Challenges and Opportunities for Qualifying Biomarkers: An Industry Perspective

October 20th, 2015

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Background

- PhRMA and BIO collaborated in 2014 on an industry survey to identify priority areas for advocacy on biomarker qualification. The survey is a first-of-its-kind effort that collected industry-wide input.
- The survey also collected information regarding the context of use that would most increase efficiency of drug development.
- Lastly, we collected expert input on what evidentiary standards could be used to support each identified context of use.

24 companies completed the survey (17 PhRMA and 7 BIO* respondent companies).

PhRMA and BIO received blinded and aggregate data.

Percentage of completion by section for 24 companies responding:

- 23 (95%) Submitted Nonclinical Safety Data
- 18 (75%) Submitted Clinical Safety Data
- 19 (79%)Submitted Clinical Efficacy Data

** BIO Companies: 7 mid-size companies*

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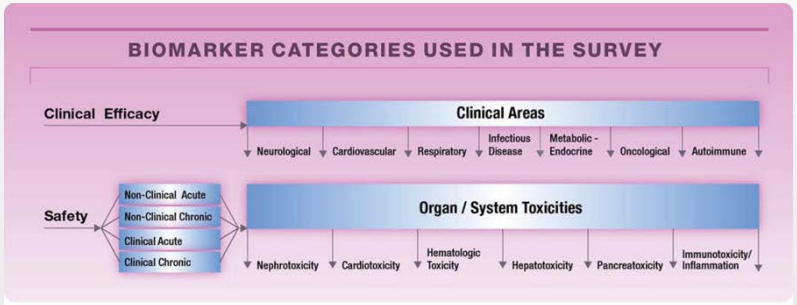
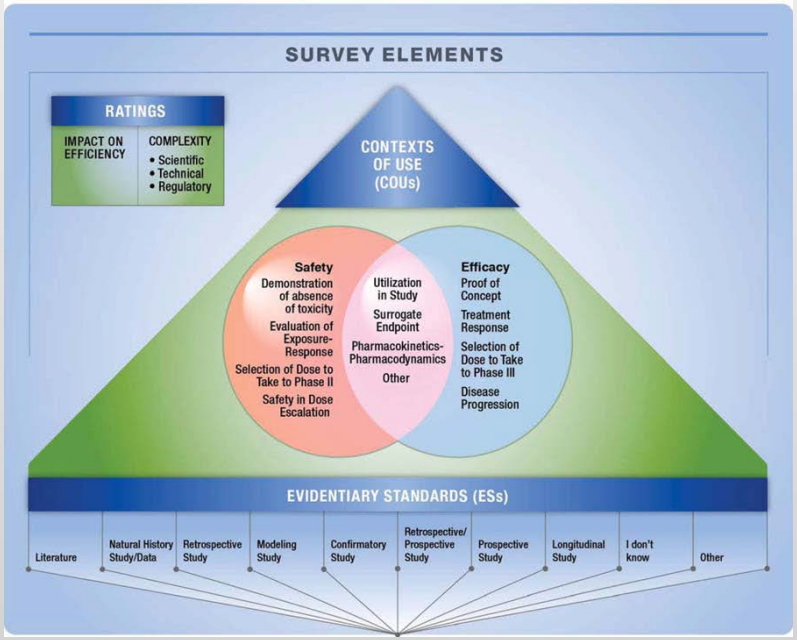
PhRMA-BIO Survey — Modules and Questions Layout





For each module we gathered data on:

1. Complexities (scientific, technical and regulatory)
2. Increase in efficiency of drug development
3. Context of Use (COUs)
4. Evidentiary Standards
5. {optional} Rationale for Evidentiary Standards selection
6. {optional} Biomarker of choice

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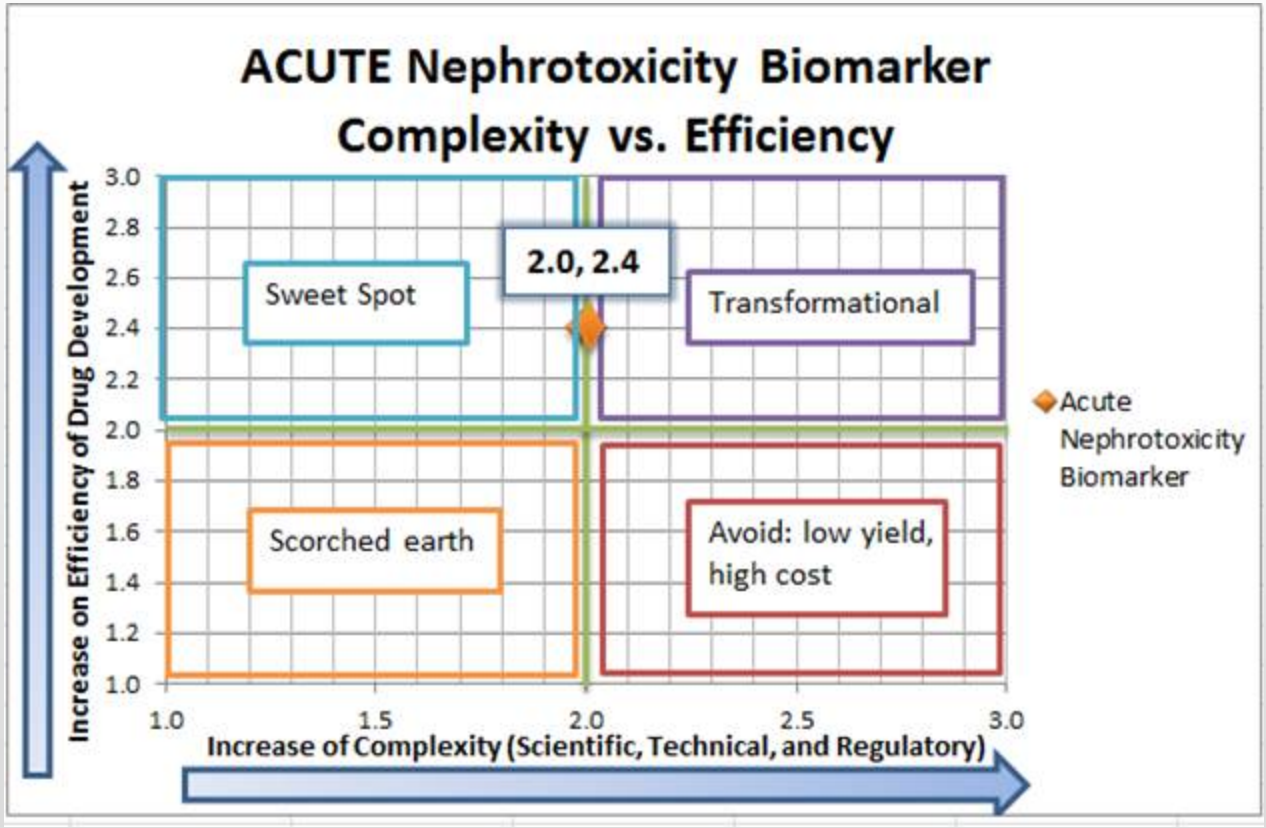
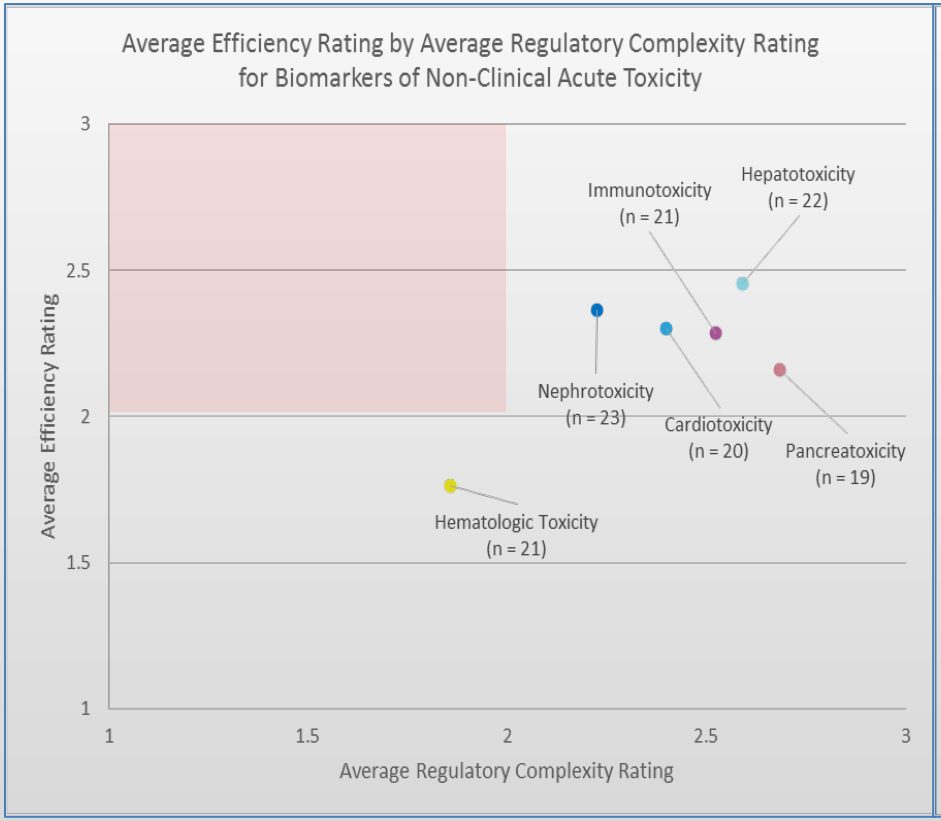
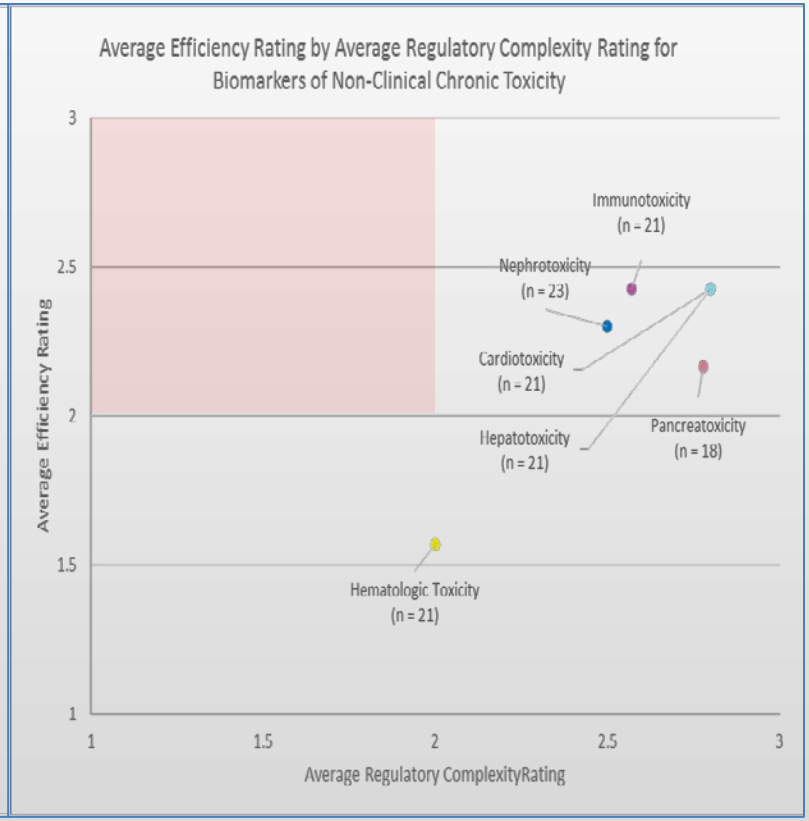
Methodology



In order to aid prioritization: The x-axis reflects the mean respondent rating for barriers to regulatory qualification, or "regulatory complexity" for biomarkers in a particular safety or efficacy category. The y-axis reflects mean respondent rating for the projected increase in efficiency of drug development, were the biomarker(s) under consideration to gain regulatory qualification. The blue quadrant of each graph represents the location of "ideal" biomarkers, or biomarkers that have the potential to have a high impact on the efficiency of drug development, but whose qualification is associated with a low level of regulatory complexity

Non-Clinical Safety Biomarkers Distribution





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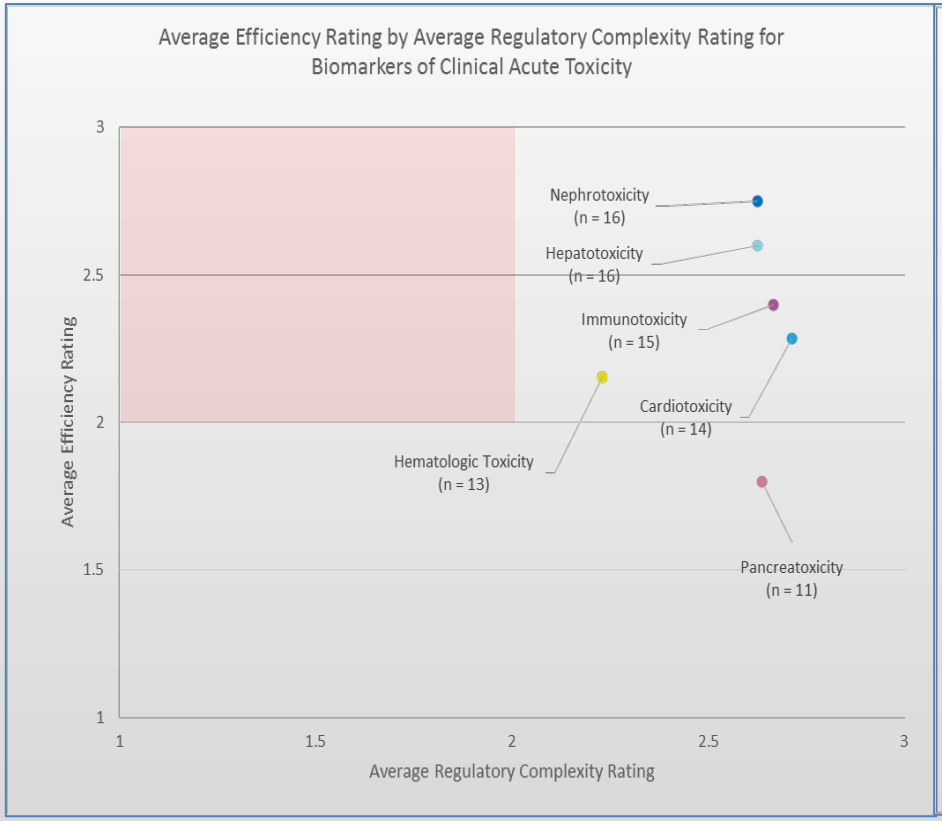
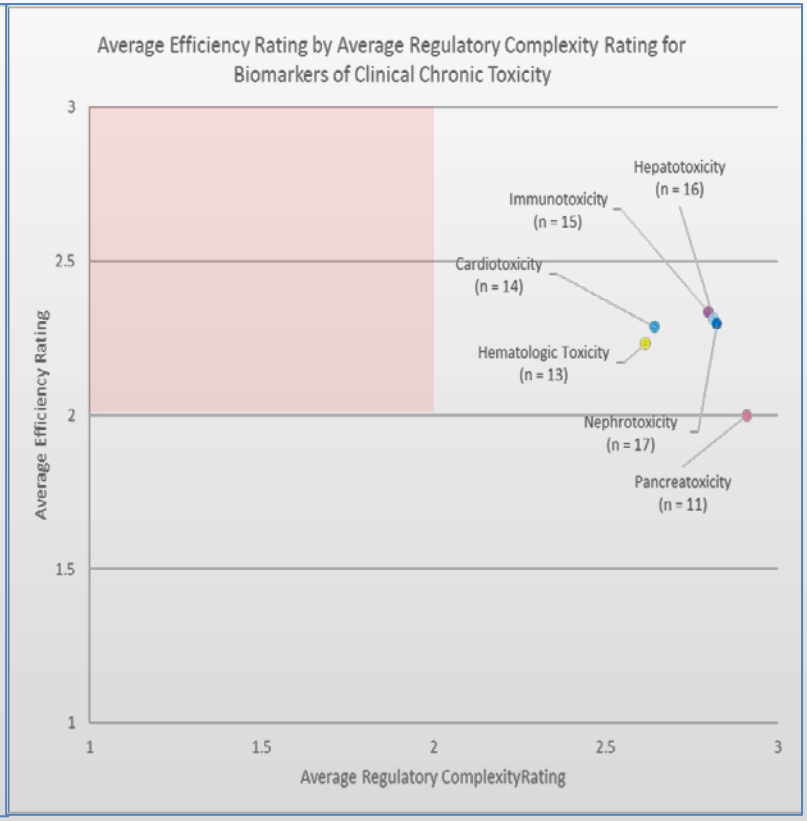
Clinical Safety Biomarkers Distribution





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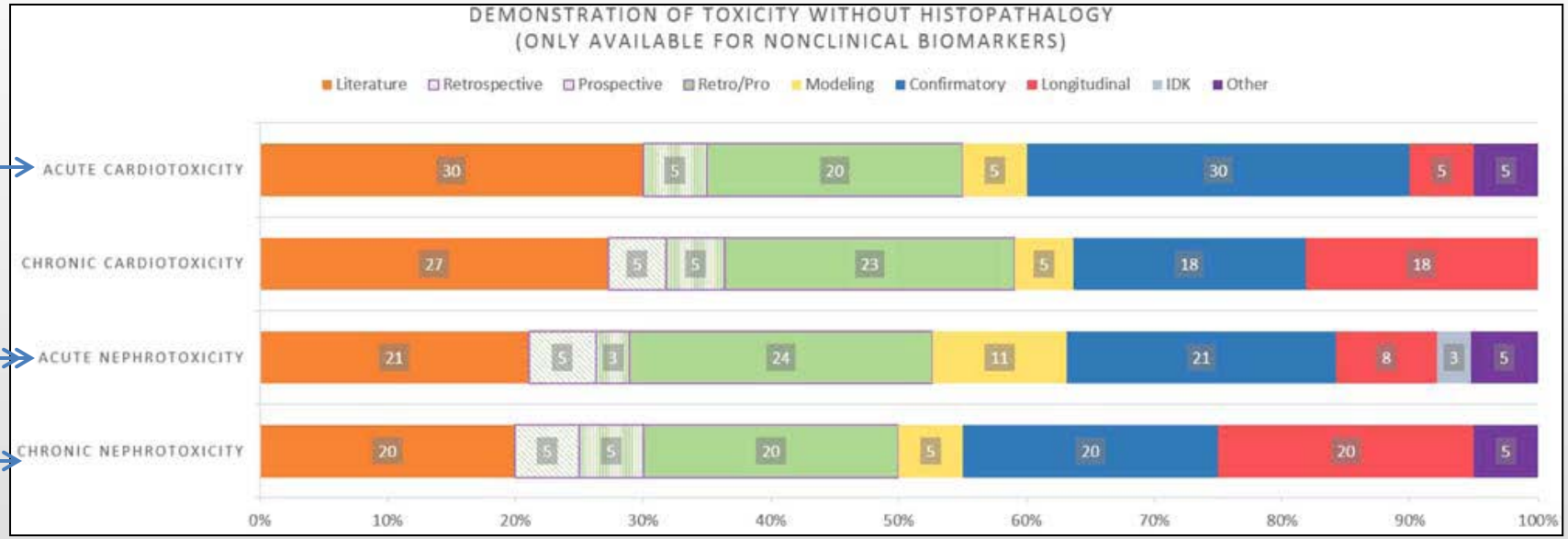
Distribution of evidentiary standard selection for a specific context of use



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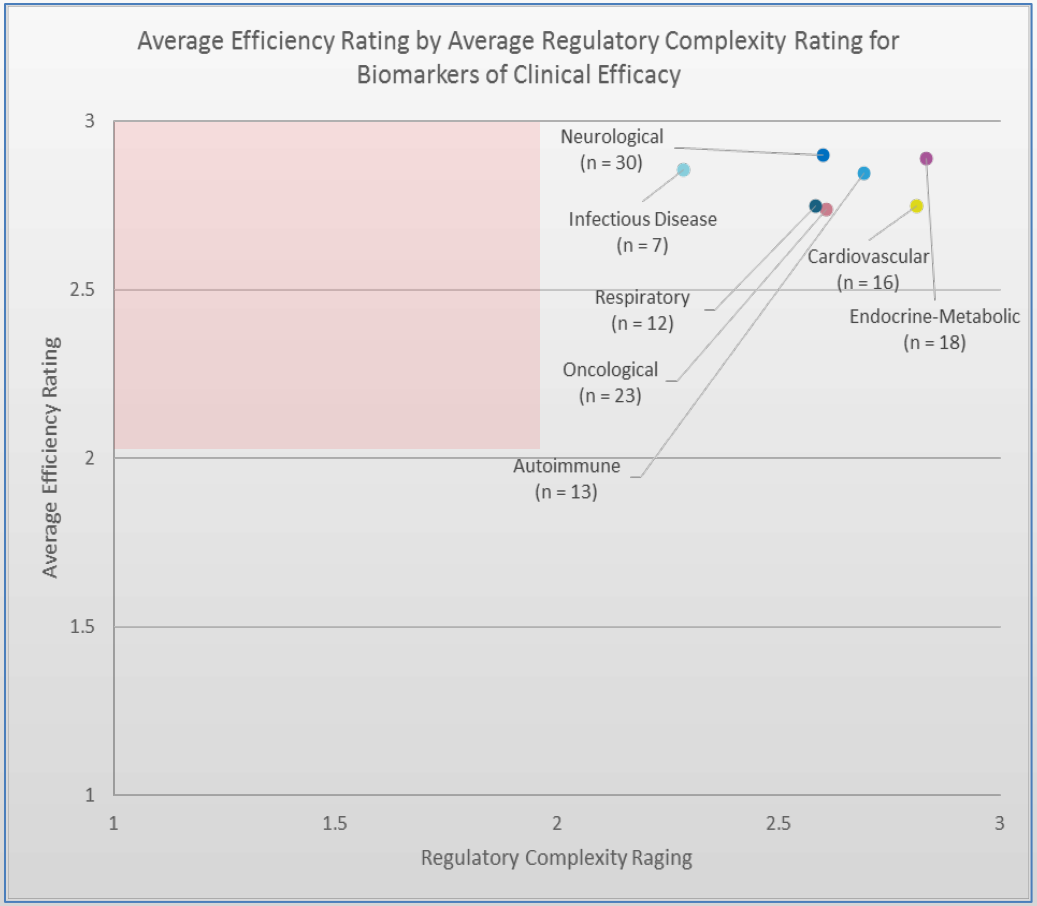
Clinical Efficacy Biomarkers Distribution



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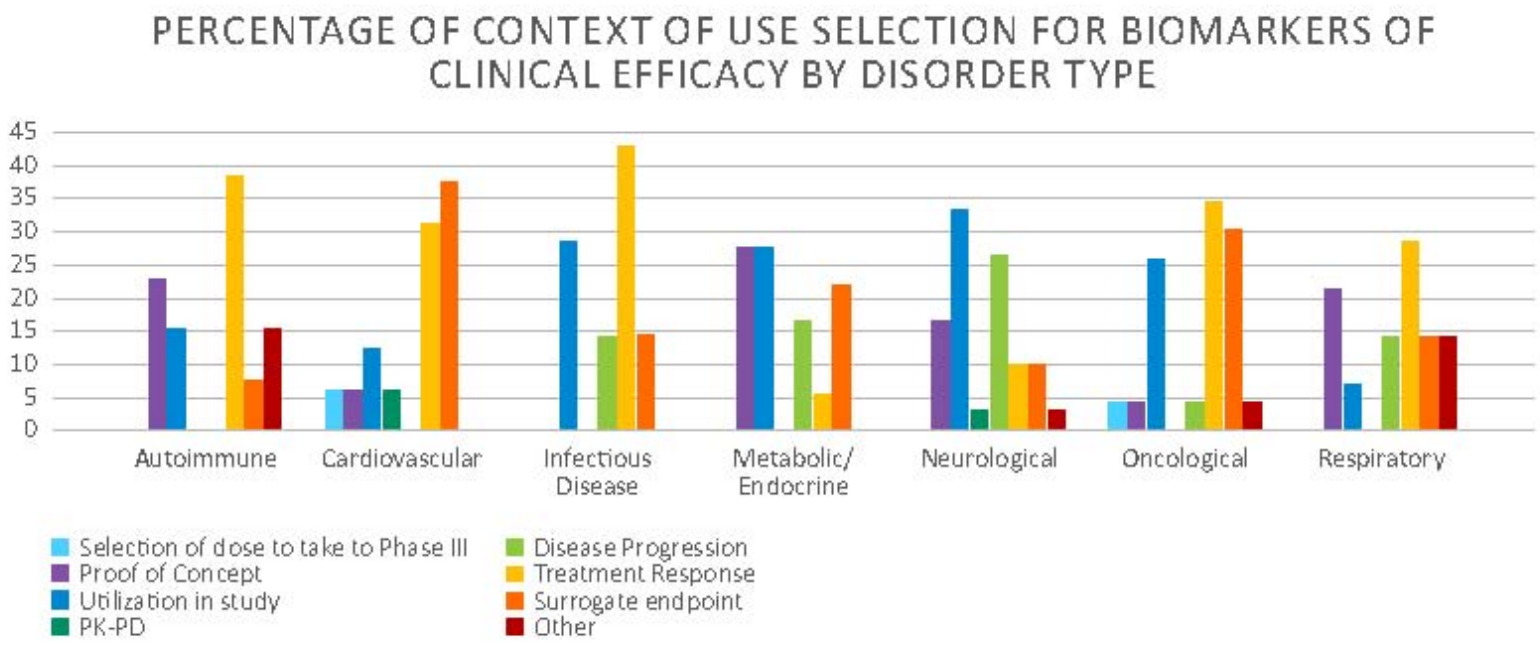
Distribution of context of use selection for efficacy biomarkers by clinical area



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Summary

In summary, survey findings included the following highlights:

- For ***nonclinical biomarkers***, respondents indicated greatest interest in acute and chronic hepatotoxicity markers, and least interest in hematological toxicity markers;
- For ***clinical safety biomarkers***, respondents indicated greatest interest in acute kidney and liver toxicity programs;
- For ***clinical efficacy biomarkers***, highest response scores for both complexity and efficiency impact were reported for central nervous system (Alzheimer's Disease and Multiple Sclerosis) and cardiovascular (heart failure and coronary artery disease).
- In the nonclinical marker areas, we observed prevalence in selecting specific COUs, like "demonstration of organ toxicity without histopathology" for nephrotoxicity, hepatotoxicity and cardiotoxicity in both acute and chronic safety.
- In the clinical marker areas, we observed that "demonstration of organ toxicity" was the most selected COU for all the organs/system in both acute and chronic safety.
- For clinical efficacy biomarkers, COUs varied according to the disease area selected; for example we have observed that for AD the most selected COU is "utilization in study" versus "disease progression" for MS.