Establishing an In Vitro Diagnostic (IVD) Claim

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Claims

- Analytical Performance
- Clinical Performance

Risk

- High – PMA – “Safe and Effective”
- Moderate – Usually 510(k) – “Substantially Equivalent”
- Low – Usually exempt
- How many patients; impact per patient
- How reliable is the test, and how will the physician/provider use the result?

Clinical Performance Claims

- Define disease state
- Detect a change in disease state
- Forecast disease state
- [Clinical study designs differ]

Define Disease State

- Initial Diagnosis
  - Screening setting
  - Definitive diagnosis setting
  - In-between setting
- Presence of Residual Disease

Detect a Change in Disease State

- Recurrence
- Progression/Regression
- [Response to Therapy]

Forecast Disease State

- Future Likelihood of Disease
- Prognosis
  - Depending on the test result, the estimate of outcome for a class of patients
  - “Natural” or other history
- Prediction
  - Depending on the test result, the estimate of an intervention’s likely effect

Setting for the Test

- Indication/Intended Use for the Test
  - Intended Use Population
  - Measurement Performed
  - Use of the Test Result
- Stand-alone Use?
  - Sensitivity/Specificity
- Adjunctive Use?
  - Improved Sensitivity, Specificity or Both
  - NOT “just another tool”

Where Does the Test "Fit" in Patient Evaluation/Management?

- Schematic likely very useful – makes the intended use concrete
- Formulation of a testable hypothesis; hence, clear labeling
- No need to elucidate all possible uses of the test – pick one for study and review

Establishing a Diagnostic Claim for the Test – Study Designs

- Study set adequately representing the intended use population
- Gold standard to assess truth of test result – sensitivity and specificity
- Lesser standard to assess truth of test result – positive and negative concordance
- Defensible success criteria

Establishing a Monitoring Claim for the Test – Study Designs

- Adequate reference for disease state (e.g. biopsy, RECIST)
- Longitudinal study
- Often multiple observations per patient
- Data analyses may be complex; please seek advice

Establishing a Prognostic Claim for the Test – Study Designs

- Well characterized study population
- Well defined outcome variate
- If retrospective, carefully assess potential sources of bias and eliminate or mitigate/compensate for them

Establishing a Predictive Claim for the Test – Study Designs

- Single-arm or only marker positive studies generally insufficient
- Coordination with CDER or CBER and OCP likely needed
- Marker by Treatment Interaction Design
- Marker-based Strategy Design
- See Sargent et al, J Clin Oncol 2005; 23:2020-2027

Finding Help

- Regulatory Consultants
- OIVD Website – http://www.fda.gov/cdrh/oivd
  - Device Advice
  - IVD Guidances
  - Many other links
- Pre-IDE Process