National Cancer Institute

caHUB
The Cancer
Human Biobank

The Revisioning of caHUB® as a Center for Biospecimen Science and Standards Development

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Executive Director, caHUB

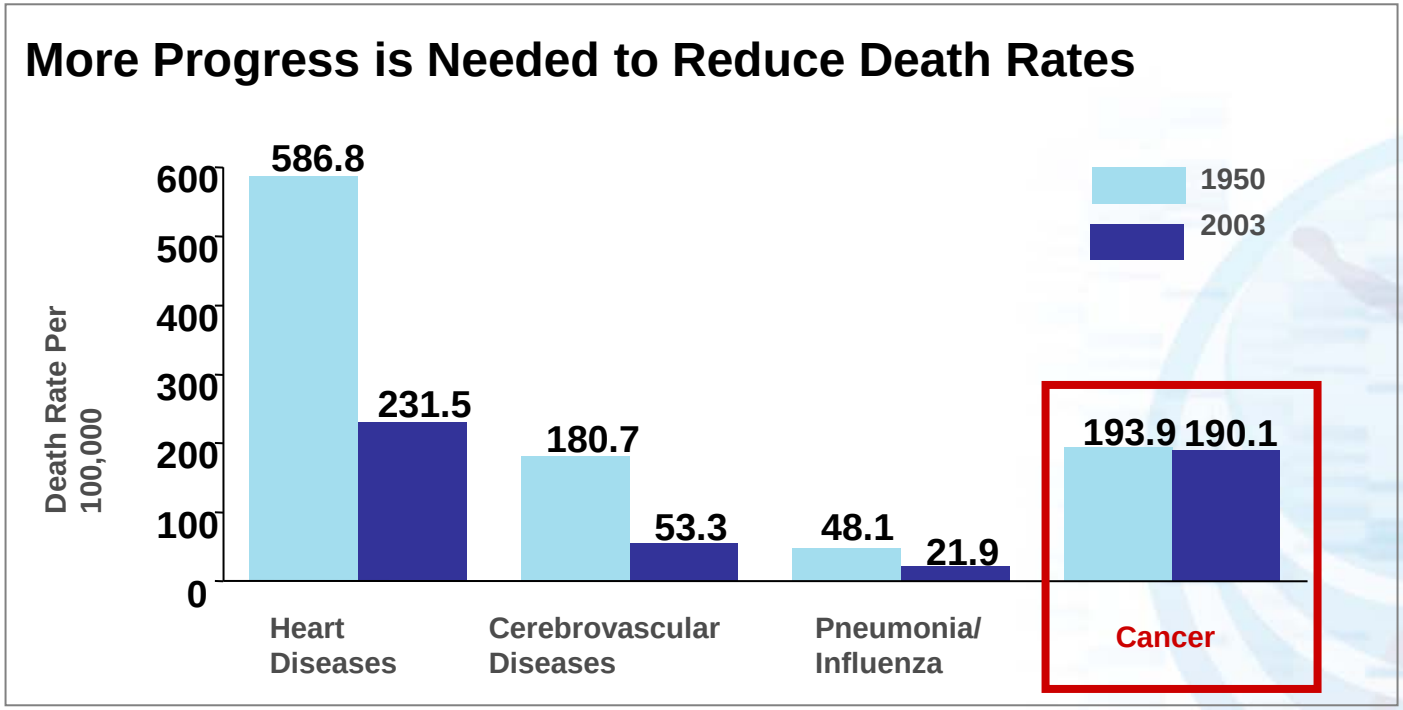
National Cancer Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Why We Are Here

- **Compared to other major disease killers, cancer death rates have changed little over the past 60 years**
- **570,280 Americans will die of cancer this year**
- **1.4 Americans will develop cancer this year**
- **1 of 3 females and 1 of 2 males will develop cancer in their lifetime**

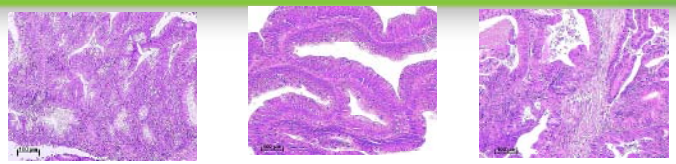


Molecular Biology, Advanced Technologies, Bioinformatics: Promise Yet Unrealized

A Defining Moment in the Nation's
"War on Cancer" —
Unprecedented Potential for Exponential Progress Toward Molecular Oncology

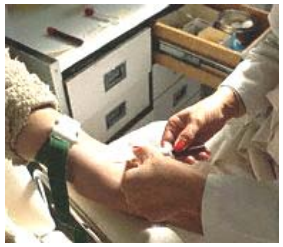
Nature, Feb. 15, 2001

Today



Tumor 1 Tumor 2 Tumor 3

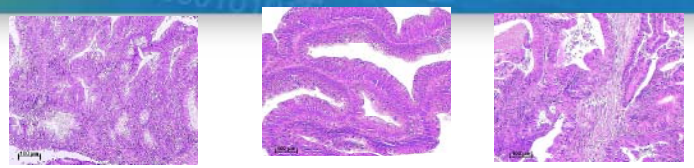
Standard Therapy



Only one of three patients benefits from cancer drug treatment
(Spear et al. (2001) Trends Molec. Med. 7, 201-203)

More effective
Less toxic
Less costly

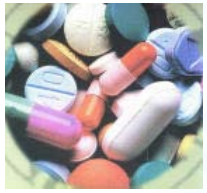
Future



Tumor 1 Tumor 2 Tumor 3

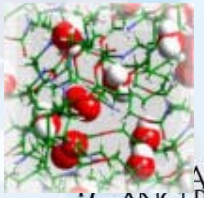
Molecular Diagnostic Assay

Therapy 1



Therapy 2

Therapy 3



caHUB The Cancer Human Biobank

Compliments of Dr. Hartmut Juhl, Indivumed GmbH, Hamburg

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NCI CANCER INSTITUTE

Getting to Personalized Medicine

Mo DETERMINES QUALITY HERE Products

Translational Research

PERSONALIZED CANCER CARE

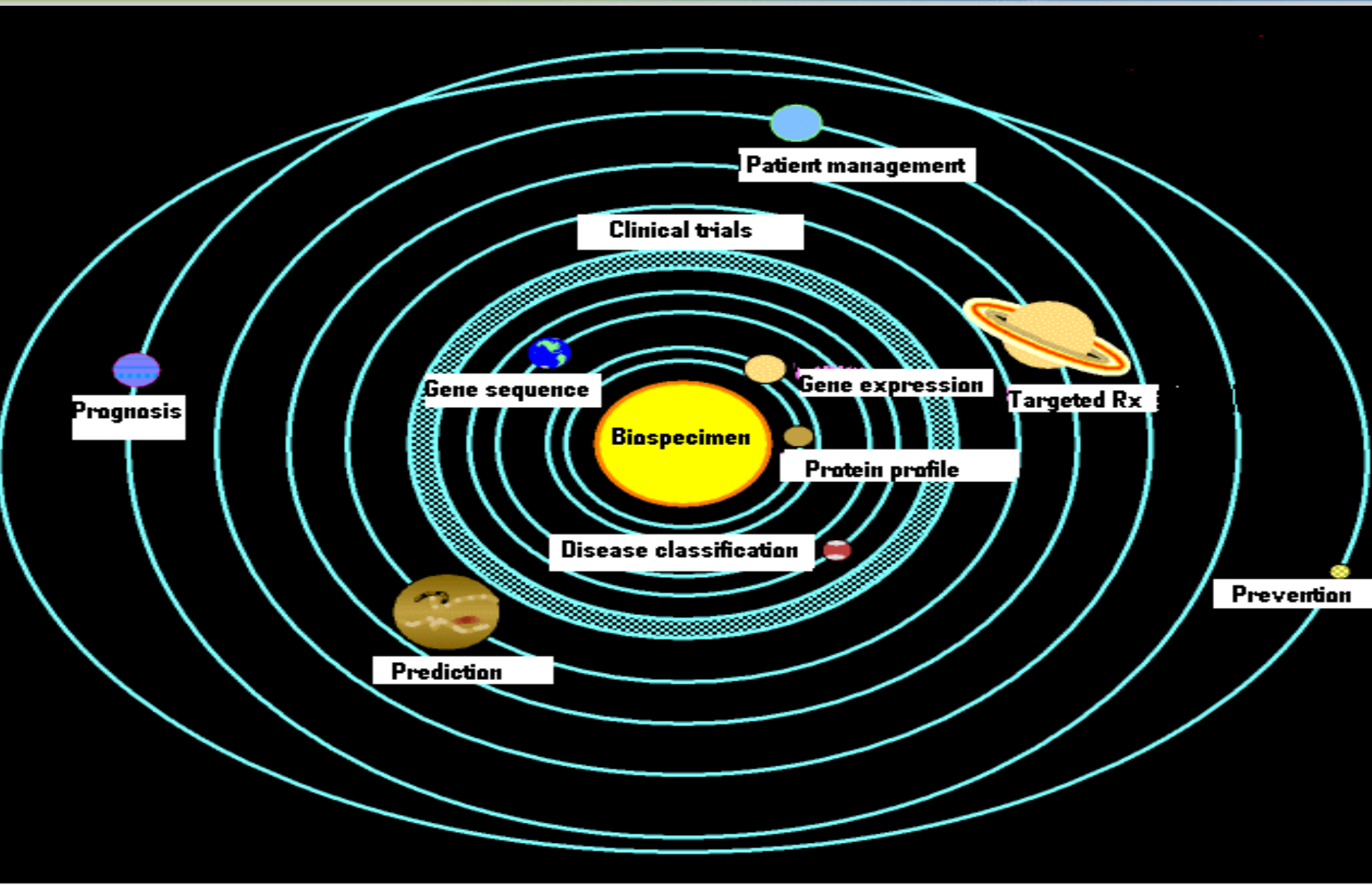
QUALITY HERE

Biospecimen Analysis

Biospecimen Collection

Biospecimen Processing and Banking

The Biospecimen Is the Center of the Personalized Medicine Universe: Those Molecular Biomarkers Are in the Biospecimens



Biospecimens Throughout a Product's Lifespan



Diagnostic Tests / Laboratory Assays

Standardized , Fit-for-Purpose Biospecimens

Define standards

- Test execution
- Tolerance for variation
- Test performance

Daily execution

- Quality Assessment
- Quality Control
- Calibration

- Decreased false negatives and false positives
- Improved Standard of Care

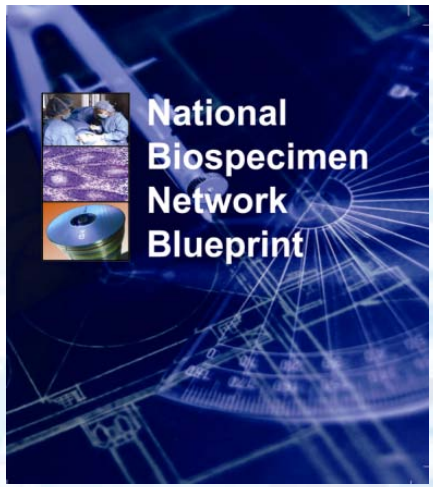


High-Quality Specimens Are Still Needed

The lack of high-quality, clinically annotated human specimens is the #1 limiting factor for translational cancer research.

NCI Outlines Principles for a National Solution

- Data-driven, standardized collection strategies
- Standardized, annotated collection, processing of all specimens
- QC and pathology analysis of every specimen
- Rich, standardized data profile for each sample
- Standardized consents and MTAs
- Supporting IT systems: open source, inter-operable
  - http://biospecimens.cancer.gov



Providing Resources for the Research Community: The Cancer Human Biobank (caHUB)

The 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

NATIONAL CANCER INSTITUTE

The caHUB Infrastructure – Essential Components

- Biospecimen Source Sites (RFPs):
  - **Cancer specimens**
  - **Normal specimens**
  - **Specimens not removed through standard of care approaches (e.g., metastases)**
- Central Biospecimen Resource (RFP)
  - **Specimen receipt and processing**
  - **Quality control**
  - **Pathology assessment**
- Central Data Resource (SAIC)
  - **Data coordination and linkage (clinical, variables, QC, molecular analysis, imaging data and image analysis)**
  - **Specimen tracking and inventory**
  - **Privacy and confidentiality**
- Comprehensive quality management program (SAIC)

What Is Total Quality Management (TQM)?

- TQM ensures that ALL activities and processes are consistent and reliable – level determined by the quality objective (GLP, GMP, etc.)

- TQM controls and monitors systems to identify and correct problems to continually improve operations; this includes:

  SOP validation • Document control • Internal audits • Process validation • Equipment qualification • Process function documentaton • Investigation of issues • Failure mode effect analysis • Corrective/ Preventive action • Auditis of contractors for compliance • Analysis of quality metrics • Customer satisfaction analysis • Training implemention & documention • Traceability maintenance• Complaint management • Experimental control • Continuous improvement • Quality control checks throughout all processes

- The caHUB is a leader in employing a comprehensive program to control all operational aspects of a biospecimen resource

caHUB Key Concepts

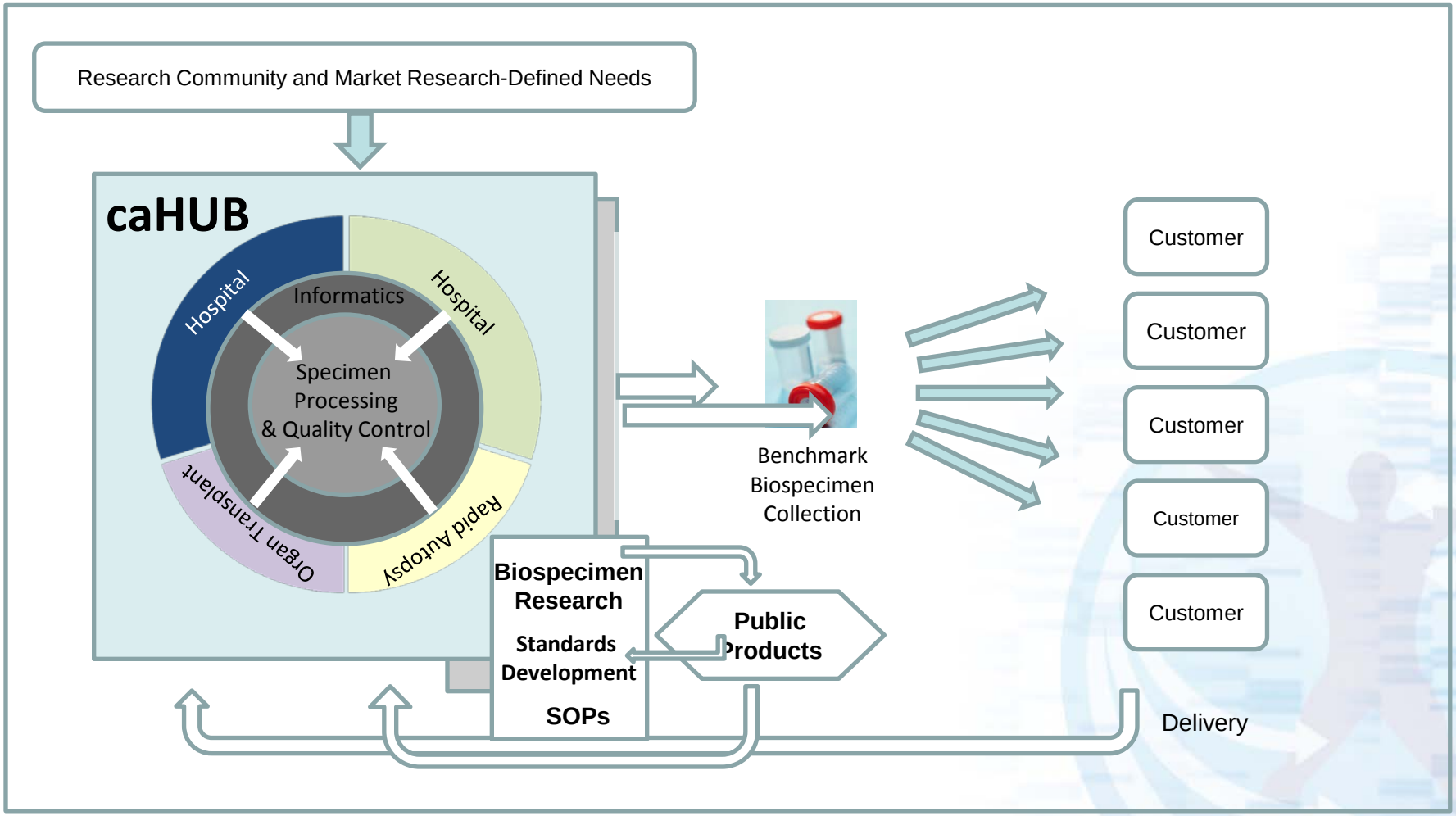
- Scientifically designed, data-driven collection strategies
- Multiple aliquots of every specimen (linking/building on previous data)
- Standardized, annotated collection, processing of all specimens
- Centralized QC and pathology analysis of every specimen
- Rich, standardized data profile for each sample
- **Research and development enabling continuous improvement**

New caHUB: Still a Transformative Initiative

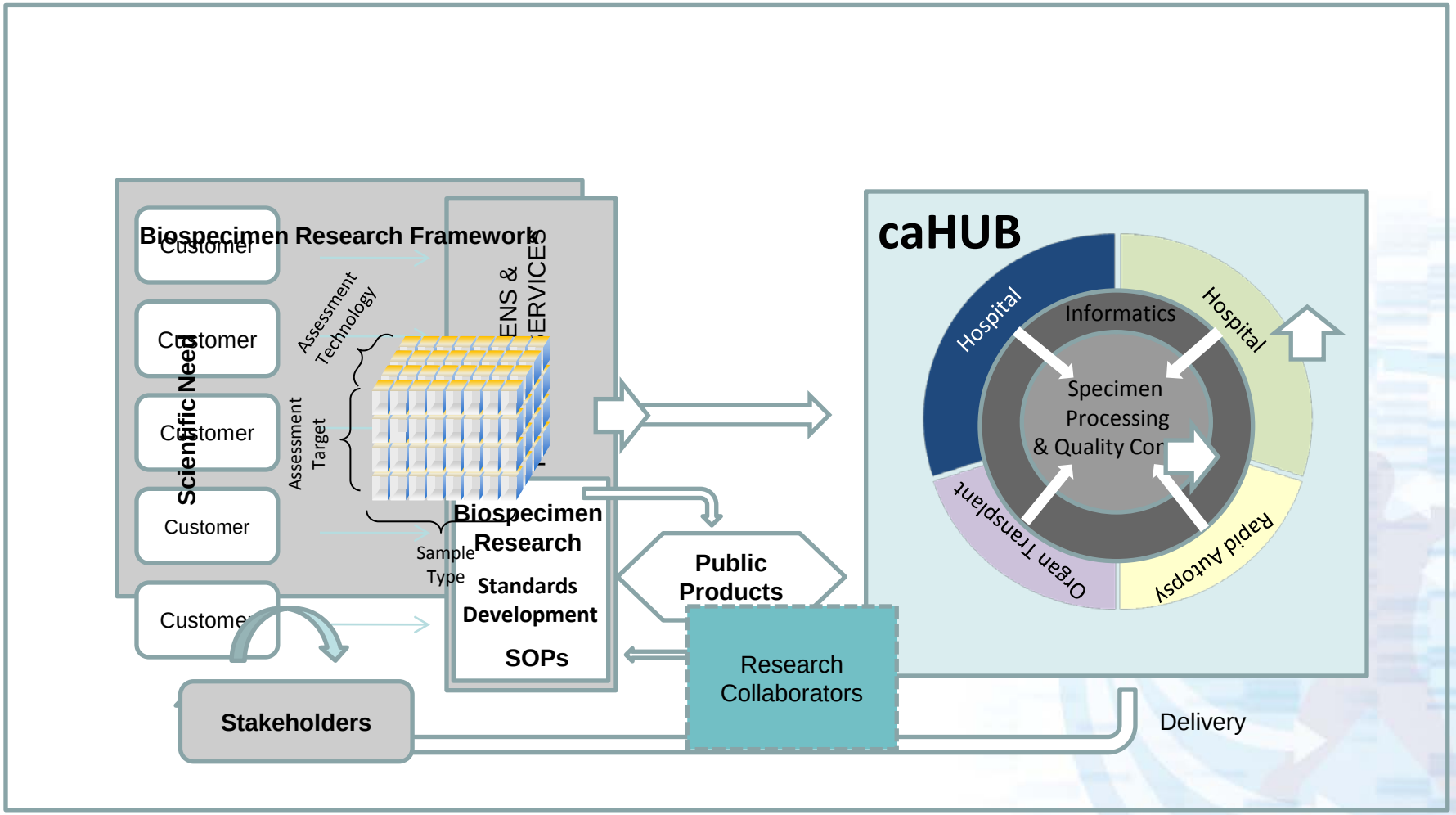
- Old approach: Provide fit-for-purpose biospecimens for the research community
  - Budget: $60 million

- New approach: Drive and coordinate the biospecimen research and standards development that will enable the research community to collect its own fit-for-purpose biospecimens
  - Budget $23.5 million

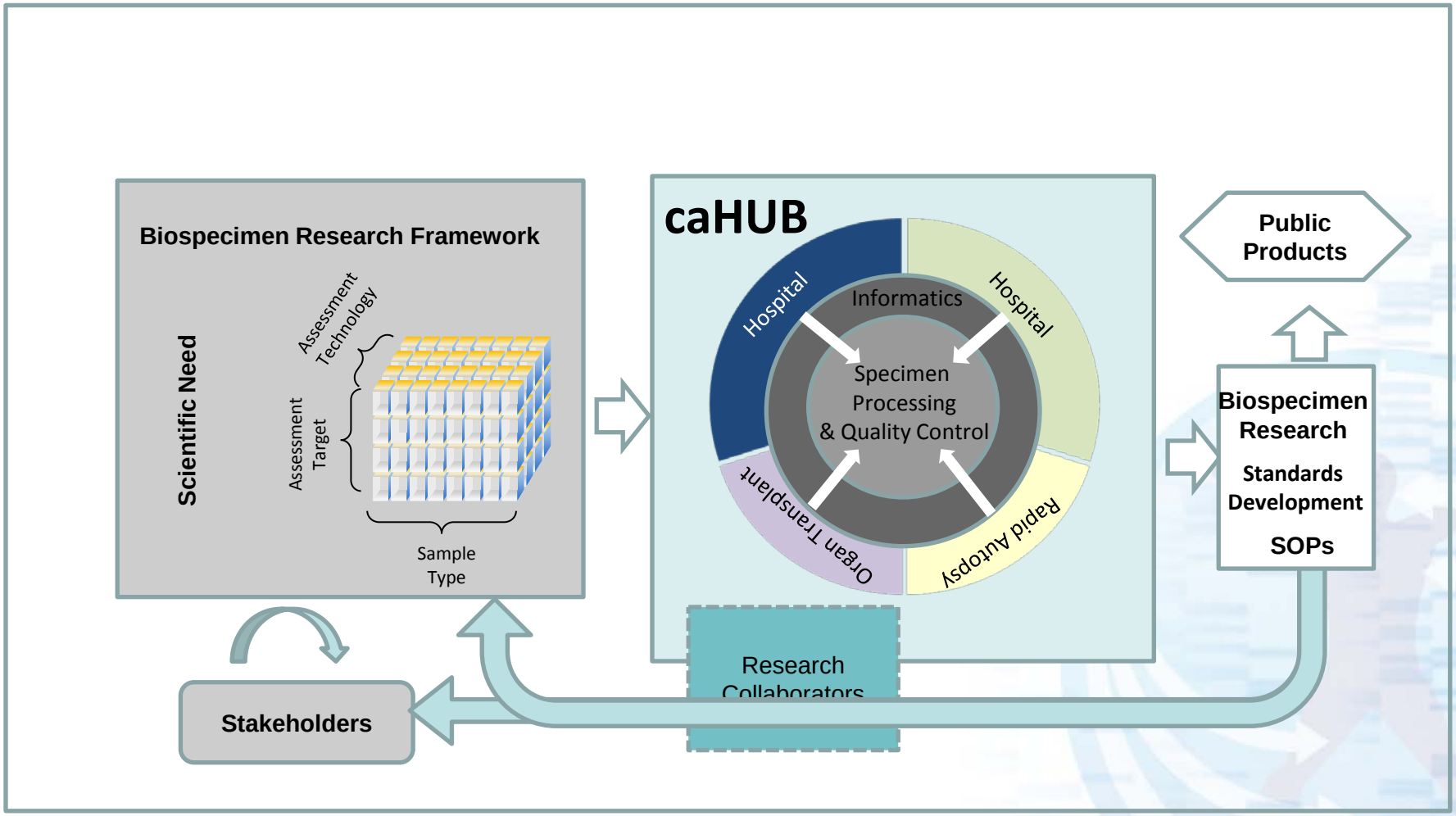
caHUB as a Benchmark Collection Provider



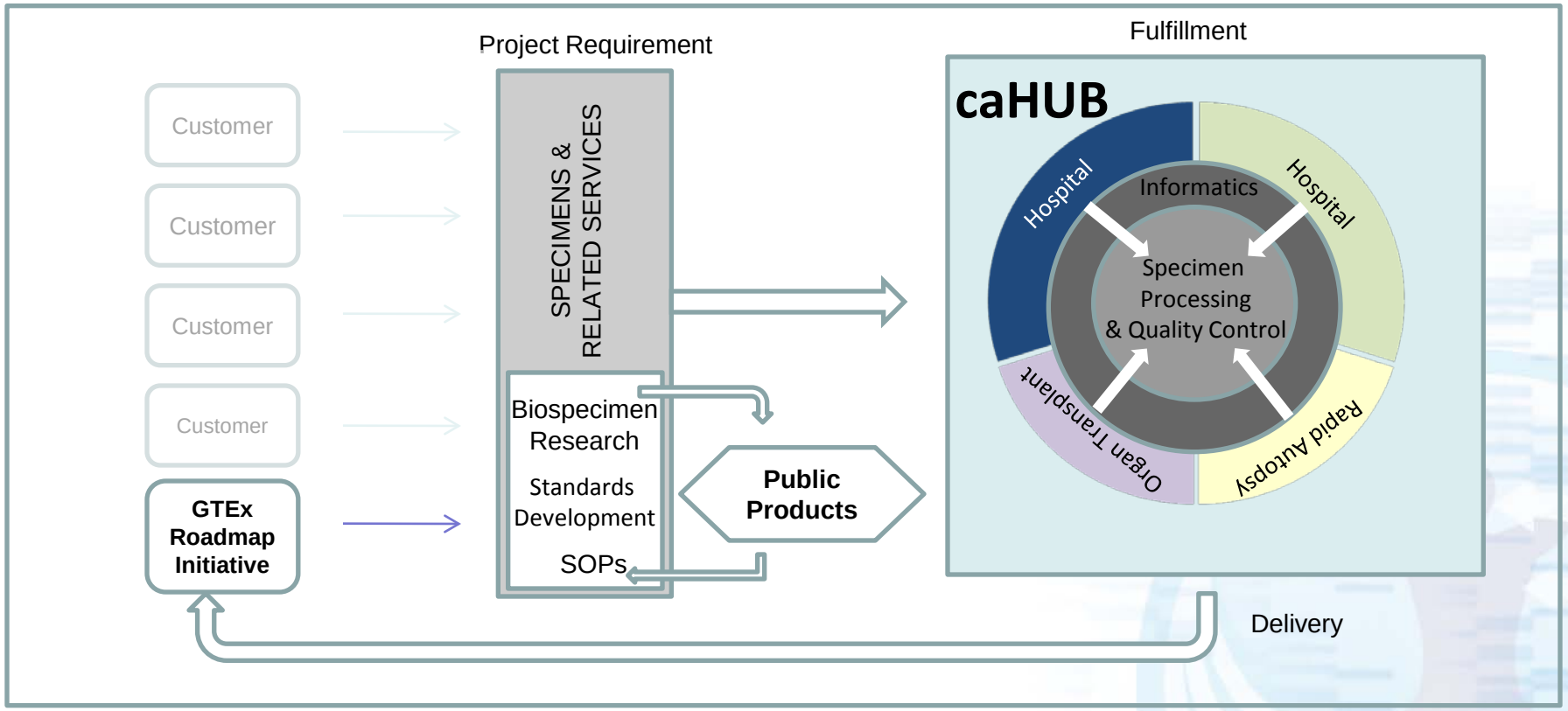
VERSION 2:
caHUB as a Service for Biospecimen Science Projects and Standards



VERSION 3:
caHUB as a Center for Biospecimen Science and Standards



VERSION 2: Customer Funded Service Provision Example: GTEx Roadmap Initiative



Genotype-Tissue Expression (GTEx): An NIH Common Fund Project

- Understand how genomic variation (SNPs) affects differential gene expression in various normal tissues (all with the same genome)
  - Normal human biology project
  - Essential knowledge: systems biology and disease susceptibility
- Team science project under auspices of NHGRI, NIMH, NCI, NHLBI, NCBI
  - Miami Brain Bank
  - Broad Institute
- Tissue acquisition challenge:
  - Statistically determined goal of collecting 30-50 different normal tissues from each of 500 males and 500 females
  - Requires innovative approaches to acquisition: rapid autopsy programs, organ procurement organizations, surgical resections for non-malignant disease
- RNA quality challenge

caHUB Supports Specimen Collection for GTEx

- caHUB biospecimen source sites – competitive procurement (RFP), site visits, QM audits, preliminary experimentation to optimize SOPs
  - Science Care, AZ
  - Roswell Park Cancer Institute, NY
  - National Disease Research Interchange, PA
- Conduct biospecimen science to create SOPs
  - Specimen Stabilization Workshop: what stabilization method produces the highest quality RNA and greatest RNA yields for normal tissues ?
  - Experiments on site with comparative results of RNA yield, RNA quality and morphological quality between Broad and caHUB
- Create collection kits for standardized collection and shipping
- Create IT infrastructure for donor/specimen data collection
- Create standardized consent form and MTA
- Create all SOPs and training modules for specimen collections
- Image all specimens and perform Pathology review
- Oversee execution of collections and performance monitoring

Pre-analytical Factors Can Affect Molecular Composition and Integrity

Factors (examples):

- Antibiotics
- Other drugs
- Type of anesthesia
- Duration of anesthesia
- Arterial clamp time

Time 0

Factors (examples):

- Time at room temperature
- Temperature of room
- Type of fixative
- Time in fixative
- Rate of freezing
- Size of aliquots

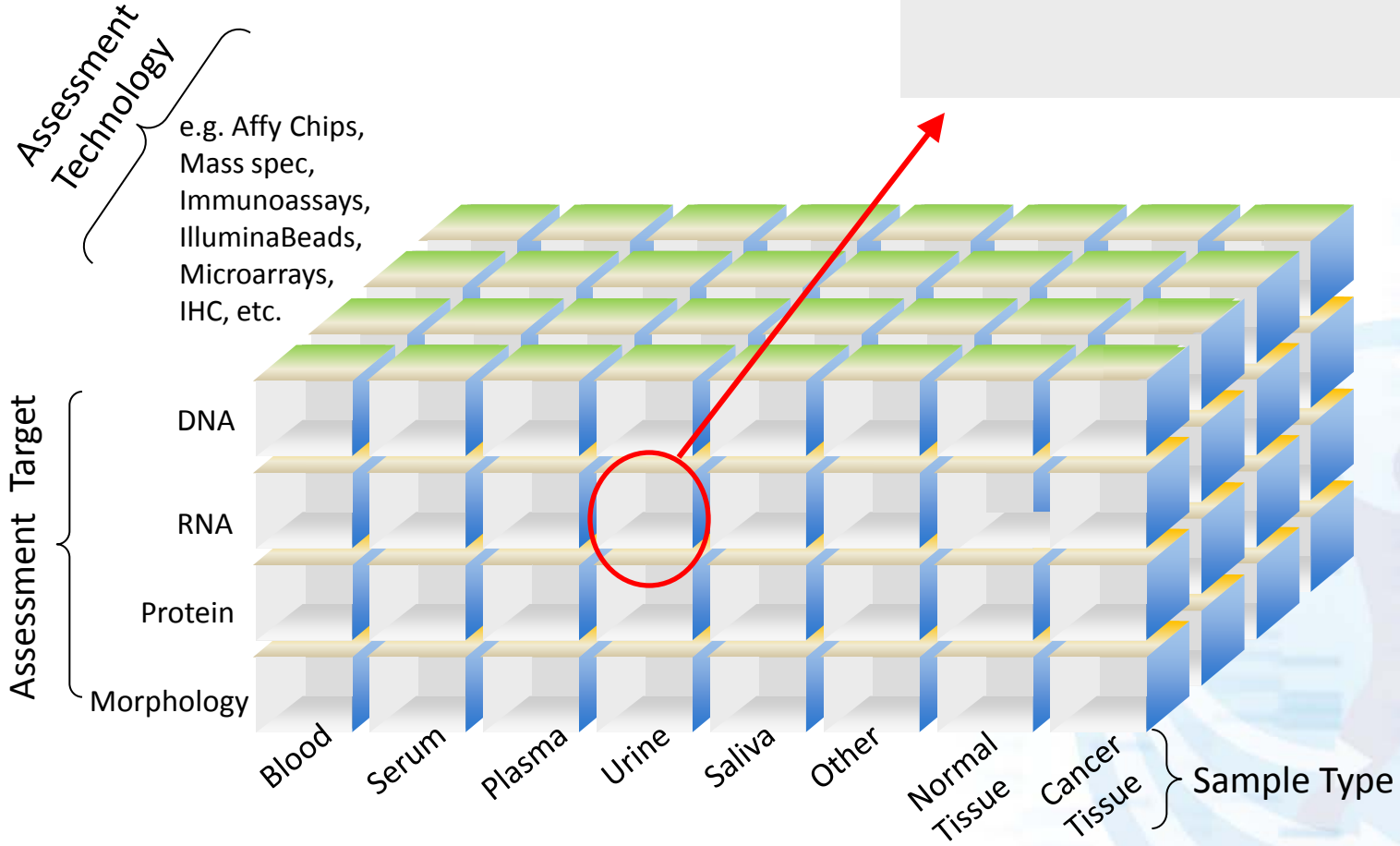
Patient	Medical/ Surgical Procedures	Acquisition	Handling/ Processing	Storage	Distribution	Scientific Analysis	Restocking Unused Sample

Pre-acquisition

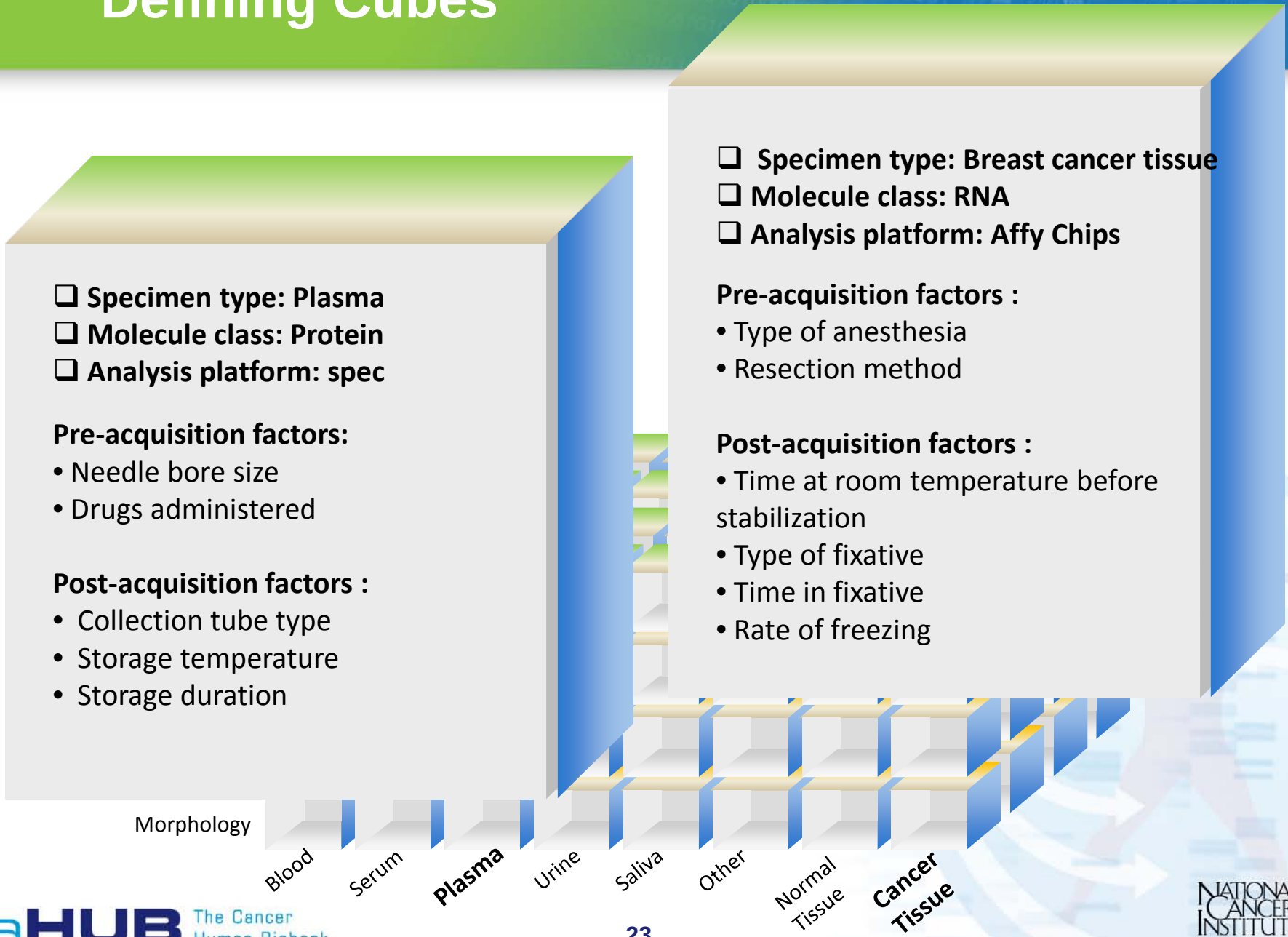
Post-acquisition

The Ice Cube Tray Model

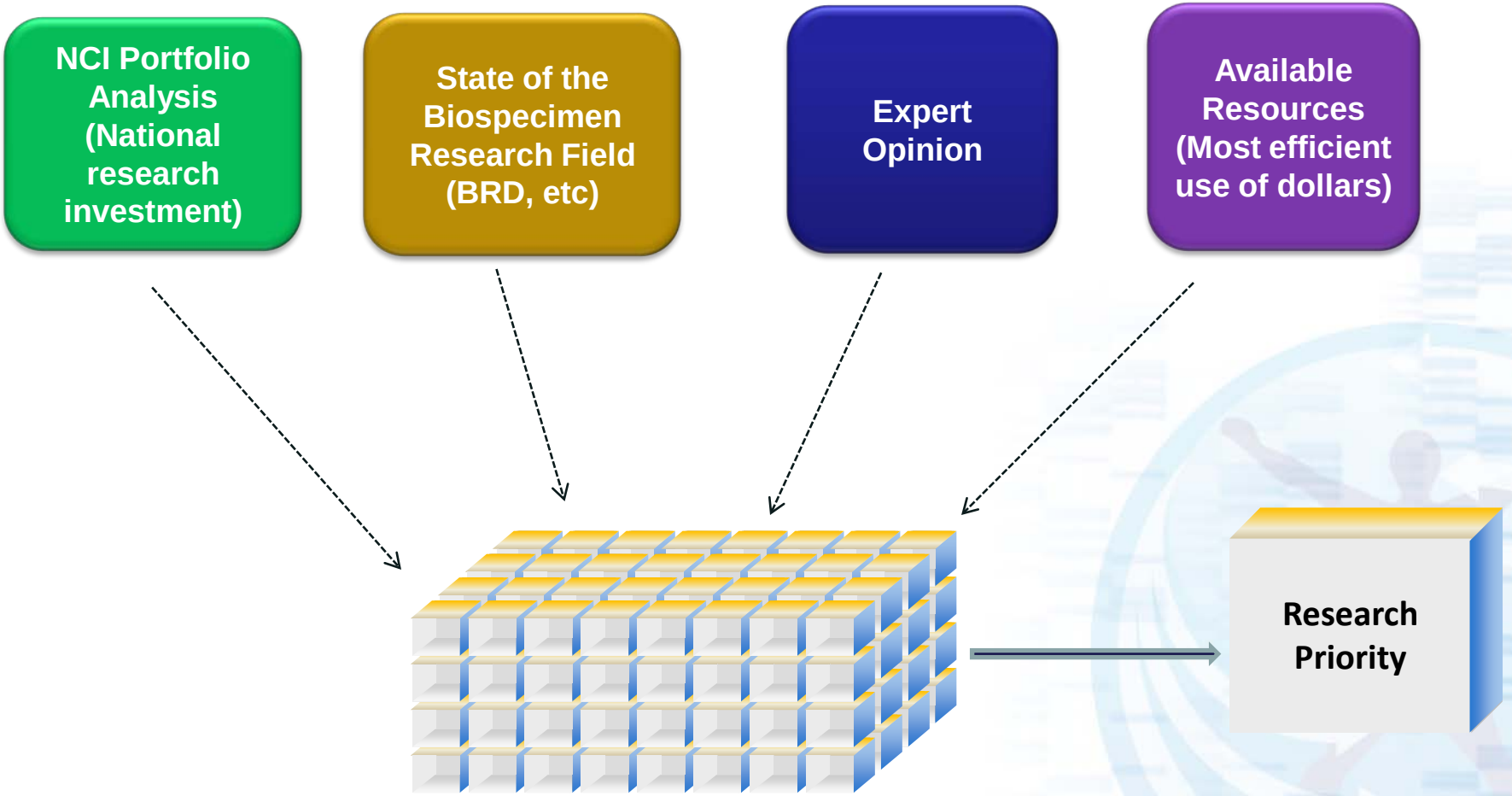
Each cube presents its own set of factors with potential impact on specimen quality or composition



Defining Cubes



caHUB Process for Identifying Biospecimen Research Priorities



Other Drivers: Advancing Biomolecular Science and Medicine Through Standards Development

- What we need to go forward: Measurable, objective standards for molecular quality in human biospecimen as the yardstick
  - The development and integration of advanced technologies (comparisons of platform performance requires a standard analyte)
  - Comparison of experimental approaches across research laboratories
  - The movement from qualitative to quantitative analysis: a convergence of the biological and physical sciences
    - Translational science
    - Regulatory science
    - Biospecimen science
    - Molecular medicine
  - Regulators need objective evidence produced from known standards

Why We Love Metrologists

- Answer: they measure things (VERY precisely) for a living
- Quantitative quality standards for different classes of biomolecules in human biospecimens are needed
- caHUB and NIST (National Institute for Standards and Technology): a bold new collaborative initiative bringing together all stakeholders to define the needs and uses for quality metrics:
  - NCI (Translational researchers and funders)
  - NIST (metrologists)
  - FDA (medical product regulators)
  - Industry (medical product /assay developers)
  - Clinical investigators and practicing clinicians
  - Statisticians
- Objective: define the experimental designs for collect ion of human biospecimen sets that will allow NIST to identify the molecular quality metrics of regulatory and clinical relevance

Coordinating Research Efforts Globally

- ***Standardization and improvement of generic pre-analytical t and procedures for in-vitro diagnostics (SPIDIA)***
  - Funded by European Union FP7 Framework Programme
  - Brings together 16 academic and international organizations and life sciences companies
  - Aims to tackle standardization and improvement of pre-analytical variables for in vitro diagnostics
  - **Signed Letter of Intent (LOI) to collaborate on setting international biobanking agenda and to share information, resources, and data**
  - **Coordinating scientific efforts so that there is no duplication, except where validation is needed**

Utilizing Public Products to Implement Best Practices on an International Level

- ***National Foundation for Cancer Research (NFCR)***
  - Co-sponsoring workshop in China on biobanking best practices
  - Workshop will include international speakers and representatives from across Asia, North America, South America, and Europe
- ***Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)***
  - Co-publishing commentaries and reviews around the importance of biobanking standards to various stakeholder audiences
  - Working to harmonize practices and procedures
- ***NCI Office of International Affairs (OIA)***
  - Coordinating efforts to reach global biobanking audiences

Gathering Stakeholder Feedback and Input

- **Stakeholder involvement is critical**
  - Identifying stakeholder needs and scientific value added
  - Utilizing stakeholders as potential research collaborators
  - Avoiding duplication of efforts, while leveraging the expertise of our collaborators
  - Defining the highest priority variables to address

- **Details for providing feedback about variables to address will be forthcoming via the OBBR and caHUB websites and listservs**
  - OBBR website: http://biospecimens.cancer.gov
  - caHUB website: http://cahub.cancer.gov
  - Email: ncicahub@mail.nih.gov

The caHUB Business Model: A Commodities and Services Model

COMMODITIES

- Specimens and data of defined quality and "variables" spectra
- Time dependent measures for research

SERVICES

- Build on existing infrastructure
- 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 private sector
  - Assay development
  - Clinical trials
- Laboratory services
  - Research support functions
  - Specialty Pathology review

caHUB Work To Date Will Yield Public Products

- ***Policies and Documents***
  - Informed Consent Template
  - MTA Template
  - SOPs for normal and diseased tissue collection
- ***Publications***
  - JNCI Monograph: Topics include the economics of biobanking, intellectual property issues, the importance of biobanking to the future of personalized medicine, etc.
  - Best Practices for Normal Tissue Acquisition
- ***Planning Groups Output***
  - Communications and Marketing, Acquiring Normal and Diseased Specimens, Building Public-Private Partnerships, Addressing ELSI Concerns, Developing SOPs, Developing Enabling Informatics Systems
- ***Lessons Learned and Information Gathered***
  - Biobanking Economics
  - Biobanking Market Research
  - Access Policy
  - Intellectual Property and Data Sharing Policy

All information will be made available as soon as possible via the caHUB website.

JNCI Monograph Coming in spring 2011

- **Main Articles:**
  - An NCI Perspective on Creating Sustainable Biospecimen Resources
  - Assessing the Need For caHUB: Findings from a National Survey with Cancer Researchers
  - Industry and Academic Researcher Needs and Reactions to the Development of a National Standardized Biospecimen Resource by NCI
  - Biobankonomics: Developing a Sustainable Business Model Approach for the Formation of a National Human Tissue Biobank
  - Biobankonomics: A Taxonomy for Quantifying the Financial Benefits that Biobanks Contribute to the Research Community and to the Public
- **Guest Commentaries:**
  - Surgical Oncologist
  - Academic Researcher
  - International Perspective
  - Pharmaceutical Industry
  - Patient Advocate

caHUB Vision

Original	Revised
caHUB will contribute to medical advances by providing high-quality human biospecimens and data.	caHUB will contribute to medical advances **through** high-quality human biospecimens and data.

caHUB Mission

Original	Revised
caHUB aims to modernize the field of biobanking and contribute to medical advances by providing high-quality human biospecimens and data as well as analysis, scientific tools, and services to the cancer research and product development communities.	caHUB aims to modernize the field of biobanking **by developing an infrastructure for collaborative biospecimen research and the production of evidence-based biospecimen standard operating procedures.** **caHUB will make the resulting data, analysis, policy documents, and scientific tools publicly available to enable the community to collect biospecimens fit for specific scientific purposes.**

caHUB Mission-Specific Action Items

Original	Revised
caHUB will provide high-quality human biospecimens and data to the research community by:	caHUB will **develop an infrastructure for collaborative biospecimen research by:**
• Designing, developing, managing, and providing access to a national cancer biospecimen resource	• Designing, developing, and managing a **national cancer biospecimen resource for biospecimen science and standardization research purposes**
•Adhering to the highest ethical and technical standards for biospecimen collection and storage	•Adhering to the highest ethical and technical standards for biospecimen collection and storage
•Developing and managing a network of biospecimen-contributing institutions	•Developing and managing a network of biospecimen-contributing institutions
•Standardizing and developing improvements to biospecimen science and best practices	•Standardizing and developing improvements to biospecimen science and best practices
•Developing enabling technologies	•Developing enabling technologies
•Providing laboratory services and online access to resources	•Providing laboratory services and online access to resources
•Fostering communication, collaboration, partnerships, education, and earning the public's trust	•Fostering communication, collaboration, partnerships, education, and earning the public's trust
•Evolving into a public-private partnership	•Evolving into a public-private partnership

caHUB Overview

Original	Revised
The National Cancer Institute (NCI) is sponsoring a unique initiative to advance cancer research and treatment through development of the cancer Human Biobank (caHUB), a national biorepository of human tissue, blood, other biological materials, and a comprehensive online database.	The National Cancer Institute (NCI) is sponsoring a unique initiative to advance cancer research and treatment through development of the cancer Human Biobank (caHUB) **as a national center for biospecimen science and standards.**
caHUB was created in response to the critical and growing shortage of high-quality, well-documented biospecimens for development of molecularly based diagnostic and therapeutic agents that will further enable personalized treatment for cancer patients.	caHUB was created in response to the critical and growing shortage of high-quality, well-documented biospecimens for development of molecularly based diagnostic and therapeutic agents that will further enable personalized treatment for cancer patients.
The caHUB initiative builds on resources already developed by the NCI, including the Biospecimen Research Network and the NCI Best Practices for Biospecimen Resources, both of which were developed to address challenges around standardization of the collection and dissemination of quality biospecimens.	The caHUB initiative builds on resources already developed by the NCI, including the Biospecimen Research Network and the NCI Best Practices for Biospecimen Resources, both of which were developed to address challenges around standardization of the collection and dissemination of quality biospecimens.

What will caHUB be a biospecimen resource?

NCI defines a biospecimen resource as a collection of human specimens and associated data for research purposes, the physical entity where the collection is stored, and all relevant processes and policies.

What will caHUB be a biospecimen resource?

- The caHUB collections will consist of specimen type-specific, variable factor-type specific specimen sets
  - Defined factors, systematically altered over a defined range
  - Collections all governed by caHUB comprehensive quality management
  - Access determined by transparent policy
- Multiple aliquots of each specimen set will allow direct comparisons of the impact of given factors on different assay types and analysis platforms

caHUB Due Diligence: Outstanding Questions

- **How should caHUB define mechanism(s) for project selection?**
  - Multiple mechanisms may exist to draw upon expertise from internal and external communities.
  - Which existing mechanisms are best fit for caHUB?
- **How do we gather external input?**
  - What mechanism could be used to establish and implement input?
- **How are research collaborators selected and engaged?**
- **How do we remain current and responsive to the evolving needs of the community?**
- **How do we integrate new caHUB vision with the existing biospecimen research framework (BRN)?**
- **How do we integrate caHUB efforts within our technology development program, Innovative Molecular Analysis Technologies (IMAT)?**

Still Our Goal

Garbage in…

…Garbage out

On the Road to Molecular Medicine…..

“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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caHUB, A Transformative Initiative

8. Biobanks

By ALICE PARK

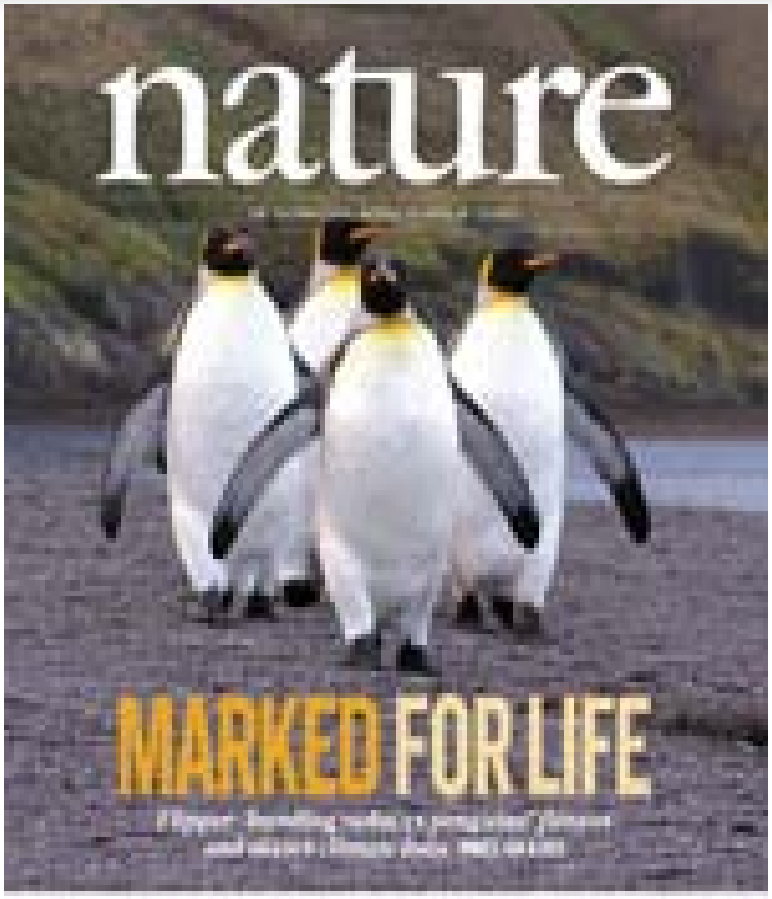
Inside Huntsman Cancer Institute's vaults: Pancreatic tumors on ice. Lance W. Clayton for TIME

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**

George Poste
Nature, Jan 13, 2011



Bring on the Biomarkers

The lack of standardization in the collection and storage of medical specimens (pictured) can hinder subsequent research.

Bring on the biomarkers

The dismal patchwork of fragmented research on disease-associated biomarkers should be replaced by a coordinated 'big science' approach, argues **George Poste**.

If researchers could establish correlations between diseases and changes in biomarkers, the ability of physicians to diagnose disease and tailor treatments to individuals would be radically improved[1]. However, research into biomarkers — disease-associated molecular changes in body tissues and fluids — hasn't yet delivered on its promise. Technologies such as proteomics and DNA microarrays have contributed a voluminous literature of more than 150,000 papers documenting thousands of claimed biomarkers, but fewer than 100 have been validated for routine clinical practice. This dismal record reflects the failure of researchers to embrace a coordinated systems-based approach.

Many chronic diseases involve changes in responses to treatment. Also, getting candidate biomarkers into large-scale validation studies poses substantial logistical and regulatory challenges. Overcoming them requires the integration of diverse skills.

Changes are needed to standardize methods and obtain the large sample sizes necessary for validation trials. The traditional model of investigator-initiated research must be replaced with the collaborative approaches typical of 'big-science' projects — such as The Cancer Genome Atlas initiative of the US National Institutes of Health (NIH) to catalogue the

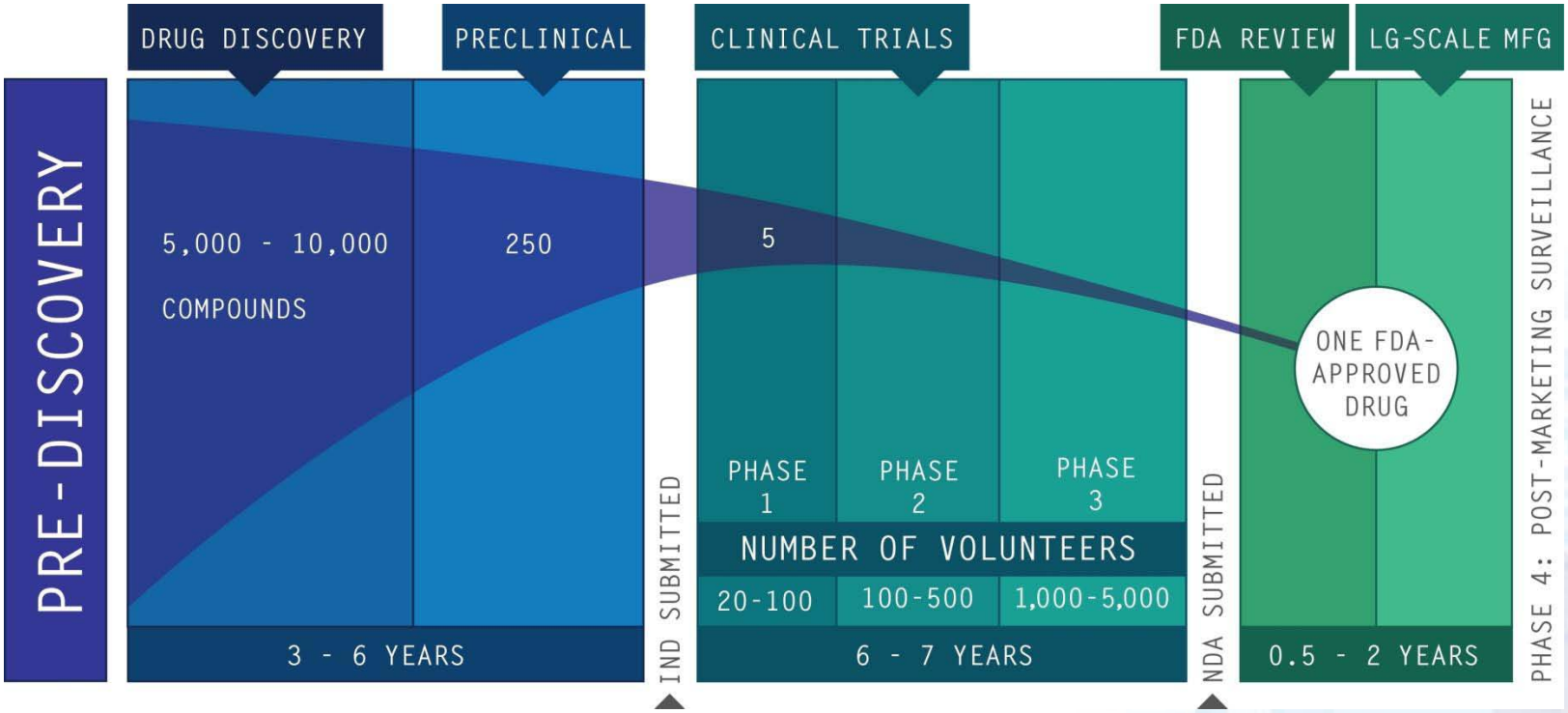
"Too many researchers rely on whatever specimens they can obtain conveniently."

key to better patient care and lower medical costs[3]. The American Society of Clinical Oncology, for example, estimates that routinely testing people with colon cancer for mutations in the *K-RAS* oncogene would save at least US$600 million a year[4]. It would also spare patients futile and potentially toxic treatments — for example, people with these mutations don't respond to drugs that inhibit epidermal growth factor receptors, which cost up to $100,000 per treatment.

APPLES AND ORANGES

A major impediment to progress in the hunt for biomarkers is the lack of standardization in how specimens are collected. Unless specimens are taken from people who are matched for as many variables as possible,

Current Reality Bleak and Unsustainable



An FDA-approved drug, start to finish:

- **10-15 years**
- **1,000 –6,000 volunteers**
- **$1-1.8 billion**