Clinical Assay Development Program

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Cancer Diagnosis Program
DCTD

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Clinical Assay Development Program

- Will improve patient outcomes by enabling the use of molecular features of malignancies to guide treatment

Goals

- To create a process to efficiently develop diagnostic tests that will address clinical needs, including co-development of targeted agents and predictive markers.
  - Meet rigorous performance standards
  - Speed evaluation of molecularly guided therapy

Background

- Advances in understanding cancer biology and the advent of technologies to characterize individual tumors promise to change the practice of medicine.
- NCI supports a large portfolio of grants to identify promising “biomarkers”, develop assays, assess clinical correlations and perform clinical trials with embedded markers.
- Unfortunately, the translation of these findings to improved clinical treatments has been inefficient. A large number of markers are reported but very few have entered practice

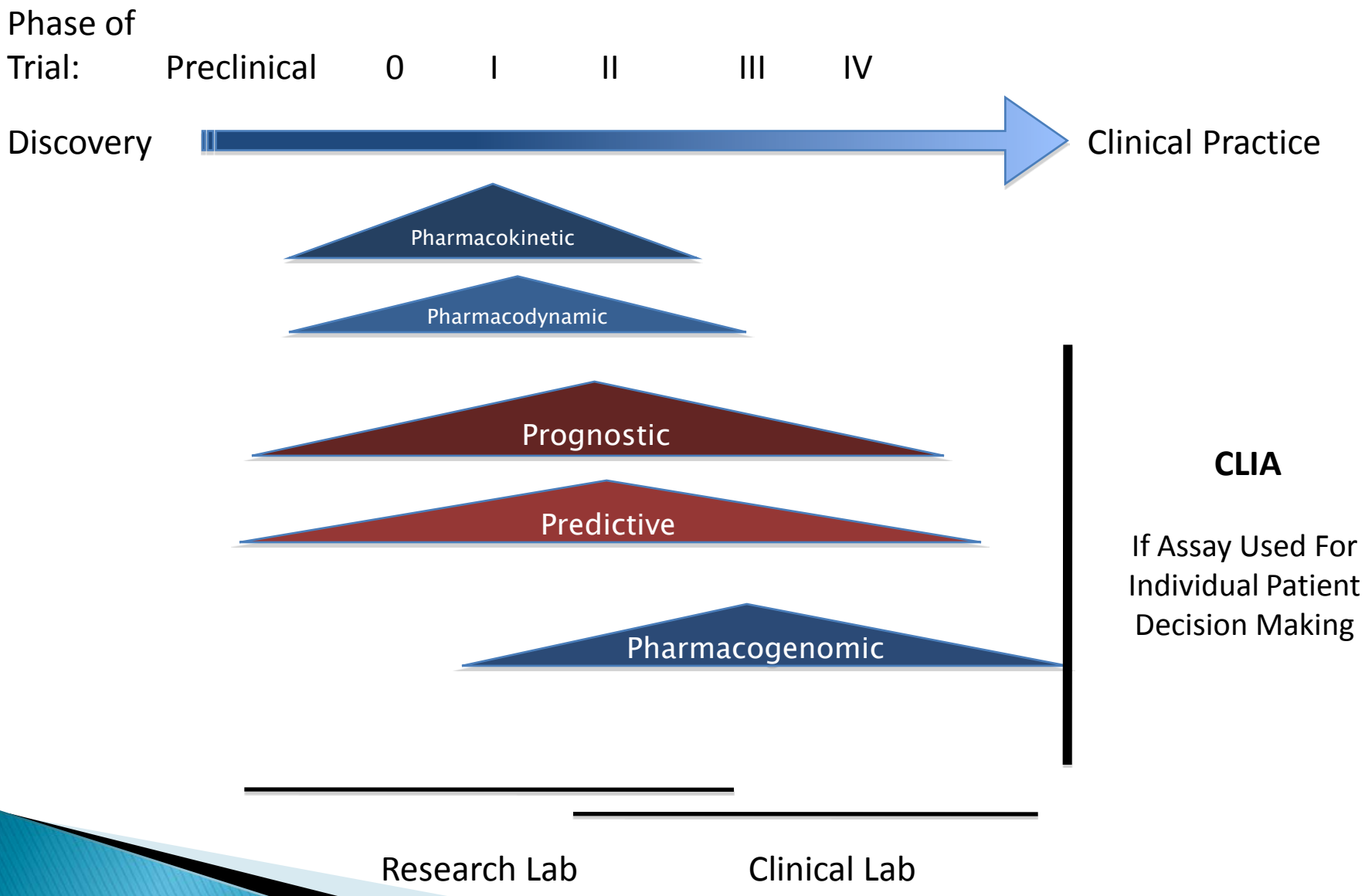
Rationale

- Clinical trial protocols often include markers for determining eligibility, stratification, or treatment assignment (integral markers)
- The assays to be used to determine these markers usually do not meet standards that are required for clinical decision making.
- Predictive markers and robust means to measure them are urgently needed in the clinic

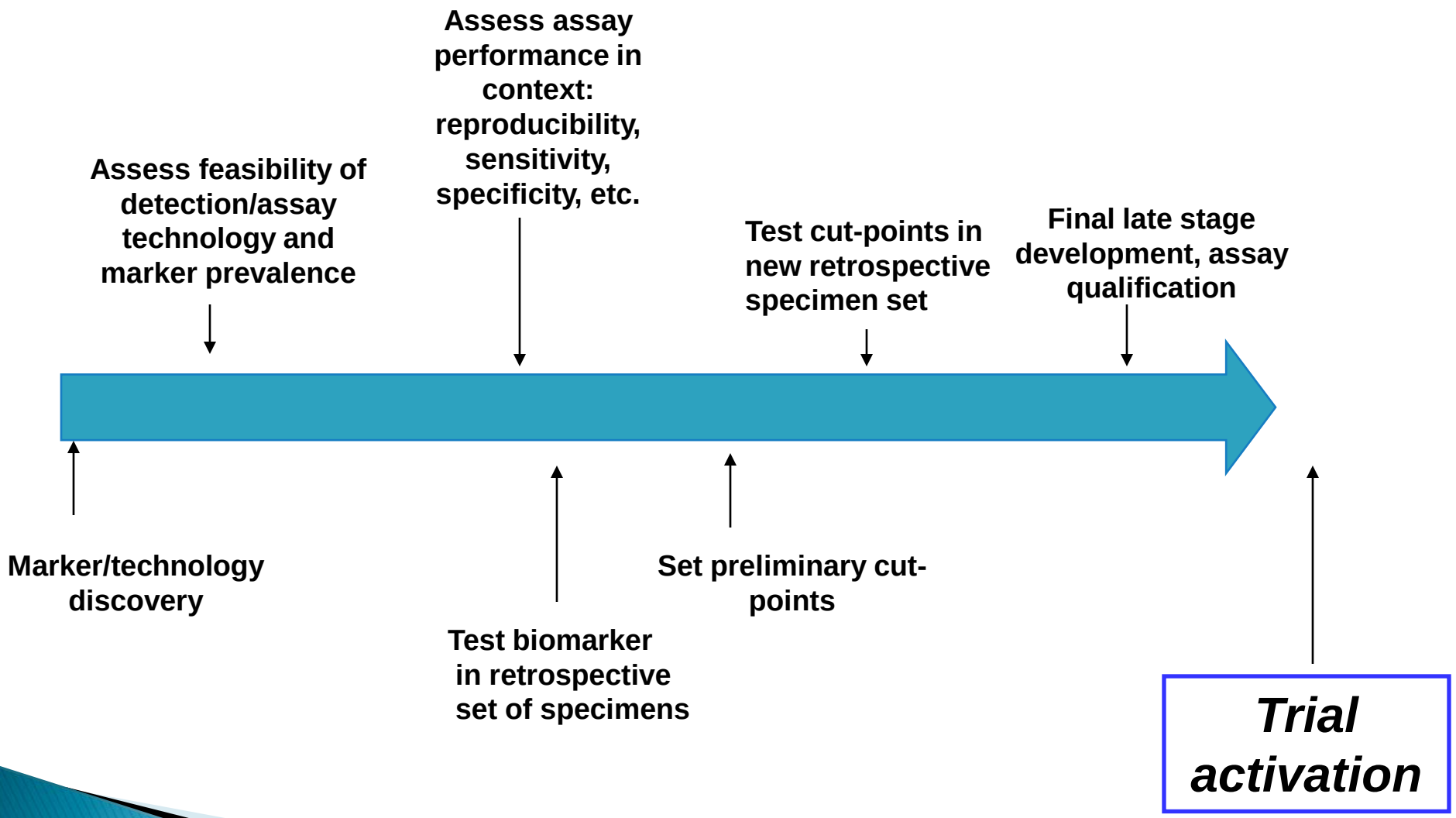
Value

- The Clinical Assay Development Program (CADP) will
  - Identify promising tests
  - Assess the needs for further development
  - Provide services to facilitate optimization of analytical performance and to establish clinical validity.

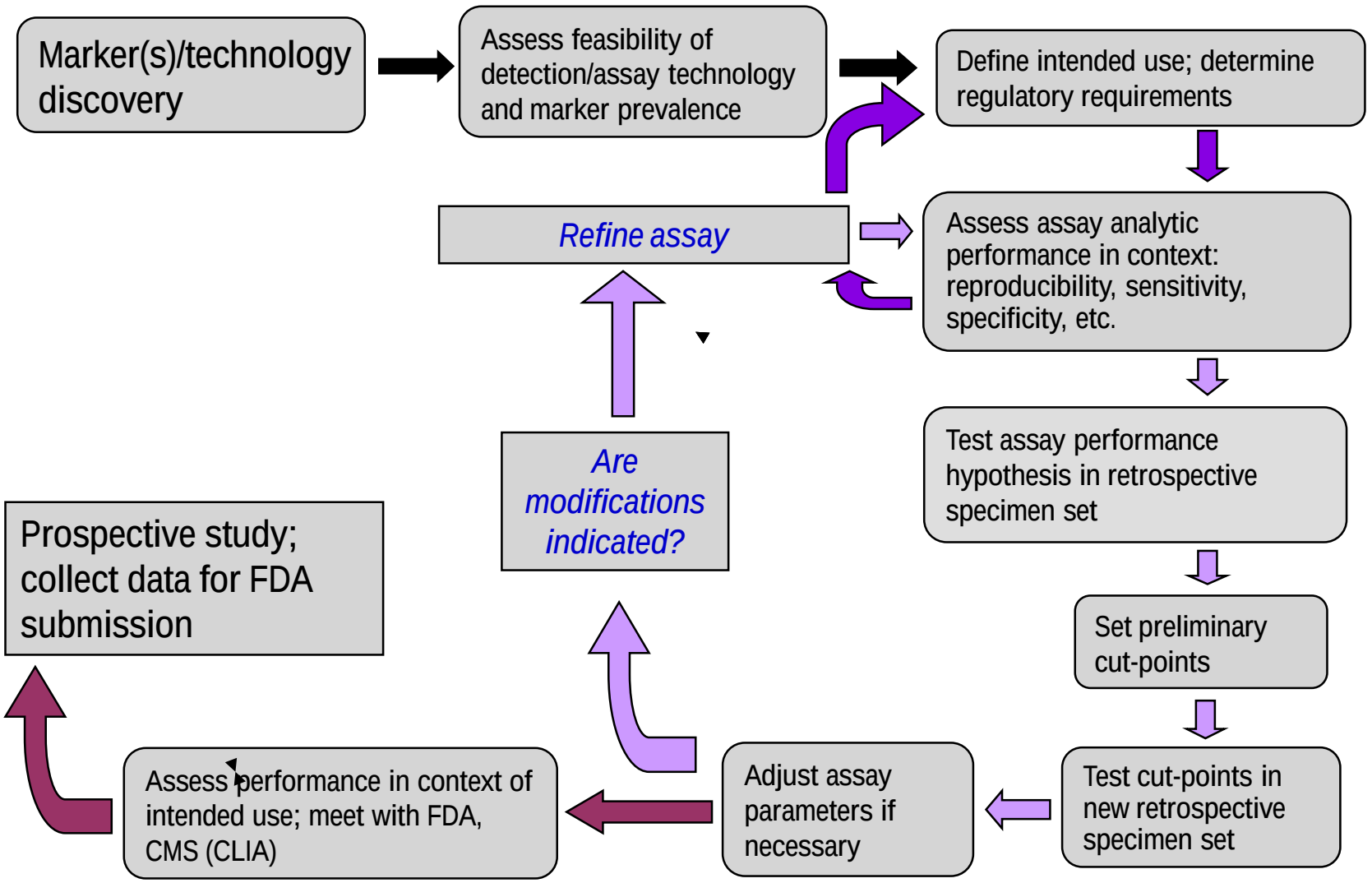
Assay & Marker Space



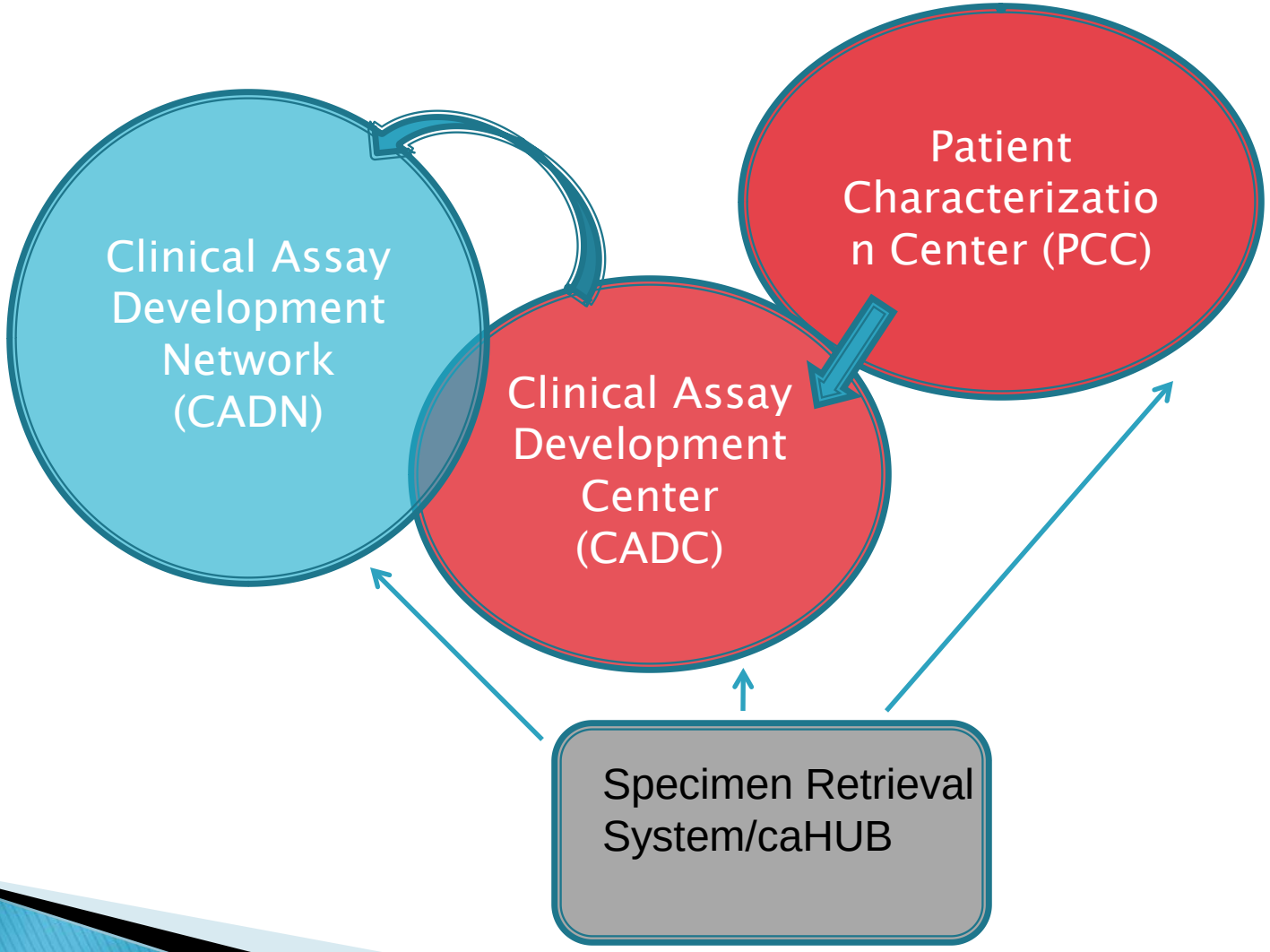
Clinical Assay Development Pipeline

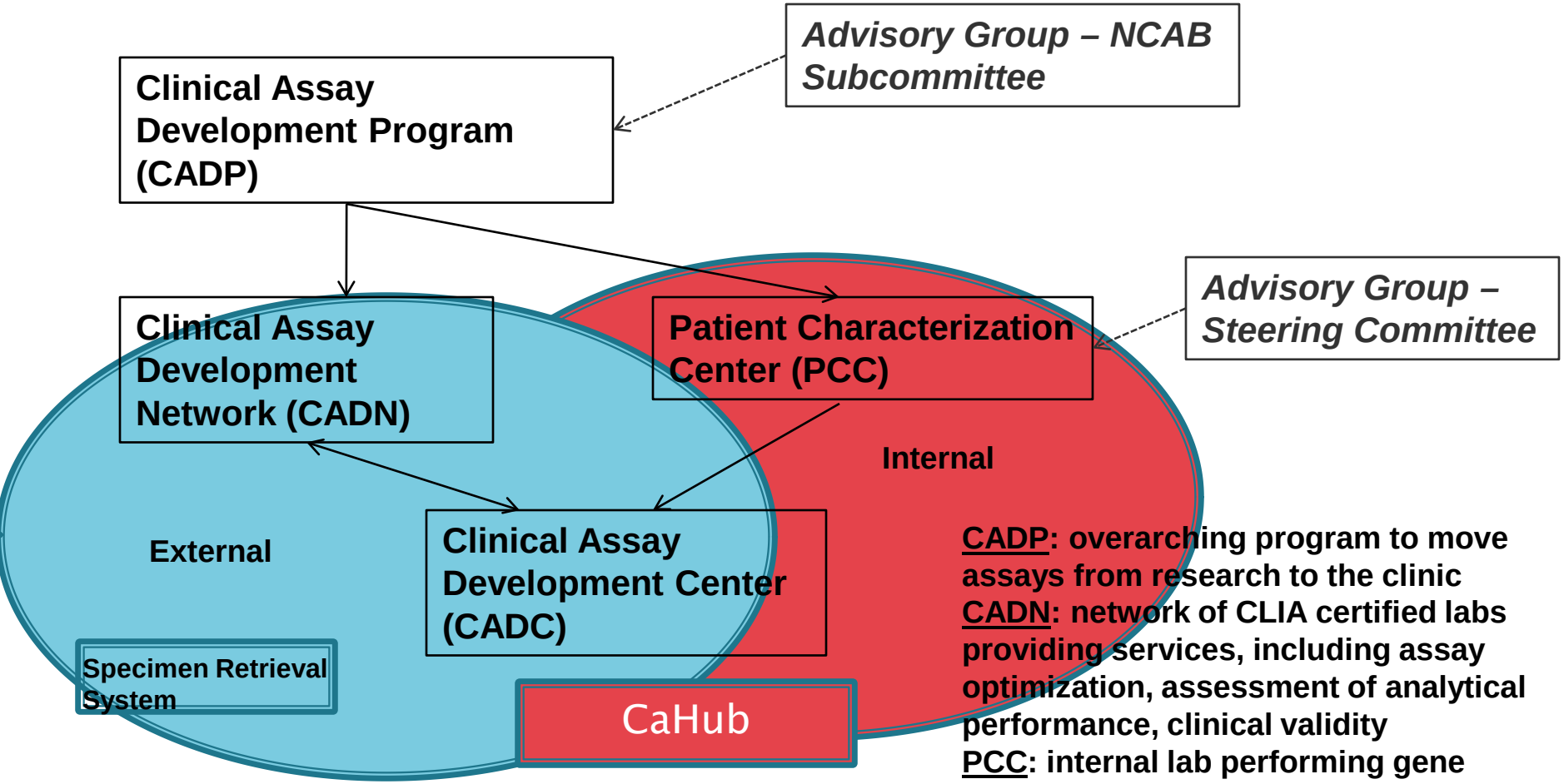


MARKER ASSAY DEVELOPMENT PROCESS



Clinical Assay Development Program





CADP: overarching program to move assays from research to the clinic
CADN: network of CLIA certified labs providing services, including assay optimization, assessment of analytical performance, clinical validity
PCC: internal lab performing gene expression profiling and somatic mutation detection using semi-quantitative NextGen sequencing on newly diagnosed cancers
CADC: internal lab that can be part of CADN and also be the assay development arm of PCC; develop standardized assays that can be disseminated

The Patient Characterization Center Will

- **Verify** biomarker discoveries (TCGA, academic investigators, literature etc.)
  - Utilize standardized genomic technologies (initially FFPET GEP and semi-quantitative targeted somatic mutation detection)
  - Utilize community samples for predictive assay verification
  - Generate SOP's including use of appropriate assay controls, calibrators and standards
  - Generate a public database of raw data, including clinical outcome when available

The Clinical Assay Development Center Will

Develop and optimize robust validated novel genomic assays and platforms for support of clinical studies

Train external sites in assay performance

Assist and participate in CADN activities

Clinical Assay Development Network

- Contracts (Basic Ordering Agreement – BOA)
- Later stage assay optimization and validation
  - CLIA certified
  - Expertise in one or more traditional assay platforms:
    - IHC
    - ELISA
    - ISH
    - qRT-PCR
    - qPCR
    - DNA sequencing

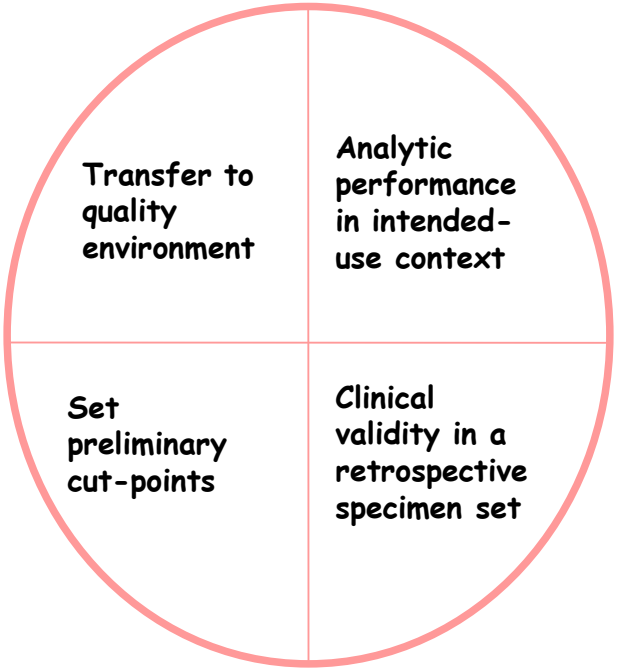
Specimen Retrieval System

- Contracts
- HMO's in the Cancer Research Network
- Community specimens with clinical and outcome data
- Resource for
  - Patient Characterization Center,
  - Clinical Assay Development Center
  - Clinical Assay Development Network

CADP Marker Development Services

Biomarker discovery and initial assay development; biomarker prevalence data; potential clinical applications; preliminary data on human tissue demonstrating a clearly defined intended clinical use

Earliest entry point →



Test cut-points in new set; retrospective test on new specimens; prospective study

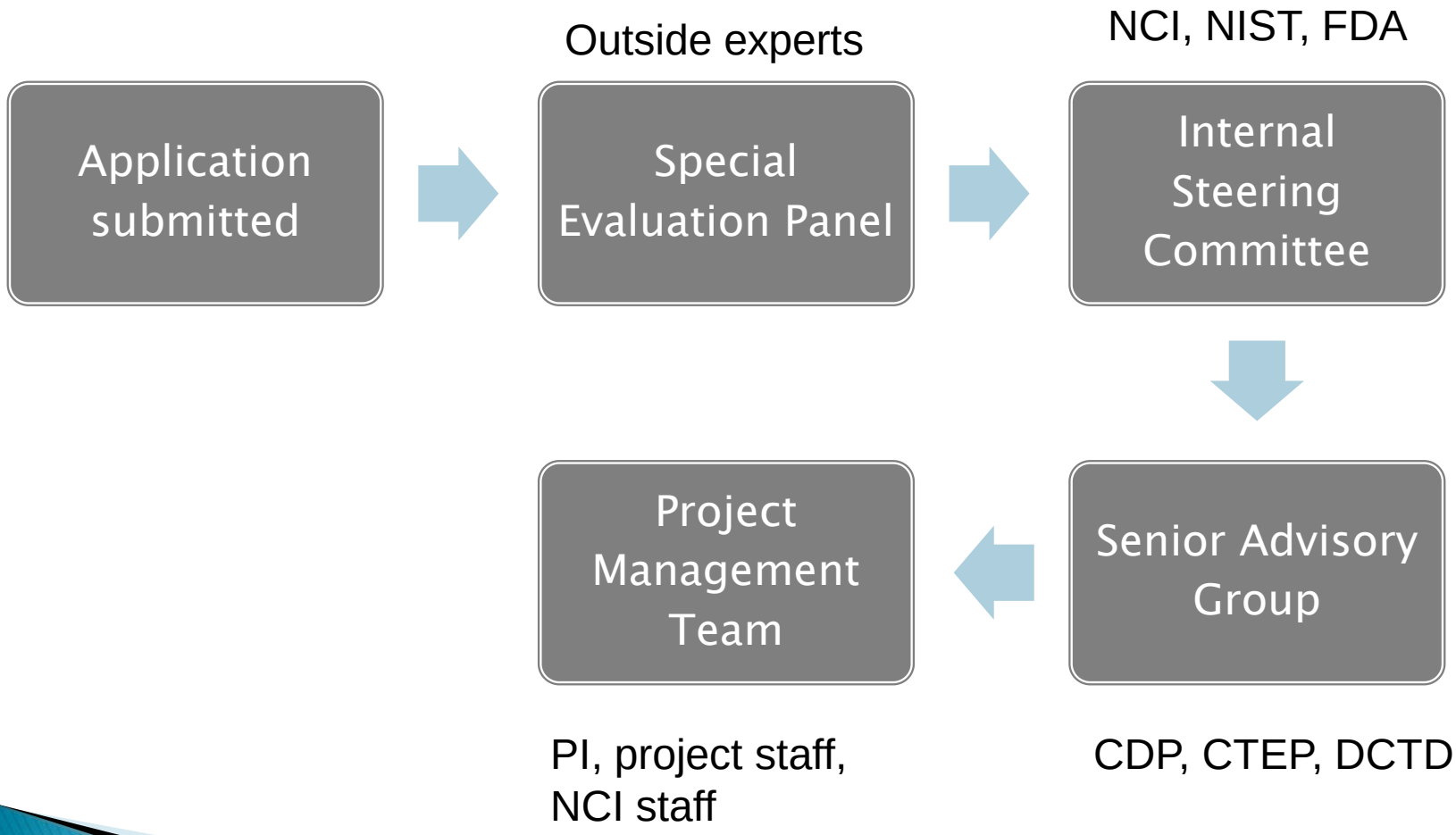
Post-discovery

- Consultation, project management
- Begin matchmaking
- Platform migration
- Assay optimization
- SOP development
- Provide or help find specimens
- Reference sets, calibrators, reagent prep
- Statistical design advice

Pre-trial

- Check data that support earlier steps
- Provide or help find specimens
- Final validation in new specimen sets
- Statistical consultation
- Facilitate transportability

CADP Process



Operation

- Earliest point of entry:
  - Working prototype assay has been developed
  - Intended clinical use for the assay is clearly defined

- Assays that have progressed further need
  - Optimization
  - Transfer to quality environment
  - Validation of analytic performance
  - Statistical Consultation
  - Help with appropriate specimens to refine cutpoints
  - Assistance with transportability

Application – Online

Technical feasibility
Clinical utility
Plans for the assay after CADP development

Who can apply

Academic investigators
Biotech firms
Clinical trials investigators

Evaluation

- Scientific Merit (40%)
  - Hypothesis sound; clinical utility
- Feasibility (30%)
  - Performance characteristics in context of intended clinical use
- Impact/Clinical Need (20%)
  - Novel insight; adds significantly to current clinical practice
- Path to Clinical Implementation (10%)

Current Status

CADP Component	Status
Clinical Assay Development Network	BOAs offered to 8 CLIA-certified labs
Patient Characterization Center & Clinical Assay Development Center	Operational 1st quarter 2011
Specimen Retrieval System	Contracts by Jan 2011
Applications	Anticipated Jan 2011