



**OBBR**

Office of Biorepositories  
and Biospecimen Research

# Update: The Cancer HUMAN Biobank (caHUB)

Carolyn C. Compton, M.D., Ph.D.

Director, Office of Biorepositories and Biospecimen Research

Meeting of the National Cancer Advisory Board  
February 18, 2010



**caHUB** The Cancer  
Human Biobank

NATIONAL  
CANCER  
INSTITUTE



## The NCI Addresses the Challenge

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### Consensus of the Broad Scientific Community:

The lack of high-quality, clinically annotated human specimens has become the limiting factor for translational cancer research.

### The NCI Moves Stepwise Towards Solutions:

- Standards
  - The *NCI's Best Practices for Biospecimen Resources*
- Science
  - The Biospecimen Research Network
- **Specimens and Service**
  - **The Cancer Human Biobank**





## Understanding the Problem: The Siloed National Biobanking Landscape

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- Collection, procession, storage procedures differ
  - Degree and type of data annotation varies
  - Scope and type of patient consent differs
  - Access policies are lacking or unknown to potential users
  - Materials transfer agreement conditions differ
  - Supporting IT structures differ in capacity and functionality
- **WIDE VARIATION IN QUALITY OF SPECIMENS AND DATA**

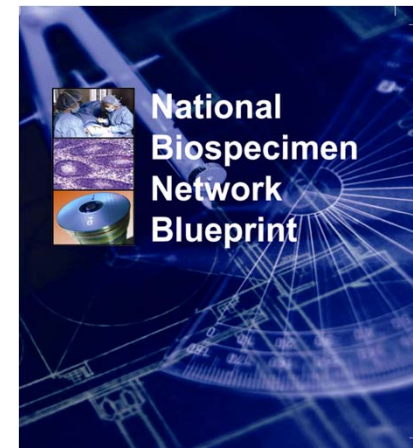


# Consensus for a Solution: The National Biospecimen Network Blueprint (2003)

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## Key principles for a national biobank:

- Standardized procedures for biospecimen collection and distribution
- Standardized data sets and data vocabulary
- Integrated information technology system to support all functions
- Harmonized approach to ethical and legal issues
  - Standardized consent, MTAs
- Transparent governance and business models
  - Transparent access policies
- Large well-designed, standardized specimen sets







## caHUB Is Founded on NBN Principles

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### The Cancer Human Biobank vision:

- unique, centralized, non-profit public resource
- source of adequate and continuous supplies of human biospecimens and associated data of *measurable, high quality* acquired within an ethical framework
- source of high-quality biobanking services for the community



**caHUB** The Cancer  
Human Biobank



## Update on Key Issues

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- **Verification of the need for caHUB**
- **Development planning**
- **Fundamental details**
  - **Who will provide the specimens**
  - **Who will use the specimens**
  - **How data will be collected and handled**
  - **How the specimens will be used (scientific purposes)**
- **Business plans and timelines**
- **Funding: \$60M ARRA funds allotted to caHUB in 2009**



## The Need for caHUB

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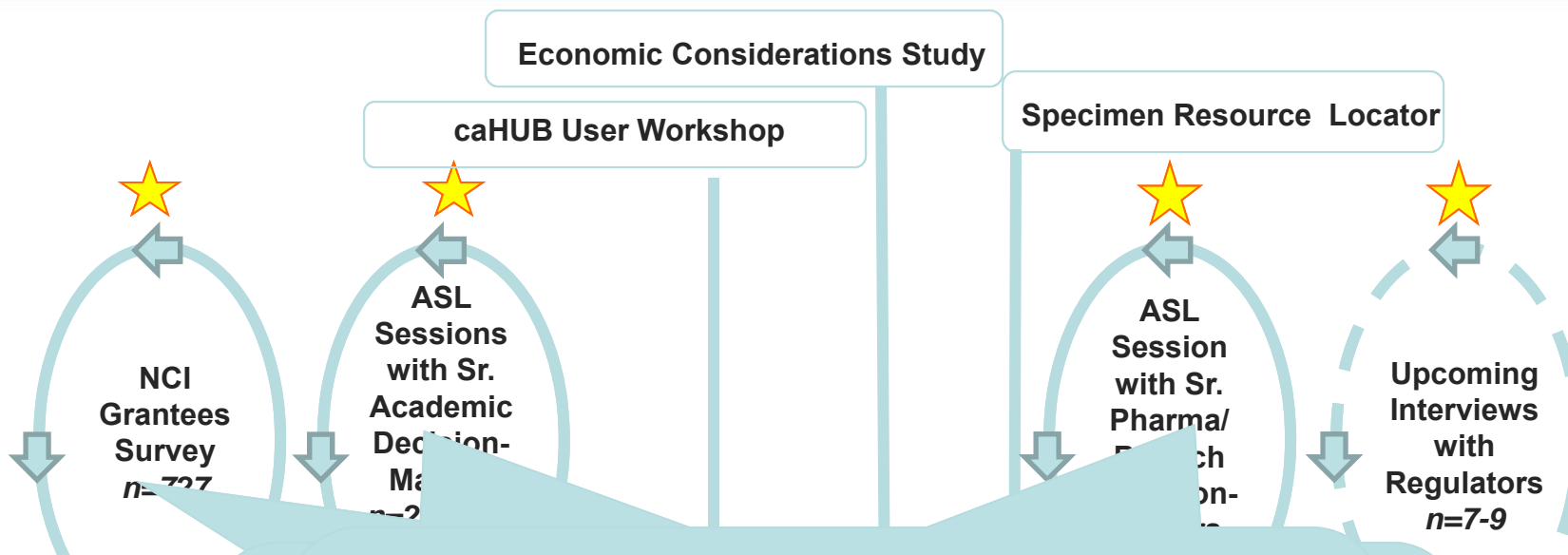
- **The need for caHUB has been clearly enunciated from all sources:**
  - **Survey of NCI investigators**
  - **Market research using focus group sessions with academia and industry decision-makers (OMB-approved; Strat@com-executed)**
    - **Focus group upcoming for regulators**
  - **Interviews with commercial tissue providers and industry users (economics considerations study by Booz Allen Hamilton)**
  - **caHUB Users Workshop**
  - **Mining of request data from the NCI Tissue Locator: last 7 years**
  - **Direct input to OBBR from potential users: CTEP, NCI Patient Characterization Center (PCC), numerous biomarkers programs**





# Stakeholder Feedback

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## Key Finding

- Biospecimen
- Both the c
- Research i
- Research :

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## Benefits of a National Biobank:

- Inspire confidence in quality of specimens
- Ensure ethical collection standards

## Development Challenges:

- IP constraints

• Strong support for a national biobank concept from all stakeholders

## Barriers to Contribute:

- IP constraints



## Summary: Strat@com Market Research Results

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- **There is clear and universal need for a National, Standardized, Human Biospecimen Resource (NSHBR)**
- **For all audiences, the level of consistency and standardization that could be offered is the most important benefit**
- **An NSHBR has the opportunity to define standard operating procedures (SOPs) for the field/industry**
  - **In fact, stakeholders are counting on it**



## The Standards for Personalized Medicine

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**“There is an opportunity for the NIH to be the ‘Statue of Liberty’ in creating a vision for how to collect, annotate, store and distribute samples in a standardized way.”**

**- Steve Gutman, FDA**



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## Importance of a National Biospecimen Resource Cited on Many Levels

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- **Genomics and Personalized Medicine Act of 2007**
- **Institute Of Medicine Report: *Cancer Biomarkers*, 2007**
- **Dept. of Health and Human Services, *Personalized Health Care Report*, Sept. 2007**
- **President's Council of Advisors on Science and Technology: *Priorities for Personalized Medicine*, Sept. 2008**
- **President's Cancer Panel Report, *Maximizing Our Nation's Investment in Cancer*, Sept. 2008**
- **Kennedy-Hutchison Cancer Bill (ALERT Bill: "War on Cancer, Part II"), 2009**
- **The NCI Bypass Budget for FY2010**

# caHUB and the Popular Press



## 8. Biobanks By ALICE PARK

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Inside Huntsman Cancer Institute's vaults: Pancreatic tumors on ice. Lance W. Clayton for TIME

Folks at the National Cancer Institute (NCI) are heading up an effort to establish the U.S.'s first national biobank — a safe house for tissue samples, tumor cells, DNA and, yes, even blood — that would be used for research into new treatments for diseases.... By fall, the group hopes to have mapped out a plan for a national biobank; the recent stimulus showered on the government by the Obama Administration might even accelerate that timetable.

*Time Magazine* March 23, 2009

*Time Magazine* November 25, 2009

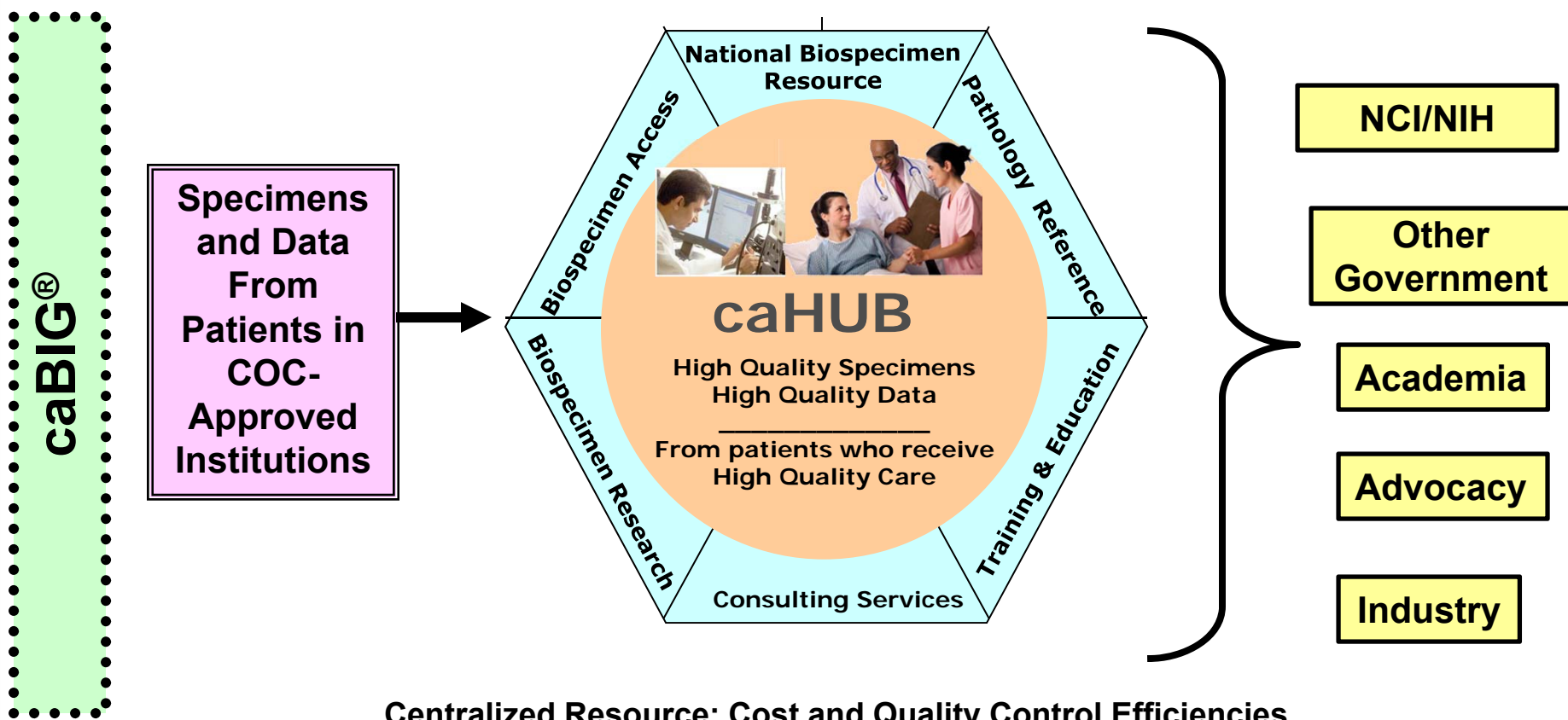




# caHUB: Centralized Model

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- HIGH QUALITY SPECIMENS • HIGH QUALITY DATA • FROM PTS RECEIVING HIGH QUALITY CARE



Centralized Resource: Cost and Quality Control Efficiencies





## caHUB Planning

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- **Planning committees operating for one year:**
  - **Administration**
  - **Strategic planning:** mission, vision, scope, organizational structure, evaluation, milestones and success factors
  - **Normal tissue acquisition:** rapid autopsy (also metastatic tumor, premalignant disease)
  - **Biospecimens:** SOPs, prioritization strategies, collection design, quality control monitors, and qualifying metrics
  - **ELSI:** Ethical, legal and social issues
  - **Facilities** requirements and design
  - **Informatics** requirements, design, and implementation
  - **Partnerships** and business models
- **210 expert contributors to the process and products**
- **Delivery of final products (white papers, SOPs, other manuscripts) scheduled for March 2010; for publication and/or availability through OBBR website**
  - Independent value to broader biobanking community



## caHUB Collection Prioritization: Process Design

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- **Process goal: Objective, realistic, quantitative**
  - **A quantitative prioritization matrix was developed using 9 criteria and a 3-tiered scoring system of importance for each**
  - **9 criteria:**
    - Ease of collection
    - Size of tumor at diagnosis
    - Treatment by surgery
    - Pre-resection treatment
    - Need for new clinical tools for diagnosis and treatment
    - Prevalence
    - Increasing incidence
    - Survival rates
    - Cost to society
  - **60 cancers selected (of 850) using NLM/SEER data**
  - **Weighting against scientific demand during launch phase**



## caHUB Collection Strategies and Standard Operating Procedures (SOPs)

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- **Completed:**
  - Tissue collection SOPs developed for 19 organs and 23 cancers
  - Specimen qualification SOPs: Morphologic, morphometric, and molecular qualification metrics
  - Blood collection SOP: Collection and processing
  - Quality monitoring: Key quality criteria for all steps of process flow
- **In progress:**
  - Identification of critical process steps that require continuous, detailed monitoring
  - Integration into the caHUB Quality Management Plan





## caHUB Collection Design: Informed by User Need

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### In high demand and short supply:

- **Benchmark samples:** biospecimens collected through standardized collection, handling, storage, processing and distribution procedures, with strict quality control and associated metrics
  - Data associated with process variables
- **Cases with multiple aliquots:** Confirmation of prior studies or the opportunity to contribute information to prior studies based on new technologies
- **Statistically valid numbers of biospecimen sets**
- **Fully defined “patient case sets”**
  - Tumor
  - Adjacent normal tissue
  - Tumor periphery (invasive border)
  - Pre- and post operative blood samples
  - Urine
  - Rich clinical data and outcome information for patients



## The caHUB Comprehensive Data Resource: Functionalities

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- **Provide user access to caHUB**
- **Ensure patient privacy and confidentiality**
- **Integrate patient and specimen data from multiple sources:**
- **Allow submission of data on caHUB specimens**
- **Perform QA/QC on all data**
- **Allow researchers to query specimen inventory based on data types**
- **Allow requesting of specimens**
- **Allow requesting, analysis, and download of datasets**

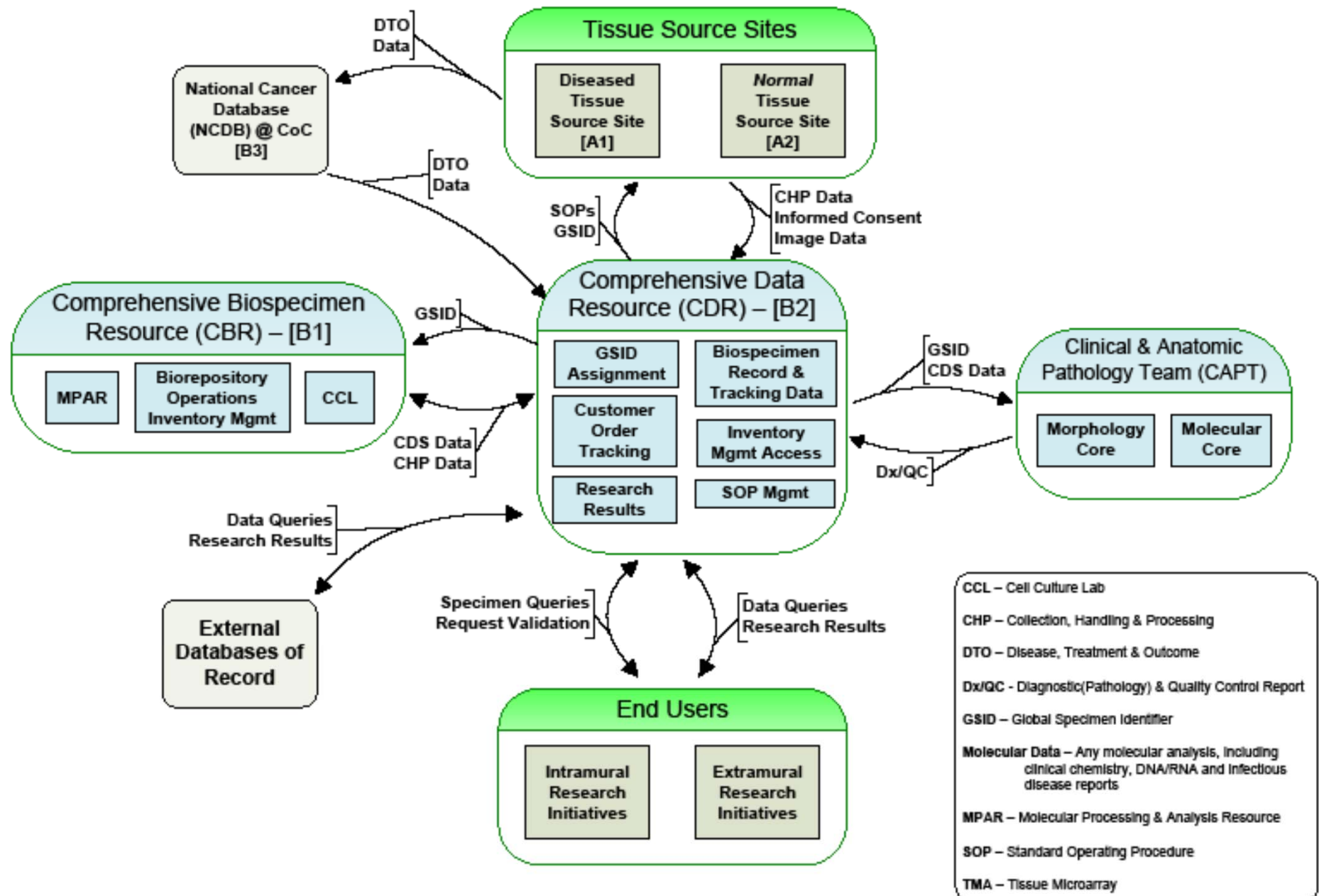


## caHUB Data: Principles, Procedures and Systems

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- **CaBIG is leading the planning/development of all informatics systems for caHUB**
- **Informatics strategies embody caBIG principles (interoperability; open source; standardized data vocabularies)**
- **caHUB Notional Informatics Architecture has been developed, reviewed, refined**
- **“Use Case” titles for the caHUB Comprehensive Data Resource are developed**
- **Data types include:**
  - Clinical data on patient including future follow-up
  - Specimen “life cycle” data: intra-operative, procurement and processing data
  - caHUB pathology review, digital imaging, and quality control data
  - Overall quality management data
  - Specimen inventory and tracking data
  - Molecular analysis data

# Comprehensive Data Resource Overview







## The caHUB Business Model: A Commodities and Services Model

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### **COMMODITIES: Cost Recovery**

#### **Distribution of specimens and data**

Increasing value of aliquots over time with increasing data richness: Time-dependent maturity

### **SERVICES: Revenue Generation**

Build on existing infrastructure and improve return on investment: Not time-dependent

- **Biobanking services to other initiatives**
  - Other NCI/NIH
  - Rare diseases
  - Advocacy
- **Education and training**
  - Pathology and laboratory functions
  - Operating room functions
  - IT and data management
  - Biostatistical and analytic methods
- **Consulting services**
  - Biobanking methods and best practices
- **Biobanking support service to industry**
  - Assay development
  - Clinical trials
- **Laboratory space and services**
  - Research incubator functions
  - Longer term in-house research contracts

## Accrual and Inventory Maturation

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Fiscal Year	Number of Tumor Cases	Number of Normal Cases	Total Number of Cases per Fiscal Year	Total Case Accrual	Total Aliquots per year	Total Aliquot Accrual
2011	1,000	600	1,600	1,600	41,440	41,440
2012	2,000	1,200	3,200	4,800	78,880	120,320
2013	3,000	1,600	4,600	9,400	109,240	229,560
2014	5,000	2,400	7,400	16,800	177,960	407,520
2015	6,000	2,400	8,400	25,200	206,160	613,680
2016	6,000	2,400	8,400	33,600	206,160	819,840
2017	3,000	900	3,900	37,500	98,460	918,300
<b>Total</b>	<b>26,000</b>	<b>11,500</b>	<b>37,500</b>		<b>918,300</b>	

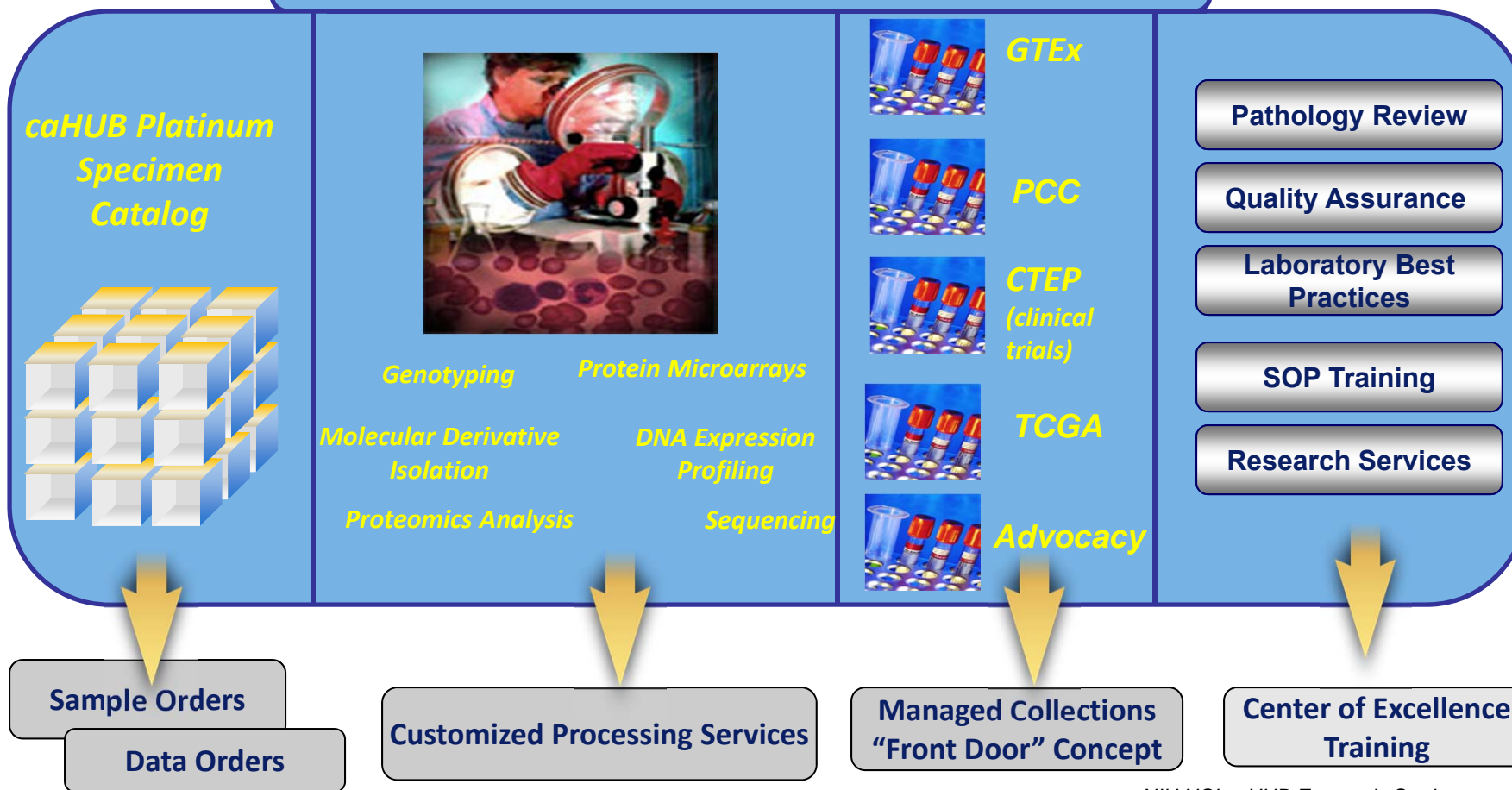
30% Optimal Case Collection = 3 Optimal Tumor Modules (6 FF/6 SC/12 SF/6 UF/3 CC) + 3 Optimal Normal Modules (6 FF/12 SF/6 UF)

40% Average Case Collection = 1 Optimal Tumor Module (2 FF/ 2 SC/ 8 SF/ 2 UF/ 1 CC) + 2 Optimal Normal Modules (4 FF/ 8 SF/ 4 UF)

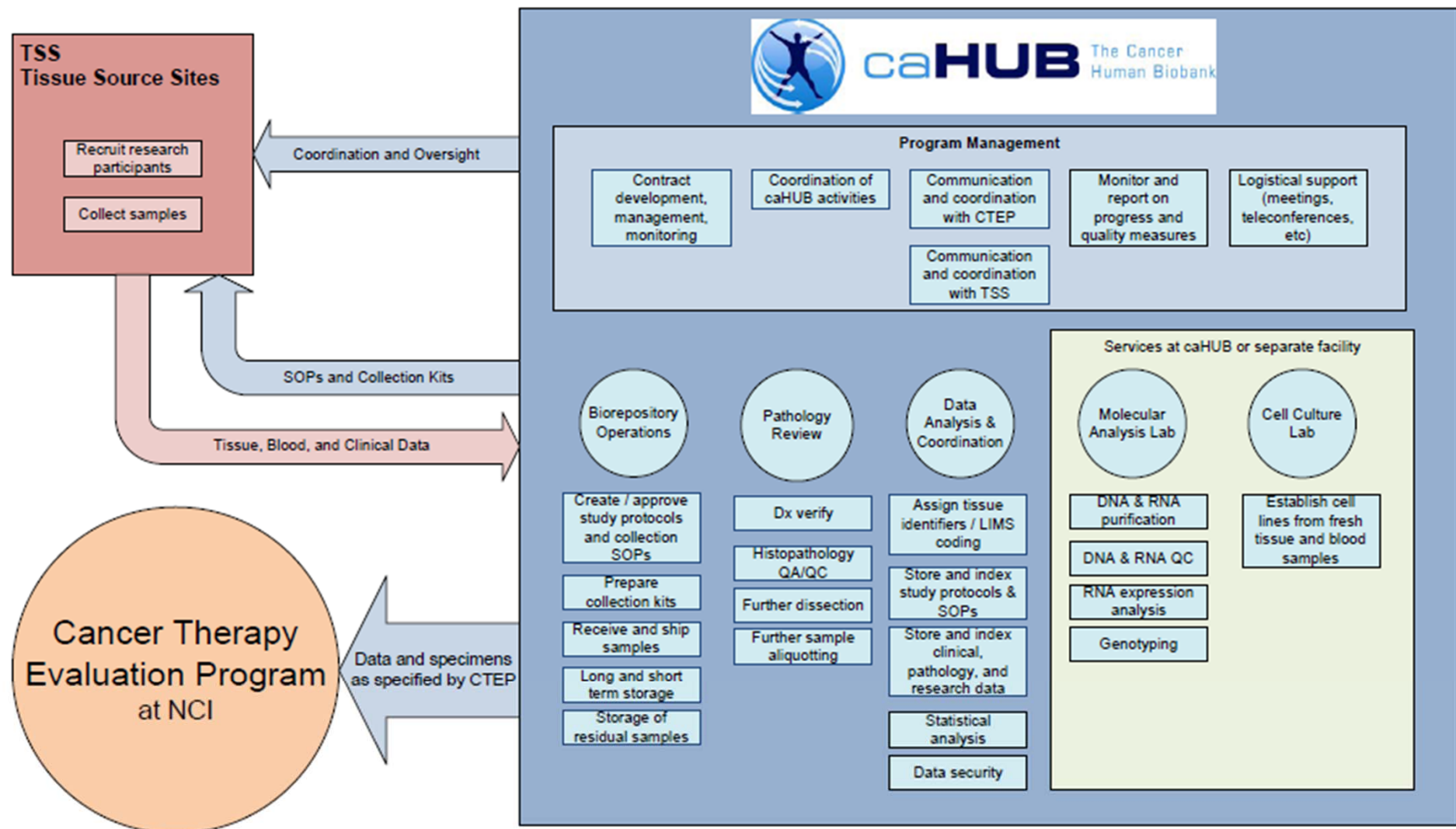
30% "Worst" Case Collection = 1 Minimal Tumor Module (1 FF/ 1 SC/ 1 SF) + 2 Minimal Normal Modules (2 FF/ 2 SF/ 2 UF)

# caHUB Business Model

## Commodities and Service-Based Model



# caHUB as Service Provider: CTEP Example







## The caHUB Business Model: Economic Considerations

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- **A detailed 15-year Total Life Cycle Cost of Ownership (TLCO) planning model for building and operating caHUB developed based on:**
  - **Comprehensive caHUB supply chain/value chain framework**
    - Encompasses all costs for (1) collection; (2) processing; (3) storage; (4) distribution; (5) infrastructure; and (6) administration
  - **Data derived from an analysis of the current biobanking landscape**
    - Interviews with >75 commercial and academic biobanking experts
  - **“Risk-based” approaches to changing business parameters and impacts on costs**
  - **An iteratively refined approach to estimated costs**
    - Cost baseline was revised and narrowed through numerous working sessions with key experts to inject realism into estimated costs
    - Continuous refinement of case flow accrual projections and processing protocols.

# 3 Fundamental Factors That Drive Pricing

## Fit for Purpose – Relationship to Pricing

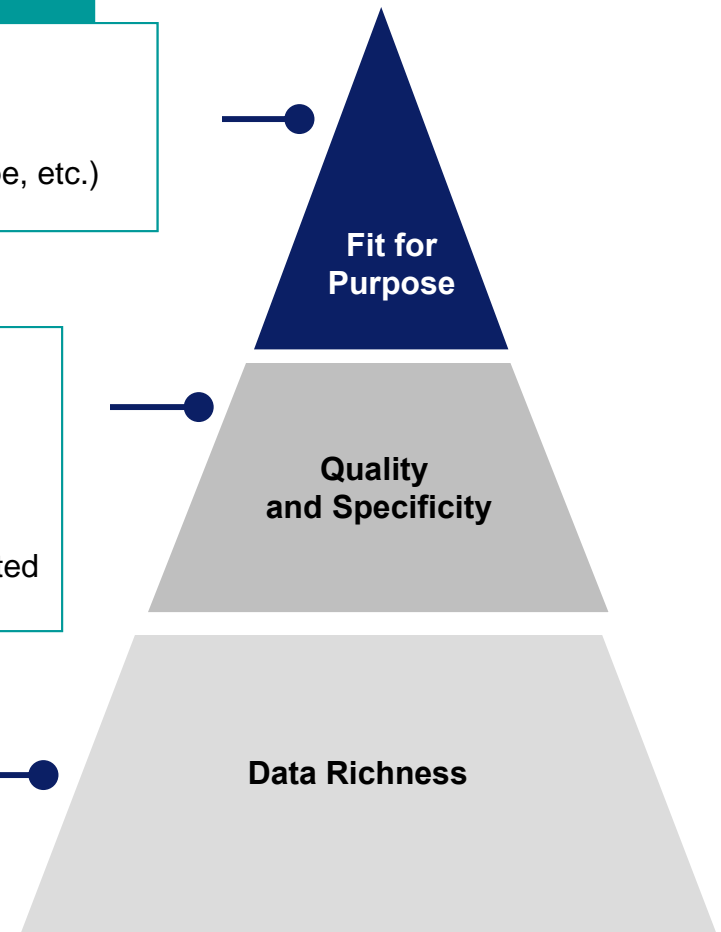
- ▶ The research application and scientific question being addressed
- ▶ Specifics of the collection protocol
- ▶ Specific project needs (e.g. normal, diseased, tissue origin, specimen type, etc.)

## Sample Quality and Specificity– Relationship to Pricing

- ▶ Quality and specificity price drivers:
  - ▶ Specimen rarity and size requirements
  - ▶ Extent of customized processing requested
  - ▶ Clinical parameters (e.g. treatments, etc.), and pathology parameters (e.g. tumor subtype, positive tissue markers) requested

## Data Richness – Relationship to Pricing

- ▶ Outcomes data are in high demand
- ▶ Comprehensive data sets may double sample price
- ▶ Customized data increases the sample price



# caHUB Cost Recovery Modeling

1 **Cost Recovery Example 1 with Highly Conservative** assumptions shows caHUB recovering 70% of costs by Year 5:

caHUB Cost and Revenue Projections (in \$000's)	ARRA	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10	Average
	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023-27
Annual Case Collection Plan	3,200	4,800	7,400	8,400	8,400	8,400	7,816	2,203	472	100	21	\$ 1
caHUB Case Inventory Turnover Rate <sup>1</sup>	10%	196	990	1,639	2,295	2,951	3,559	3,709	3,741	3,747	3,749	\$ 3,749
Estimated Sample Revenue at Avg Price of <sup>2</sup>	\$ 250	\$ 8,500	\$ 18,000	\$ 29,865	\$ 41,827	\$ 53,782	\$ 64,865	\$ 67,603	\$ 68,171	\$ 68,293	\$ 68,318	\$ 68,325
Customized Processing Services/Orders <sup>3</sup>	\$ 25,000	15	30	39	45	48	51	54	57	60	65	74
Estimated Revenue from Customized Services		\$ 375	\$ 750	\$ 975	\$ 1,125	\$ 1,200	\$ 1,275	\$ 1,350	\$ 1,425	\$ 1,500	\$ 1,625	\$ 1,850
Total Estimated Revenue		\$ 3,943	\$ 18,785	\$ 30,840	\$ 42,952	\$ 54,982	\$ 66,140	\$ 68,953	\$ 69,596	\$ 69,793	\$ 69,943	\$ 70,175
Estimated Annual caHUB Operating Costs <sup>4</sup>		\$ 50,608	\$ 60,729	\$ 71,577	\$ 75,685	\$ 79,955	\$ 59,388	\$ 44,385	\$ 40,293	\$ 40,243	\$ 41,099	\$ 44,640
caHUB Operating Costs Recovered (%)		8%	31%	43%	57%	69%	111%	155%	173%	173%	170%	157%

2 The **More Realistic Example 2** uses going-market price data for samples, and demonstrates the potential for caHUB to achieve **Full Cost Recovery** by Year 3 just from the sale of commodities alone:

caHUB Cost and Revenue Projections (in \$000's)	ARRA	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10	Average
	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023-27
Estimated Sample Revenue at Avg Price of <sup>2</sup>	\$ 600	\$ 8,500	\$ 43,283	\$ 71,676	\$ 100,384	\$ 129,077	\$ 155,675	\$ 162,247	\$ 163,610	\$ 163,902	\$ 163,964	\$ 163,980
100% Cost Recovery Achieved By Year 3 Post-ARRA		17%	71%	100%	133%	161%	262%	366%	406%	407%	399%	368%

<sup>1</sup> Case turnover (e.g. sales) is expected to exceed 10% due to caHUB's managed collections, and would lift revenue above the projections illustrated.

<sup>2</sup> The \$200 avg. sample price example illustrates a very conservative scenario assuming turnover was attributed mainly to cheaper priced commodities (fluids).

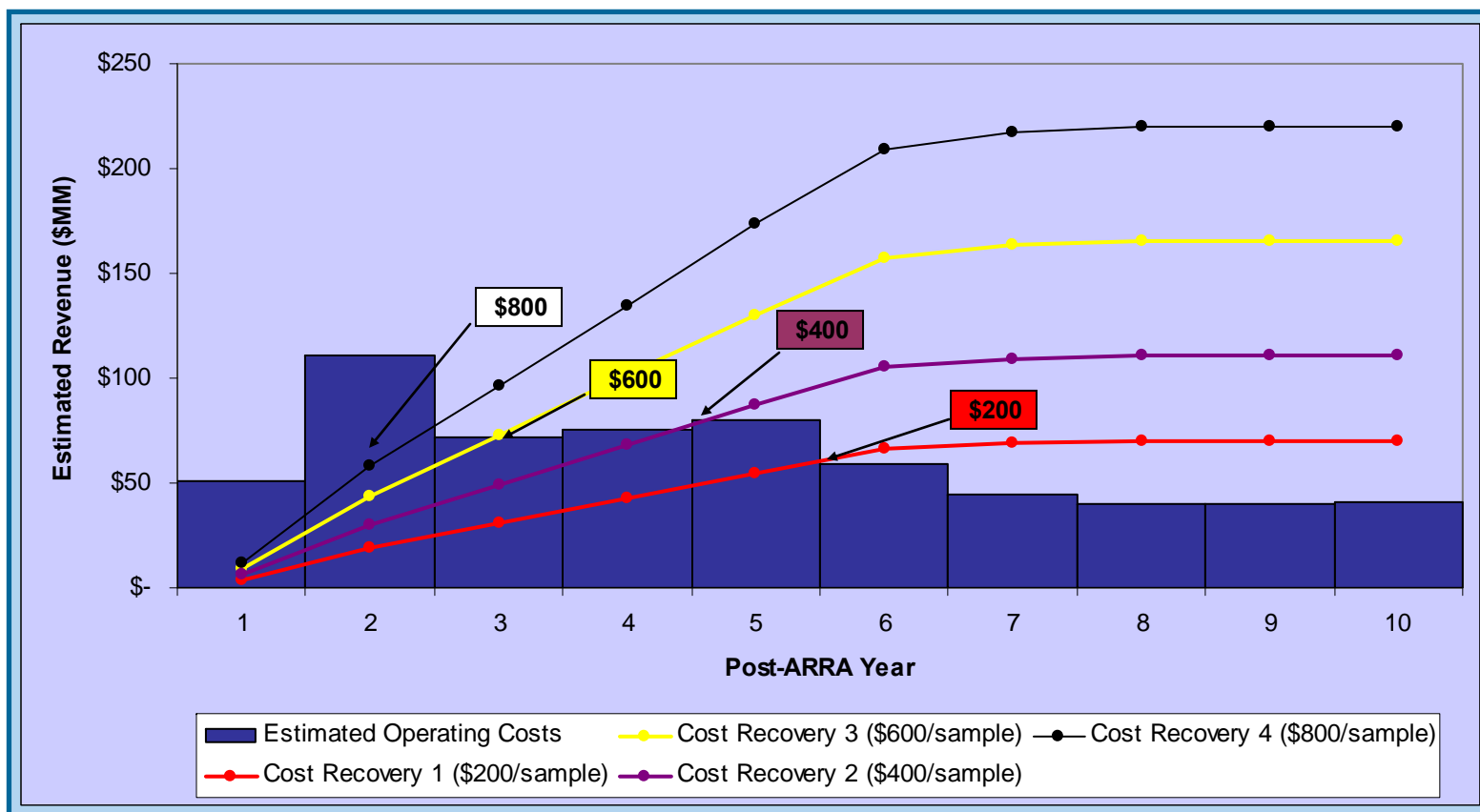
<sup>2</sup> The \$600 avg. price is more realistic given a market range of \$500-\$1,200 across the tumor tissue spectrum, and evidence of prices paid previously by TCGA.

<sup>3</sup> Customized processing services (proteomic analysis, DNA microarrays, molecular analysis genotyping etc.) will supplement sample commodity sales.

<sup>4</sup> Cost estimates assume the construction of a permanent caHUB facility in the fall 2012 timeframe.

# caHUB Cost Recovery Modeling

## caHUB Cost Recovery Breakeven Point Given Various Average Prices Per Sample





# caHUB Contracted Components in Phase 1

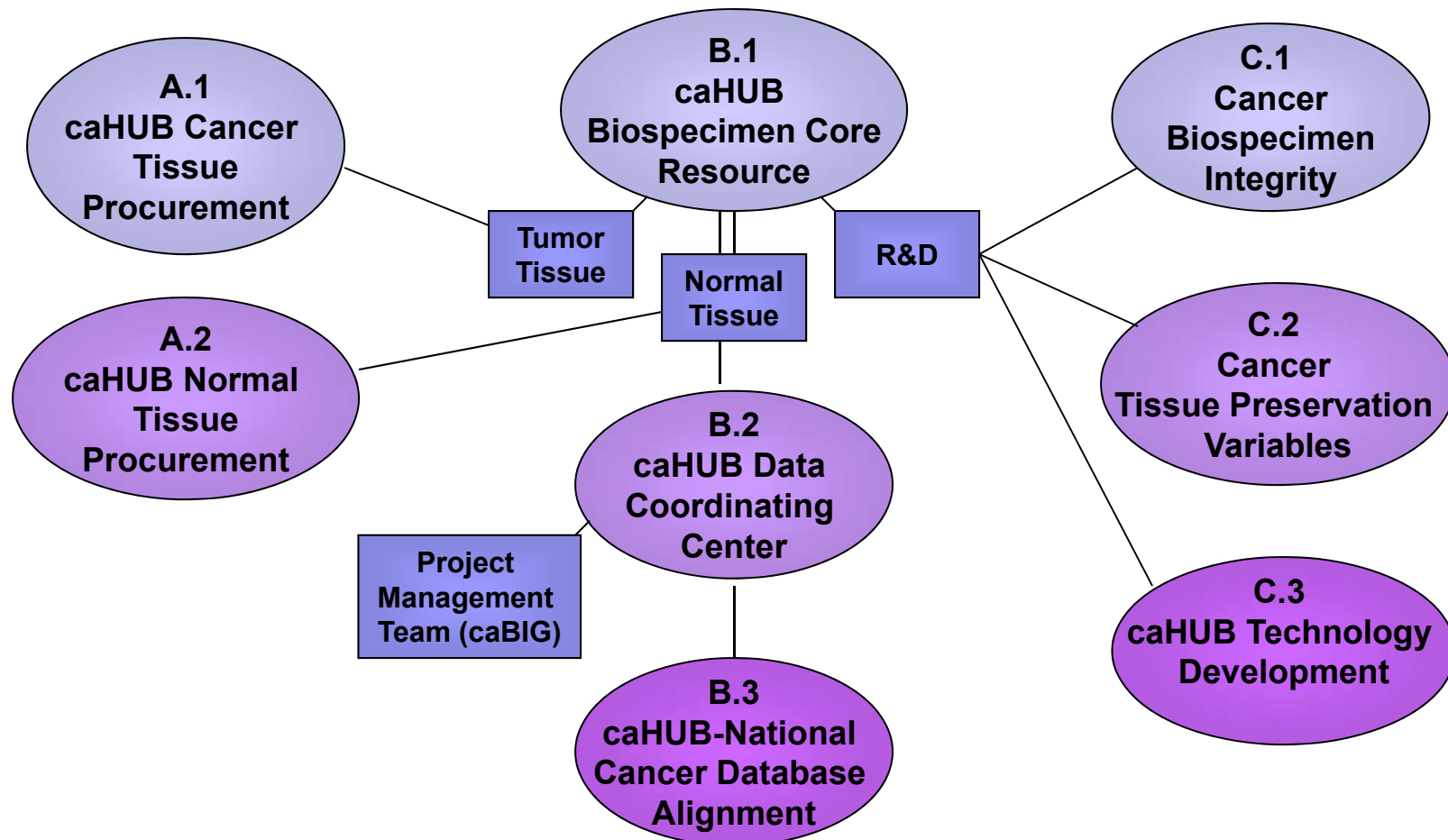


atories  
Research

## A. Tissue Procurement

## B. caHUB Central Functions

## C. Biospecimen R & D



# caHUB Functional Organization (ARRA Period)

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## Communication and Outreach

- Partnerships Management
- Education and outreach
- TSS relations and management
- End user relations management

## Services/Tools

- Best Practices
- Biospecimen science training
- Biospecimen resource evaluation tools
- Specimen Locator tool
- Biospecimen Research Database (BRD)

## Administration

- Finance - Funding model (Public-Private)
- Personnel
- Technical and administrative operations
- Quality management
- Policies and procedures
- Reporting

## Comprehensive Data Resource

- IT Infrastructure and caBIG
- Clinical data from NCDB
- Research data from R&D
- Molecular analysis data from QC and end users

## Pathology Reference Center

- Sample receiving / quality control
- Sample accessioning – case file / labeling / inventory
- Sample profiling / processing
- Diagnostic confirmation
- Extensive pathology review and reporting
- Sample annotation (data to data repository)
- Sample storage and end user distribution

## Ethical / Legal / Policy

- Federal, state, local regulations
- DHHS policies
- NIH / NCI policies
- caHUB policies
  - Access
  - Protection
  - Consent

## R&D

- Evidence-based SOPs and quality metrics (BRN)
- Technology development / validation (IMAT)
- Technology integration



## Continuous Process Improvement

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- **caHUB will establish policies and procedures that will ensure its continued responsiveness to the changing needs of the research and product development communities**
  - Goals for performance metrics and success factors
  - Routine assessment of performance against metrics
  - Customer Satisfaction Program
  - Ongoing market analysis to be responsive to trends in translational research and advances in biomedical technology
  - Transparent mechanism for receiving and responding to public input





# caHUB Timeline

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## Planning

- Pathology Resource Center
- Working Groups
- Cost Recovery
- Market Research

## Phase 1

- caHUB pilot
  - procurement
  - operations
  - data coordination
  - R&D
- PPP Development

## Phase 2

- Centralization
- Expansion
- Special Collections
- Training Services





## caHUB, A Transformative Initiative

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### More Efficient Research



- Reduction in re-experimentation due to higher quality samples
- Avoided cost of incremental labor from PIs and lab technicians, researchers
- Avoided cost of replacing failed samples because of higher sample quality
- Avoided time delays and labor costs for recontact and recontact of patients for new studies

### More Efficient Use of Resources



- User leverage of caHUB's systems infrastructure, reducing the need to purchase and maintain requisite infrastructure
- User leverage of caHUB goods and services, decreasing labor costs to process samples in order to meet research requirements

### Ensured Implementation of Best Practices



- Increased comparability (quality and uniformity) of specimen and data sets
- Ensures compliance reducing implementation and monitoring costs

### Stronger Clinical Correlation



- Quality and uniformity of data promotes more accurate modeling
- Avoided re-collection of data, saving time and cost



## caHUB, A Transformative Initiative

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More Efficient  
Product  
Development and  
Regulatory Approval



- Higher quality samples helps advance biomarker research
- Higher quality specimens helps reduce clinical trials timeframes and costs
- FDA recognition of “platinum” status specimens may lead to more rapid approvals for new drugs and diagnostics

More Efficient  
Technology  
Development and  
Clinical  
Implementation



- Standardized biospecimens allows direct performance comparisons
- Benchmark biospecimens allows calibration, performance monitoring and operator proficiency testing

Added Clinical  
Value: Improved  
Standards of Care



- Speed the transition from research standards to standards of care
- More rapid implementation and standardization of diagnostic assays in clinical laboratories

Improved  
Outcomes for  
Cancer Patients



- **Increase in lives saved**
- **Improvements in quality of life**
- **Positive impact on personal economics**
- **Savings to healthcare systems**
- **Positive impact on national economics (GDP, tax revenues)**



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