therapeutic product;
- Identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or
- Monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness.



Predictive (and potentially prognostic) CDx

Selective CDx

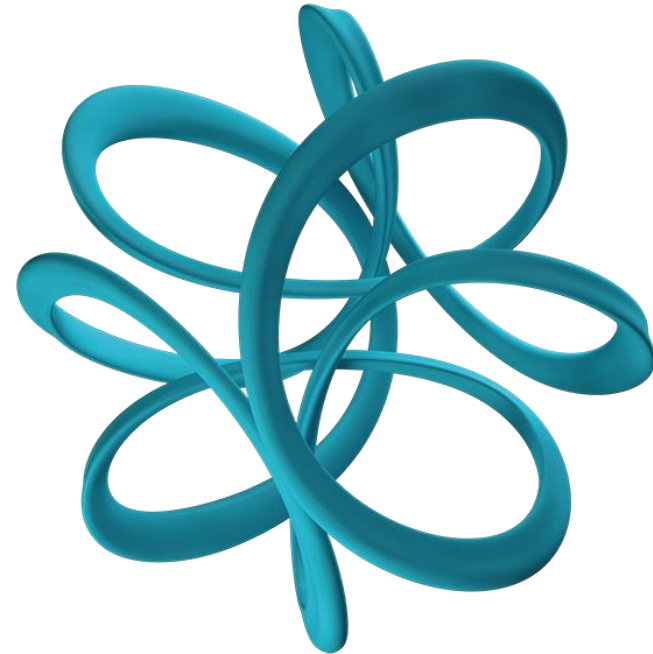


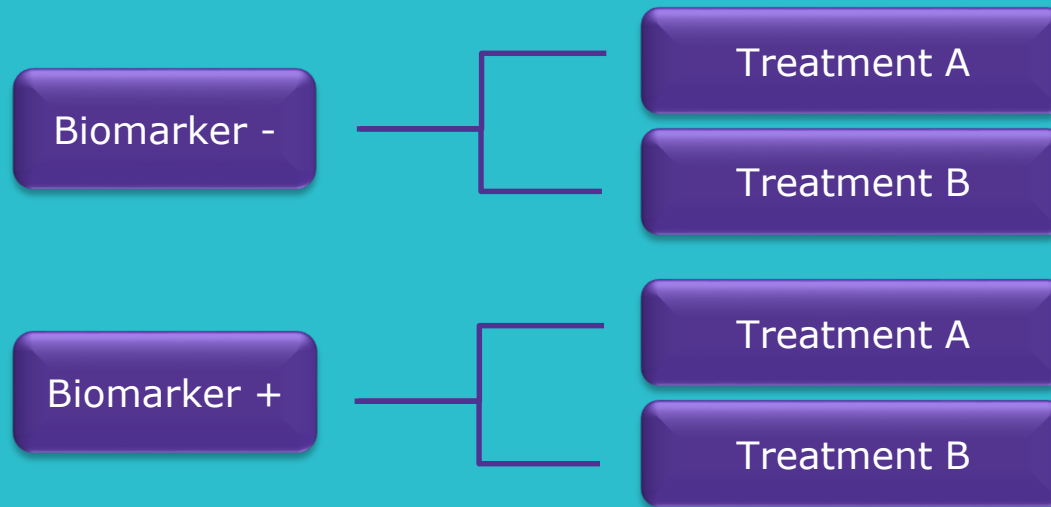
Selective CDx (historic control)



# Complementary Diagnostic (CoDx)

- Not essential for the safe and efficacious use of a corresponding drug
- Provide additional information about how a drug might be used
- To date, not a very well defined regulatory concept





### Use of historic control:



# Questions

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