Diagnostics 101 For SAS Professionals

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OVERVIEW

- CDISC
- Approval Process
- Biomarker
- Challenges
- Types of Studies
- Conclusion

CDISC

- 6 New SDTM Domains for Devices
  - Device Information
  - Device In-Use Properties
  - Device Subject-Relationship
  - Device Events
  - Device Exposure
  - Device Tracking and Disposition

CDISC

- Work on Diagnostics is in Progress
  - Lab data
    - How to handle run controls
    - Sample-based (no subjects) clinical trials

Approval Process

- Classification of Devices
  - *intended use* of the device and also upon *indications for use*
  - Class I - minimal risk
  - Class II - moderate risk
  - Class III - severe risk

Approval Process

- Center for Devices and Radiologic Health (CDRH)
  - 510(k)
    - Predicate device
  - PMA

Approval Process

- Combination Product
  - A diagnostic assay that is intended for use only with an approved drug where both are required to achieve the intended use or effect and that will be labeled as such upon approval.

Approval Process

- Combination Product
  - Joint submission
    - Pharma – CDER/CBER
    - Diagnostics - CDRH

Biomarker

- Biomarker – "…a substance used as an indication of a biological state. It is a characteristic that is objectively measured and evaluated as an indicator of:
  - A normal biological process
  - Pathogenic processes
  - Pharmacological responses to therapeutic intervention"

Biomarker

- To predict the likelihood of a cancer responding to a specific therapy
  - an existing therapy
  - an novel targeted therapy in development - THIS IS CoDX (companion diagnostics)

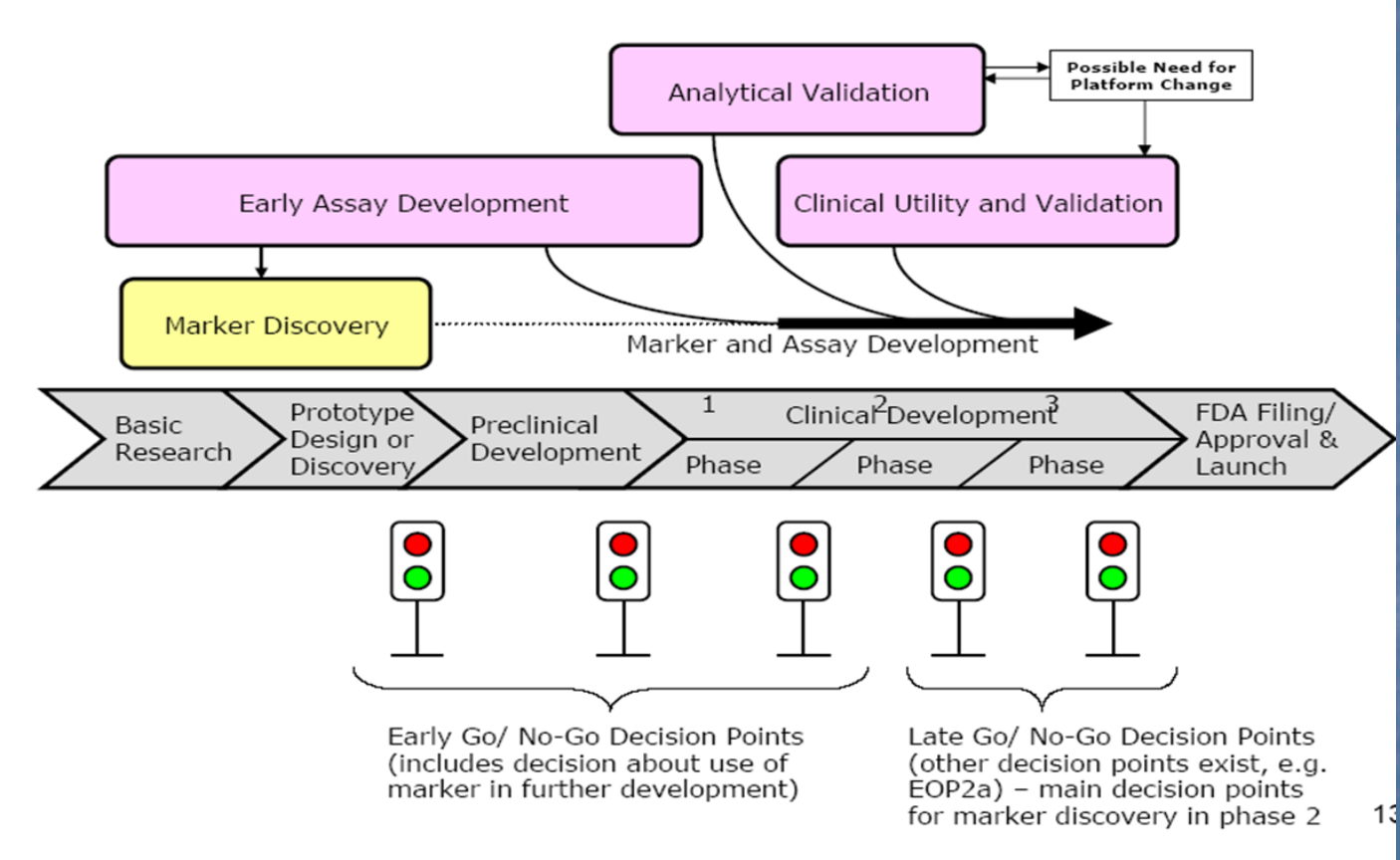
Biomarker

- Problem
  - Biomarkers need to be developed (qualified) in the context of their intended use.
    - The clinical phases of the drug development program will provide evidence of clinical utility (i.e., value) of the diagnostic test.
  - We do not know how good the marker/test is before going into clinical studies - context of use!

Challenges: CoDX Development

- Instrument Platform
- Software
- Algorithms
- Test Kits

Challenges: CoDX Development



Types of Studies

- Reproducibility
- Clinical Utility

Types of Studies

- Reproducibility
  - Accuracy and precision of an assay
  - Coefficient of variation
  - Components of variance (PROC MIXED)
  - Short: typically 4 weeks

Expected Concentration (Log10)	N	Total Standard Deviation	Percentage of Total Variance (Lognormal CV[%]) Lot	Site/ Instrument	Operator	Day/Run	Within-Run	Lognormal Total CV(%)
x.xxx	xxx	x.xx	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xxx.x
x.xxx	xxx	x.xx	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xxx.x
x.xxx	xxx	x.xx	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xxx.x
x.xxx	xxx	x.xx	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xxx.x
x.xxx	xxx	x.xx	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xxx.x
x.xxx	xxx	x.xx	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xx.x% (xxx.x)	xxx.x

Types of Studies

- Clinical Utility
  - Real-life use of an assay in clinical practice
  - Sensitivity, specificity, negative predictive value, positive predictive value (2x2 tables)
    - Assess analytic performance of the assay versus a reference method.
  - Longer: typically 1 – 4 months

Investigational Method	Reference Method		
	Positive	**Negative**	**Total**
Positive	xxx	xxx	xxx
Negative	xxx	xxx	xxx
Total	xxx(xx.x%)	xxx(xx.x%)	xxx
Positive Percent Agreement (95% CI)	xx.x% (xx.x%, xx.x%)		
Negative Percent Agreement (95% CI)	xx.x% (xx.x%, xx.x%)		
Overall Percent Agreement (95% CI)	xx.x% (xx.x%, xx.x%)		

CONCLUSION

- CoDX Challenges
  - Development of Assay
    - Within its intended use
  - Approval Process
    - Joint Submission
  - Types of Studies
    - Reference method

CONTACT INFORMATION

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