Biomarker Qualification

What it means, What it is for, What it is not

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Categories of Biomarkers

- Prognostic
- Predictive
- Pharmacodynamic
  - Efficacy-response (Surrogate endpoint)

- An individual biomarker may have uses in more than one category

How have Biomarkers become accepted?

- Case by case
  - Within a specific IND/NDA/BLA/Labeling Update
  - For a specific drug
  - Driven by a specific drug developer's needs
- General use accepted over extended period
  - Scientific experience accumulates through varied uses
  - Usually very extended time-frame
  - Evidence collection not cohesively directed

How can biomarkers become accepted?

- Co-development of drug and test
  - Companion diagnostics
  - Guidance in development

- Biomarker Qualification Process
  - Developing program within CDER
  - Opportunity for a new way to establish use of biomarkers
  - Outgrowth of Critical Path Initiative
  - Process Guidance published (Draft)

Biomarker Qualification

- A conclusion that within a carefully and specifically stated “context of use” the biomarker has been demonstrated to reliably support a specified manner of interpretation and application in drug development

- The qualified biomarker can be applied in drug development programs without the need for submission of extensive biomarker-supportive information to each IND, and re-evaluation to confirm that application is justified

What becomes Qualified?

- Biomarker is a ‘substance’, analyte, or otherwise a ‘thing’
  - Assay methods are needed to measure the biomarker
  - Assay method is not the biomarker
- One biomarker may have multiple assays that are capable of measuring the biomarker
  - Assay method/device performance characteristics are important
- CDRH clears or approves commercial testing devices for clinical measurements
- CDRH clearance does not equal CDER qualification
  - Different purposes

Context of Use

- Biomarkers are qualified for a very specific context of use
- A comprehensive statement of the manner of use and the purpose, including how to apply results to decision making
- May include identifying limits of established reliability

- Biomarker may also have utility outside the currently qualified context of use
  - Accept on case by case (IND specific) basis
  - May expand qualified context of use as further data justifies

Qualification Utility

- Utility in drug development, particularly regulatory decisions, is central to purpose of qualification
- Particularly for biomarkers expected to have application in multiple different drug development programs
- Qualified biomarkers may make some drug development programs less intractable, and more attractive to undertake
- Qualified biomarkers may avoid slowing down drug development when the individual drug sponsor would have needed to develop evidence on the biomarker during the drug development program

Qualification's Place in Therapeutic Development

- Qualification is not required
  - Case by case approach for accepting use in a single IND/NDA/BLA program remains valuable
- Qualification is voluntary
  - Holder of biomarker data can choose to pursue or not pursue qualification
- Qualification is intended for biomarkers that will be used in multiple drug development programs
  - Public knowledge and availability essential
  - Consortia or collaborative groups likely to be source of biomarkers for qualification

Qualification Process within CDER

- 'Submitter' proposes project to FDA
  - Identifies biomarker and proposed context of use
  - FDA decides whether this project has sufficient potential to justify Agency resources be devoted to actively working with submitter

- Interdisciplinary working team assembled within CDER & FDA
  - Working team will guide submitter, and ultimately review the complete evidence regarding the biomarker

Qualification Process within CDER

- Advice & Consultation stage begins

- Summaries of available information reviewed
  - Advice to submitter on how to advance development for intended use
  - Additional studies conducted as needed
- Summary results discussed with submitter as developed
  - Advice on next steps for development
  - Cycles of Briefing Document / Meeting / Conducting next steps as needed
  - Ultimately development is thought complete

Qualification Process within CDER

- Biomarker Review stage begins

- Submission of full data package
- Full review and CDER decision on qualification
- Formal qualification granted if appropriate

- Qualification statements made public on FDA website as appendix to Guidance on process for development of Drug Development Tools
  - Initially as “draft” guidance statement; subsequently finalized