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# Performance Standards for Clinical Trial Marker Assays

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# Performance Standards for Clinical Trial Marker Assays

- **Clinical Trials Working Group (CTWG) identified the need to establish standards for marker assays in phase II/III clinical trials**
- **The Cancer Diagnosis Program (CDP) was charged with developing the standards**
- **Performance Standards Document was developed by the Strategic Group of the Program for the Assessment of Clinical Cancer Tests (PACCT)**
- **Standards document approved in draft form by CTAC in July 2007**

# Rationale

- **The need to ensure that marker assays are sufficiently well validated to be used to make a clinical decision; patient stratification assignment to therapy, etc.**

- **The need to ensure that tests used in trials can be rapidly translated to clinical practice for patient benefit**

# Rationale con't

- **The need to adhere to regulations that apply to tests to be used to guide clinical decisions**
- **The principle that use of precious and non-renewable specimens collected in randomized trials should lead to clearly interpretable results that move the field forward**

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# Levels of Evidence Needed Vary with the Assay Type

- **Integral assays refer to tests that must be performed for the trial to proceed**
- **Integrated assays include assays that will be performed on all samples or cases (for imaging studies) but are not required for the trial to proceed and will not inform treatment decisions or actions within the current trial**

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# Integral Assays

- ***In vitro*** **assay(s) must be performed in laboratories with at least a CLIA Certificate of Compliance**
- **Required information includes the same categories of data as required for submission for FDA clearance (510k – substantial equivalence) or approval (premarket application)**

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# Integral *In Vitro* Assays

## Information and Data to be Included

- The role the assay will play in the trial (analogous to FDA 'intended use')
- Assay Description
  - Is test quantitative, semi-quantitative, or qualitative?
  - What platform will be used?
  - What is to be measured?
  - What are the controls?
  - What is the scoring procedure? (The values that will be used (e.g., pos vs neg; 1+, 2+ 3+); interpretation; etc.)
- specimen type(s)
  - preparation/handling/ shipping SOPs, including definition for acceptability of a sample

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# Integral *In Vitro* Assays

## Information and Data to be Included, cont

- Measurements of precision and reproducibility (within lab and between labs if more than one lab will be performing the assay)
- Data to support proposed cut-point(s) if assay results are not reported as a continuous variable
- Analytic sensitivity (limits of detection) and analytic specificity (cross-reacting substances, interfering substances, etc.)
- Accuracy measurements

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# Integral *In Vitro* Assays

## Information and Data to be Included, cont

- information about the statistical design used to establish the correlation with the clinical parameter of interest
- procedures in case of assay results that are not interpretable or are discrepant

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# Integral Imaging Assays

- **The in vivo imaging assay must be performed using standardized guidelines for image acquisition, analysis and interpretation (detailed SOPs)**
- **Information to support the use of the imaging assay:**
  - **The role the imaging test will play in the trial**
  - **Measurements of precision and reproducibility (within lab and between labs if more than one lab will be performing the assay)**
  - **Data to support proposed cut-point(s) if assay results are not reported as a continuous variable**
  - **Assay sensitivity (limits of detection) and specificity.**
  - **Accuracy measurements**

# Implementation

- **Two immediate needs**
  - **Biomarker, Imaging and Quality of Life Studies Funding Program (BIQSFP)**
  - **Integral Assay in Phase III trials concepts and protocols**
- **Additional need**
  - **To inform the prioritization of assays that will receive MoDEL services once MoDEL is implemented**

# Implementation Plan

- Checklist that captures the data elements for concepts that are submitted to CTEP has been developed
- Checklist incorporated into BIQSFP solicitation
- Standards Document and Checklist provided to Clinical Co-operative Group Chairs
- Planning to ensure distribution to Clinical Co-operative Group members who need to see it
- Discussions on going with CTEP staff on incorporation of checklist into guidelines for concept and protocol development
- Discussions on the development of an Assay Data Templates for capturing data during concept and protocol development