

**Seeking a “Signature” of Early Cardiotoxicity  
Industry View**

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# Overview

- **Preclinical uses of biomarkers of cardiotoxicity**
  - Mechanism of action
  - Toxicology
- **Clinical application of biomarkers of cardiotoxicity**
  - Monitoring safety
  - Signal detection

## Key questions

- **What is the clinical significance of an increase in a cardiotoxicity marker (i.e., troponin)**
  - What magnitude of the change in a biomarker is significant?
  - How does the biomarker relate to functional myocardial changes
- **Are biomarkers of cardiotoxicity occurring too late in the process?**

# Preclinical

- **Identify and evaluating potential mechanism based toxicity**
  - Enhance understanding of the molecular mechanism of cardiotoxicity
  - Same target or off-target
  - Specificity of compound
  - Optimization of chemical leads
  - Reliability of markers
  - Upstream/earlier biomarkers
- **Toxicology**
  - Margins
  - False negative rates

# Clinical

- **Safety monitoring of patients**
  - What change in a biomarker is clinically significant?
  - Rules for discontinuation
  - Are the imaging tools sensitive enough?
  - Potential benefit/risk evaluation
- **Signal detection**
  - Define the normal range – is any increase significant?
  - What is the specificity of a very small increase
  - Interpreting signals in conditions with elevated levels of the marker (e.g., heart failure)