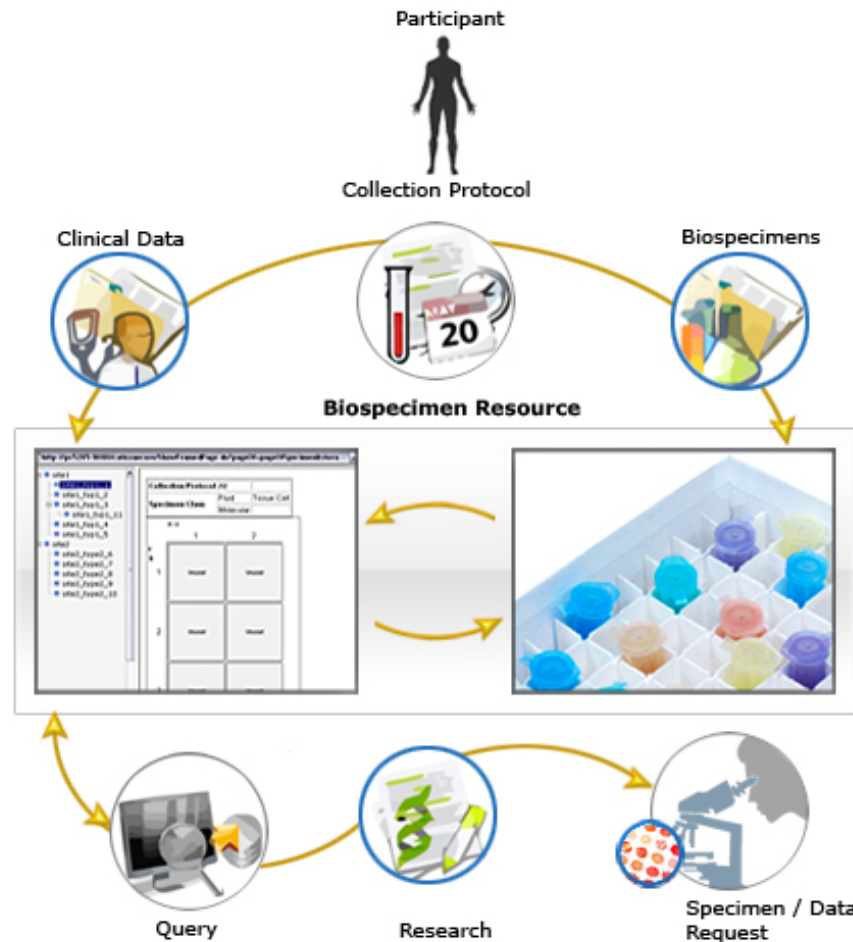


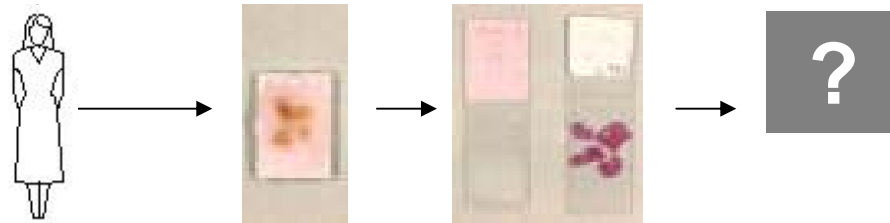
# Development and Real-World Use of a System for Tracking Biospecimens and Biospecimen Data



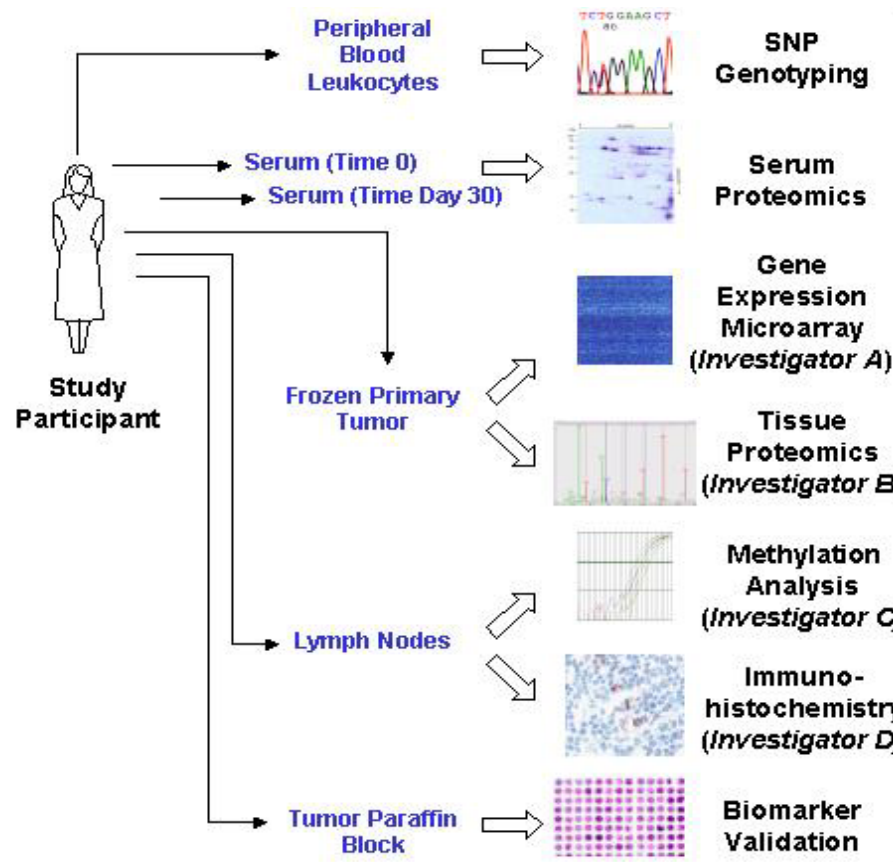
Mark A. Watson, M.D., Ph.D.  
 Rakesh Nagarajan, M.D., Ph.D.  
 Dept. Pathology and Immunology

# The Evolution of Biospecimen Banking

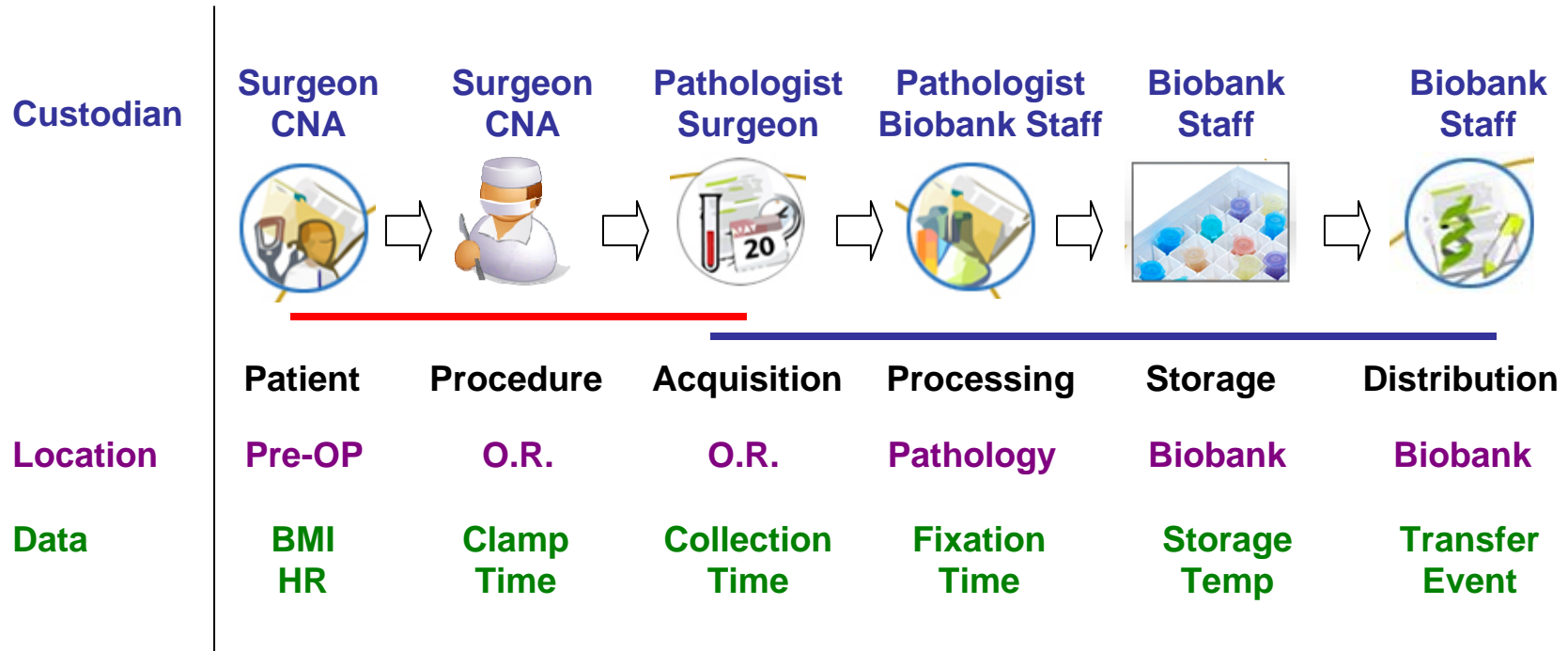
• 1988



• 2010



# The Biospecimen Lifecycle



# Generic Biospecimen (Tumor) Bank

- Pre-operative consent is obtained and operative frozen tissue specimens (tumor and non-malignant) are collected from surgical discards.



Consent Patient  
Register to Protocol  
Provide Diagnosis  
Provide Operative Date

**CRA**



Collect Specimen

**Pathologist**



Receive Specimen  
Store Specimen

**Biobank**

Participant Details

Social Security Number (SSN)

Name: Last, First, Middle

Birth Date: [MM/DD/YYYY]

Vital Status:  Alive  Dead  Unknown  Unspecified

Death Date: [MM/DD/YYYY]

Gender:  Female Gender  Male Gender  Unknown  Unspecified

Sex: Genotype: [Unknown]

Race: [Select: American Indian or Alaska Nat., Asian, Black or African American]

Ethnicity: [Unknown]

Medical Identifier(s)

Protocol Registrations(s)

Select Collection Protocol	Participant Protocol ID	Registration Date	Activity Status	Consent
<input checked="" type="checkbox"/>	X Bank	04-09-2009	Active	Enter Response

Specimen Collection Group: X Bank\_728\_1478

Collection Protocol Title: X Bank

Specimen Group Name: X Bank\_728\_1478

Study Calendar Event Point: 1.0 Surgery

Clinical Diagnosis: Adenocarcinoma of sigmoid colon

Activity Status: Active

Events

Collected	Received
Collector: Admin, Admin	Receiver: Admin, Admin
Date: 04-24-2009	Date: 04-24-2009
Time: 11:55 AM	Time: 11:55 AM

Specimen Collection Group successfully updated for X Bank\_728\_1478.

Specimen details

Label	Barcode	Type	Qty	Cont.	Location	Apply First to All	Collected
122843	8301553	Frozen Tissue	1.0	Auto	Res_4_BTTB_F15	<input type="checkbox"/>	<input type="checkbox"/>
122844	8301554	Frozen Tissue	1.0	Auto	Res_4_BTTB_F15	<input type="checkbox"/>	<input type="checkbox"/>

Child specimens not defined.

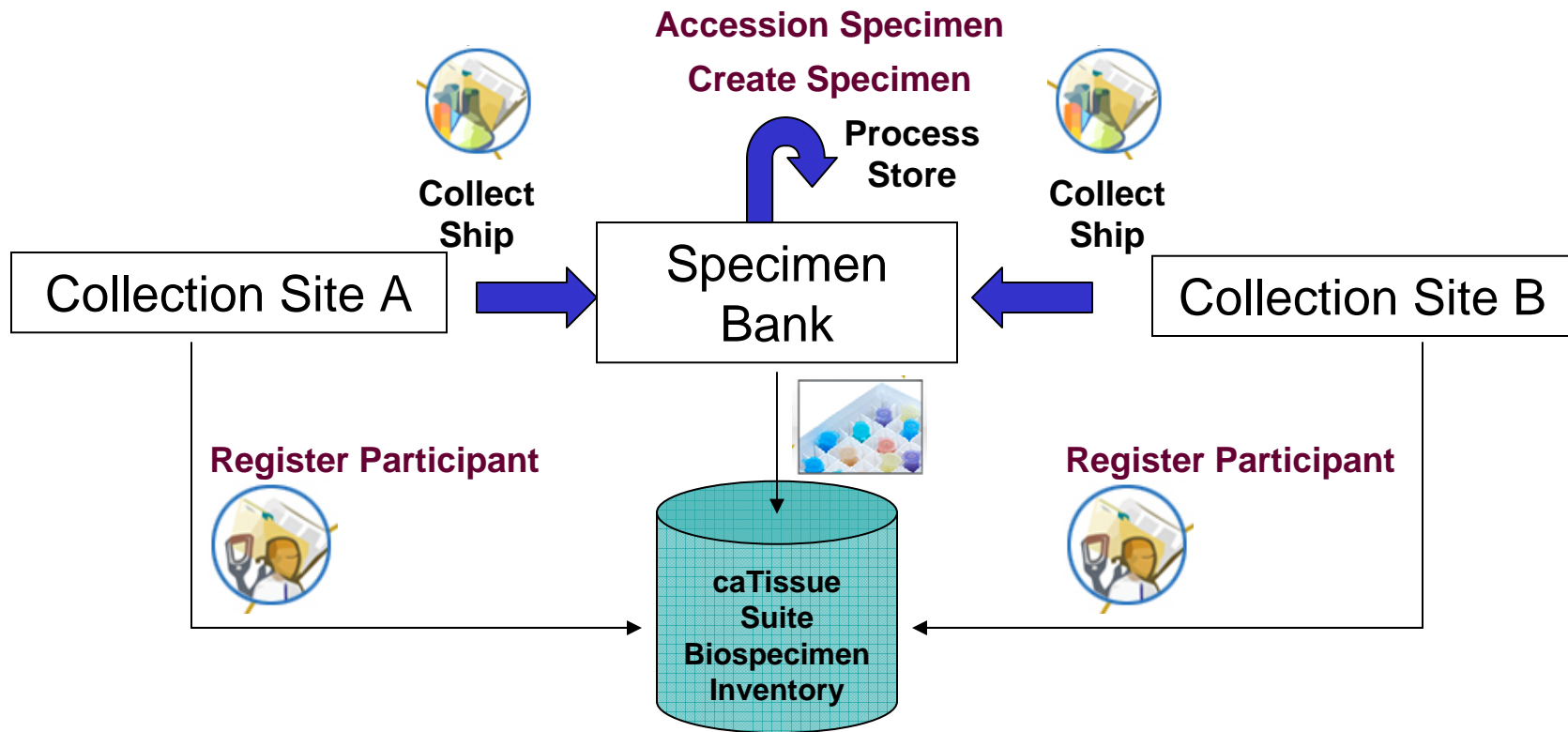
Print Labels Submit Add To My List

**TIME**



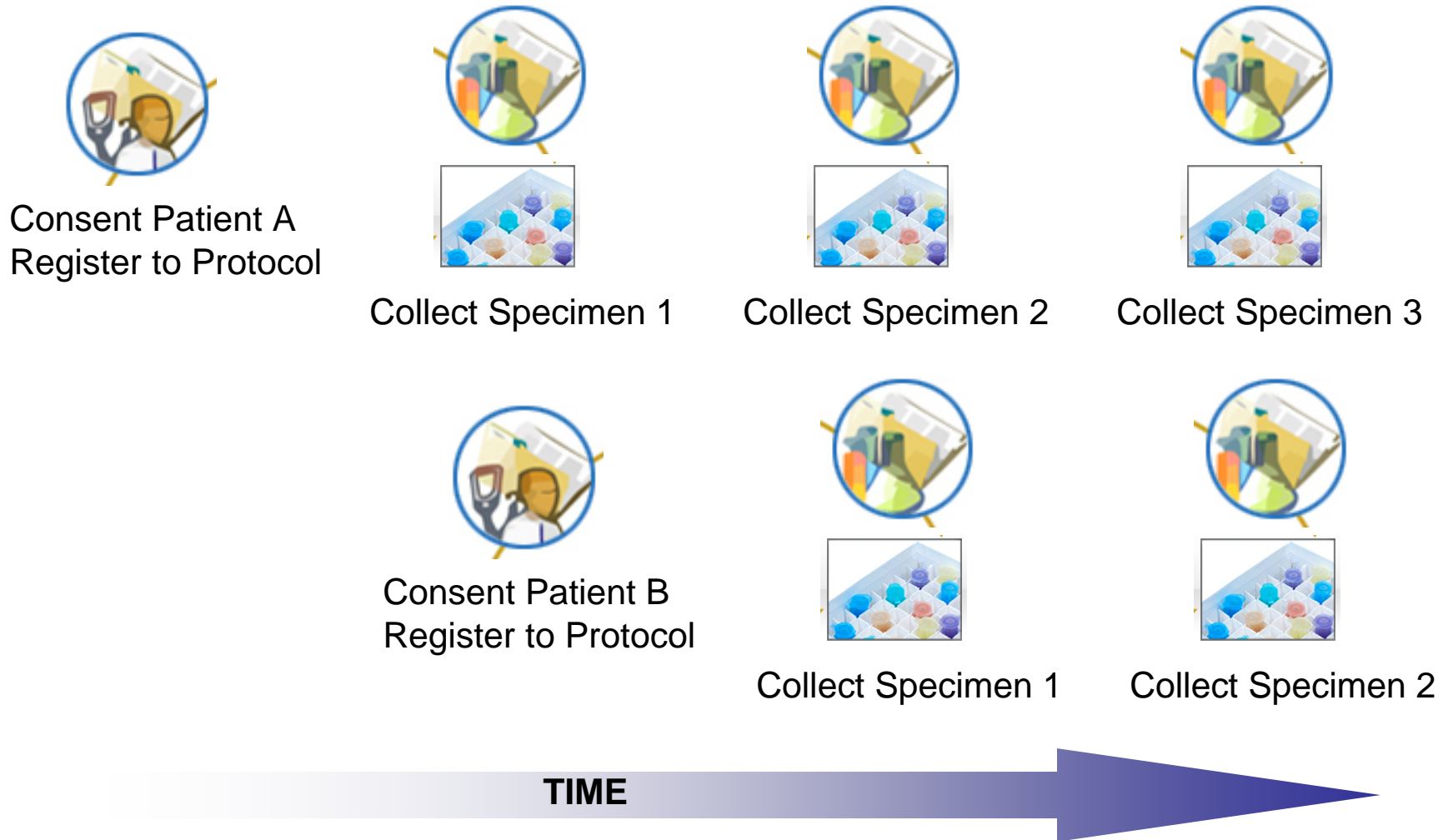
# Multisite Trial

- *Participants are registered, specimens collected, and then processed at independent sites by different users over time.*



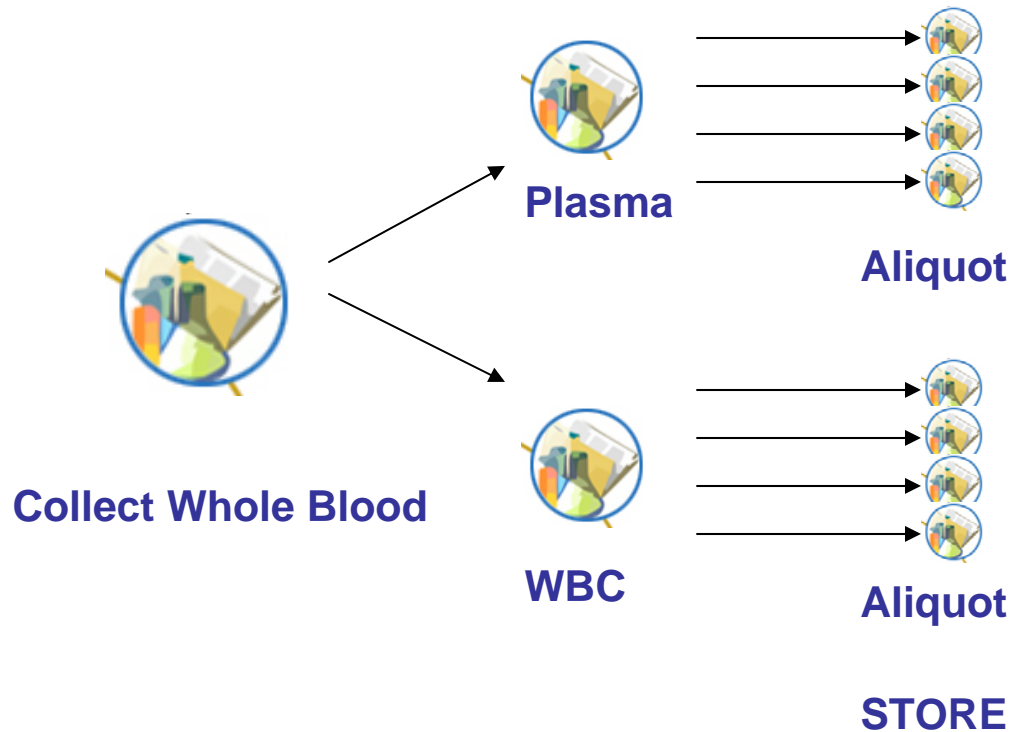
# Multiple Time Point Clinical Trial

- *Specimens are collected at multiple time points from a participant who is independently registered to a clinical trial.*



# Multi-Component Blood Protocol

- A tube of whole blood is collected which is then processed and aliquoted into individual components, as per a unique SOP for that protocol.



Specimen details

Label	Barcode	Type	Qty	Conc.	Location	<input type="checkbox"/> Apply First to All	Coll
123846	8301556	Whole Blood	10.0		Virtual	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Derivative Details

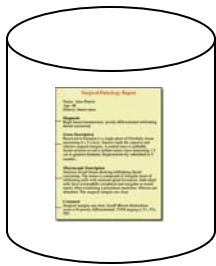
Parent	Label	Barcode	Type	Qty	Conc.	Location	<input type="checkbox"/> Apply First to All	<input checked="" type="checkbox"/> Co
123846	123847	8301557	Plasma	4.0		Virtual	<input type="checkbox"/>	<input checked="" type="checkbox"/>
123846	123848	8301558	Frozen Cell Pelle	4.0E7		Virtual	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Aliquot Details

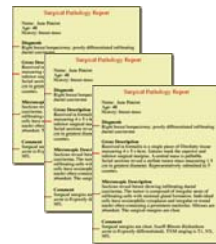
Parent	Label	Barcode	Type	Qty	Conc.	Location	<input type="checkbox"/> Apply First to All	<input checked="" type="checkbox"/> Co
123847	123847_1	8301557_1	Plasma	1.0		Auto	<input type="checkbox"/>	<input checked="" type="checkbox"/>
123847	123847_2	8301557_2	Plasma	1.0		Auto	<input type="checkbox"/>	<input checked="" type="checkbox"/>
123847	123847_3	8301557_3	Plasma	1.0		Auto	<input type="checkbox"/>	<input checked="" type="checkbox"/>
123847	123847_4	8301557_4	Plasma	1.0		Auto	<input type="checkbox"/>	<input checked="" type="checkbox"/>
123848	123848_1	8301558_1	Frozen Cell Pelle	1.0E7		Auto	<input type="checkbox"/>	<input checked="" type="checkbox"/>

# Surgical Pathology Block Archive

- Pathology report texts that are loaded into the system are the basis for a search and block request. Blocks are requested, deidentified, sectioned, and distributed for a study.



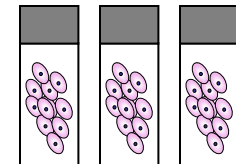
Path Report Loading



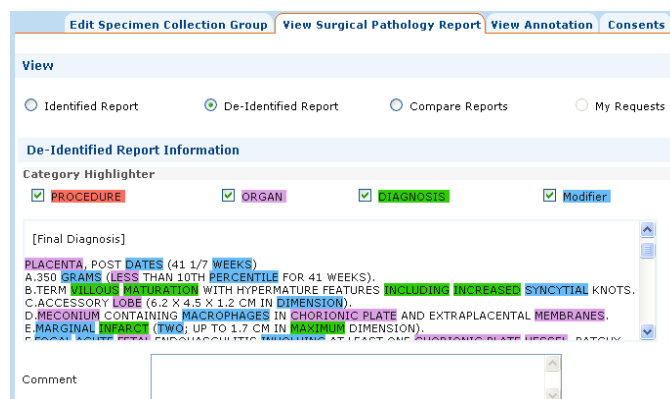
Search for cases based on path report



Retrieve requested blocks from pathology and accession as new specimens



Cut slides and distribute

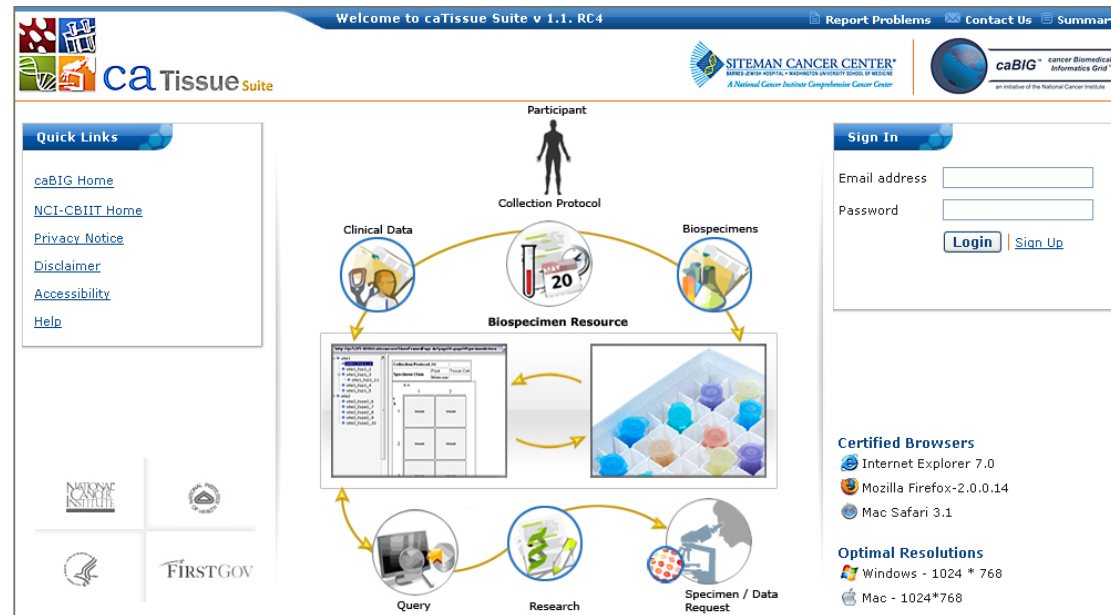




# Challenges in Biospecimen Informatics

- **Workflows that are facility-specific**
- **Workflows that are protocol-specific**
- **Requirement for flexibility and extensibility**
- **Access by multiple user roles for diverse purposes**
- **Requirement to accurately gather large amounts of data**
- **Data can be diverse, complex, and hierarchical**
- **Limited personnel / financial resources for data entry**
- **Requirement for data sharing using common vocabularies**

# caTissue Suite v1.1(P4.1)



- **Web-based application for biospecimen information management**
- **Professional approach to software design**
- **Open source / Open access (Free)**
- **Iterative development cycle (Always improving)**
- **Flexible to meet the needs of varying biobank environments**
- **Multiple sources of electronic and human support**
- **Tracks many events in the biospecimen lifecycle**

# Lifecycle: Collection / Receipt

caTissueSuite

Home Administrative Data Biospecimen Data Search

Collection Protocol: TPCF- Full Consent

Participant (Protocol ID): N/A (10470)

Specimen Details for N/A (10470)

T1.0: Undefined: 03-10-2005

**Edit Specimen Collection Group**

\* Collection Protocol Title: TPCF- Full Consent

\* Specimen Group Name: 8525

\* Study Calendar Event Point: 1.0, Undefined Days

\* Clinical Diagnosis: Not Specified

\* Activity Status: Active

\* Participant Name (Protocol ID):

\* Collection Site: Barnes Jewish - South

\* Clinical Status: New Diagnosis

\* Collection Status: Complete

**Specimen Collection Group**  
(Applies to all specimens collected in the group)

When / who collected from the participant:  
**Surgeon**  
**Clinician**  
**CRA**  
**Pathologist**

**Collected**

\* Collector: Abbey, Elliot

\* Date: 03-10-2005 [MM-DD-YYYY]

\* Time: 00 Hr. 00 Min.

\* Procedure: Not Specified

**Received**

\* Receiver: Abbey, Elliot

\* Date: 03-10-

\* Time: 00

\* Quality: Accept

When / who received the specimen:  
**Pathologist**  
**Pathology Assistant**  
**Biospecimen Bank Staff**

# Lifecycle: Tracking Collection Timepoints

The screenshot displays the 'caTissue Suite' web interface. The top navigation bar includes 'Home', 'Administrative Data', 'Biospecimen Data', 'Search', and 'Help'. The main content area is titled 'Edit Specimen Collection Group' and shows details for Collection Protocol Z1031 and Participant P, E(16202). The 'Specimen Details for P, E (16202)' section lists timepoints: T0.0 (Baseline), T14.0 (Week 2), T30.0 (Week 4), T56.0 (8 Week), and T130.0 (Surgery). The T30.0 timepoint is highlighted with a gold border. Below it, a list of specimens is shown: 0813815P (purple), 0813816P (purple), 0813817P (purple), 0813818P (purple), and two 'Whole Blood' specimens (black). The 'Events' section is divided into 'Collected' and 'Received' tabs, both showing details for the 09-03-2008 collection event. The 'Collection Status' is set to 'Incomplete'. Three callout boxes provide context: 'Time point with specimens collected (gold)' points to the T30.0 timepoint; 'Collected specimen (purple)' points to the specimen list; 'Pending or not collected specimen (black)' points to the 'Whole Blood' specimens; and 'Status of collection time point' points to the 'Collection Status' dropdown.

**Time point with specimens collected (gold)**

**Collected specimen (purple)**

**Pending or not collected specimen (black)**

**Status of collection time point**

# Lifecycle: Specimen Processing Events

caTissue Suite

Home Administrative Data Biospecimen Data Search Help

Specimen Details Events View Surgical Pathology Report View Annotation Consents

Existing events for the specimen with label '23496'

Identifier	Event Parameter	User	Date / Time
446274	Collection	Abbey Elliot	03-10-200500:00
446273	Received Event	Abbey Elliot	03-10-200500:00

Select Specimen Event To Add

Event Details "Frozen Event"

\*User: Watson, Mark

\*Date: 01-21-2010

\*Method: Not Specified

Comments

Submit

Recordable specimen events

Recording when / who / how specimen was frozen

# Lifecycle: Creating a Biospecimen CV

The screenshot shows the 'caTissue Suite' web application interface. The top navigation bar includes 'Home', 'Administrative Data', 'Biospecimen Data', 'Search', and 'Help'. The left sidebar shows 'Collection Protocol: TPCF- Full Consent' and 'Participant (Protocol ID): Register New'. The main content area is titled 'Existing events for the specimen with label '8010500806641'' and contains a table with the following data:

Event Parameter	User	Date / Time
Collection	Fleshman James	01-21-2010 13:00
Received Event	Brink Amy	01-21-2010 13:47
Frozen	Brink Amy	01-21-2010 13:54

Below the table, there is a 'Select Specimen Event To Add' dropdown menu currently set to '-- Select --'. Three callout boxes are overlaid on the left side of the table, pointing to the 'Collection', 'Received Event', and 'Frozen' rows respectively.

Resected by surgeon (Fleshman)

Received in repository (Brink)

Frozen (Brink)

# Lifecycle: Biospecimen QA

The screenshot displays the 'caTissue Suite' web application interface. The top navigation bar includes 'Home', 'Administrative Data', 'Biospecimen Data', 'Search', and 'Help'. The main content area is divided into a left sidebar and a right main panel.

**Left Sidebar:**

- Collection Protocol:** Z1031
- Participant (Protocol ID):** C, M (16545)
- Specimen Details for C, M (16545):**
  - T0.0: Radiology (Baseline): 06-20-2009
  - 0916337P
  - 0916339P
  - 0916342P** (highlighted)
  - 0916343P
  - 0916340P
  - 0916341P
  - T14.0: Week 2 : 08-15-1975
  - T30.0: Week 4: 07-20-2009
  - T56.0: 8 Week: 08-15-2009
  - T130.0: Surgery: 10-28-2009

**Main Panel:**

- Navigation:** Specimen Details, Events, View Surgical Pathology Report, View Annotation, Consents
- Section:** Existing events for the specimen with label '0916342P'
- Table:**

Identifier	Event Parameter	User	Date / Time
1506594	Received Event	Brink Amy	06-20-2009 14:27
1506595	Collection	Brink Amy	06-20-2009 14:27
1738861	Tissue Specimen Review	Deschryver Katherine	12-07-2009 08:35
- Event Details "Tissue Specimen Review Event":**
  - \* User: Deschryver, Katherine
  - \* Date: 12-07-2009 [MM-DD-YYYY]
  - \* Time: 8 Hr., 35 Min.
  - Neo Plastic Cellularity Percentage: 70.0
  - Lymphocytic Percentage: 0.0
  - Histological Quality: Good- Definable Cellular Data
  - Comments: [Empty text area]
  - Necrosis Percentage: 0.0
  - Total Cellularity Percentage: 60.0

# Lifecycle: Biospecimen QA

caTissue Suite

Home Administrative Data Biospecimen Data Search Help

TitLi Search TitLi Search Report Problems Contact Us Summary Logout

Specimen Details Events View Surgical Pathology Report View Annotation Consents

Existing events for the specimen with label 'T812473'

Identifier	Event Parameter	User	Date / Time
1347225	Collection	Brink Amy	08-01-2008 15:33
1347226	Received Event	Brink Amy	08-01-2008 15:33
1347645	Molecular Specimen Review	Giuntoli Therese	06-02-2009 15:27

Molecular Specimen Review Event- Who / When

Select Specimen Event To Add -- Select --

Event Details "Molecular Specimen Review Event"

\* User: Giuntoli, Therese

\* Date: 06-02-2009 [MM-DD-YYYY]

\* Time: 15 Hr. 27 Min.

Gel Image URL:

Quality Index:

Gel Number:

Lane Number:

Absorbance At 260: 2.858

Absorbance At 280: 1.361

Ratio 28S To 18S:

Comments:

Details

Collection Protocol: Z1031

Participant (Protocol ID): B, D (16135)

View Participant

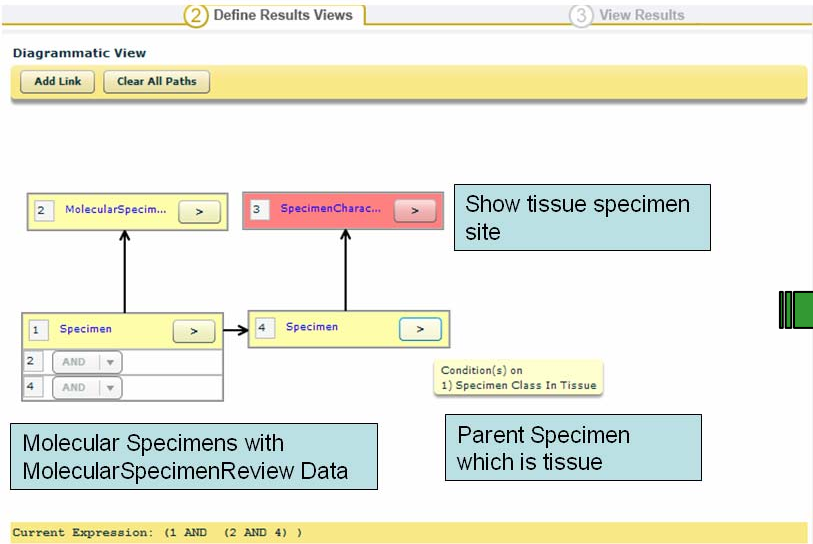
Specimen Details for B, D (16135)

- T0.0: Radiology (Baseline): 06-04-2008
- 0809672P
- 0812471P
- 0812472P
- 0812473P
- T812473
- D812473
- 0812474P
- 0812475P
- 0812476P
- T14.0: Week 2 : 08-15-1975
- T30.0: Week 4: 08-15-1975
- T56.0: 8 Week: 08-15-1975
- T130.0: Surgery: 10-30-2008

DNA derived from frozen tumor tissue



# Lifecycle: Biospecimen QA



1 Add Limits 2 Define Results Views 3 View Results

Records Per Page 100 1 - 100 of 4425 1 2 3 4 5 6 7 8 9 10 >>

Specimen Label	Abstract Specimen Type	Abstract Initial Quantity	Molec Absorb At260	Molec Absorb At280	Molec Quality Index	Molec Ratio 285 To185	Abstract Specimen Type	Abstract Pathological Status	Specimen Ch Tissue Site
✓ P8305	RNA	9.7	5.378	2.558			Fixed Tissue	Malignant	Breast NOS
✓ P8315	RNA	4.8	2.68	1.289			Fixed Tissue	Malignant	Breast NOS
✓ P8325	RNA	5.9	3.302	1.591			Fixed Tissue	Malignant	Breast NOS
✓ P8335	RNA	1.66	0.895	0.458			Fixed Tissue	Malignant	Breast NOS
✓ P8345	RNA	4.2	2.294	1.106			Fixed Tissue	Malignant	Breast NOS
✓ P8355	RNA	2.5	1.36	0.666			Fixed Tissue	Malignant	Breast NOS
✓ P8385	RNA	1.38	0.737	0.372			Fixed Tissue	Malignant	Breast NOS
✓ P8395	RNA	1.7	0.93	0.573			Fixed Tissue	Malignant	Breast NOS
✓ P8405	RNA	5.8	3.6	1.722			Fixed Tissue	Malignant	Breast NOS
✓ P8415	RNA	3.4	2.028	0.972			Fixed Tissue	Malignant	Breast NOS
✓ P8425	RNA	13.5	8.05	3.852			Fixed Tissue	Malignant	Breast NOS
✓ 085622	RNA	53.11			8.6		Frozen Tissue	Malignant	Lung NOS
✓ 100468	DNA	29.5					Frozen Tissue	Non-Malignant	Skin NOS
✓ 100469	DNA	31.5					Frozen Tissue	Non-Malignant	Skin NOS
✓ 100470	DNA	38.2					Frozen Tissue	Non-Malignant	Skin NOS
✓ 100471	DNA	21.86					Frozen Tissue	Non-Malignant	Skin NOS
✓ 100472	DNA	30.2					Frozen Tissue	Non-Malignant	Skin NOS
✓ 100473	DNA	35.9					Fresh Tissue	Non-Malignant	Skin NOS
✓ 100474	DNA	25.4					Fresh Tissue	Non-Malignant	Skin NOS

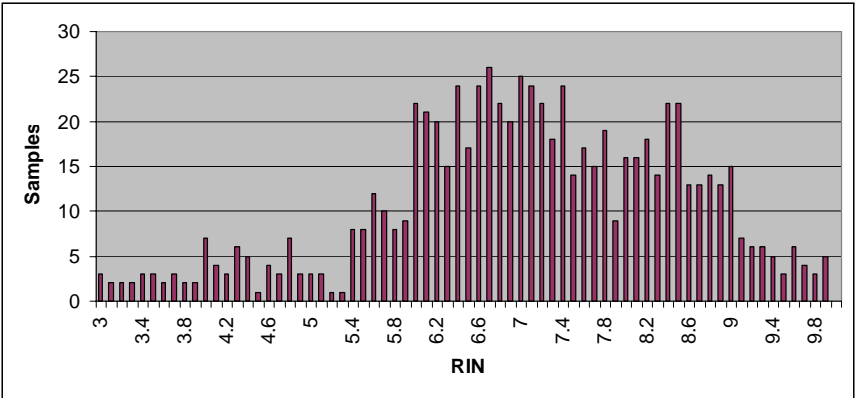
Save Previous

Check All On This Page  Check All

Add To My List Export Define View Redefine Query

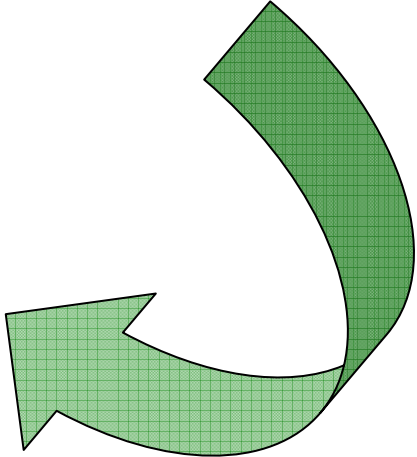
## QUERY

## REPORT



## ANALYZE

Distribution of RNA RIN Scores for Frozen Tissue Specimens




- Filter based on:
- RNA / DNA
  - Fixed / Frozen Tissue
  - Tissue Site
  - Collector
  - Collection Date
  - Collection Site
  - Processing Technician

# Deploying caTissue at WUMC

Welcome to caTissue Suite v1.1.p4.1

HOME Report Problems Contact Us Summary

**Summary**

**Administrative Records**

Total Registered Users:	1021	Total Collection Sites:	68
Total Collection Protocols:	289	Total Repository Sites:	15
Total Distribution Protocols:	195	Total Laboratory Sites:	48

**Specimens Details**

**Total Specimens: 426856**

**Total Cell Specimens: 88775**

Frozen Cell Pellet	68746
Cryopreserved Cells	19086
Not Specified	655
Slide	187
Frozen Cell Block	101

**Total Fluid Specimens: 186702**

Plasma	83170
Serum	42349
Cerebrospinal Fluid	29287
Whole Blood	24765
Urine	3370
Bone Marrow Plasma	1396
Whole Bone Marrow	1046
Lavage	580
Body Cavity Fluid	303
Feces	153

**Total Tissue Specimens: 110329**

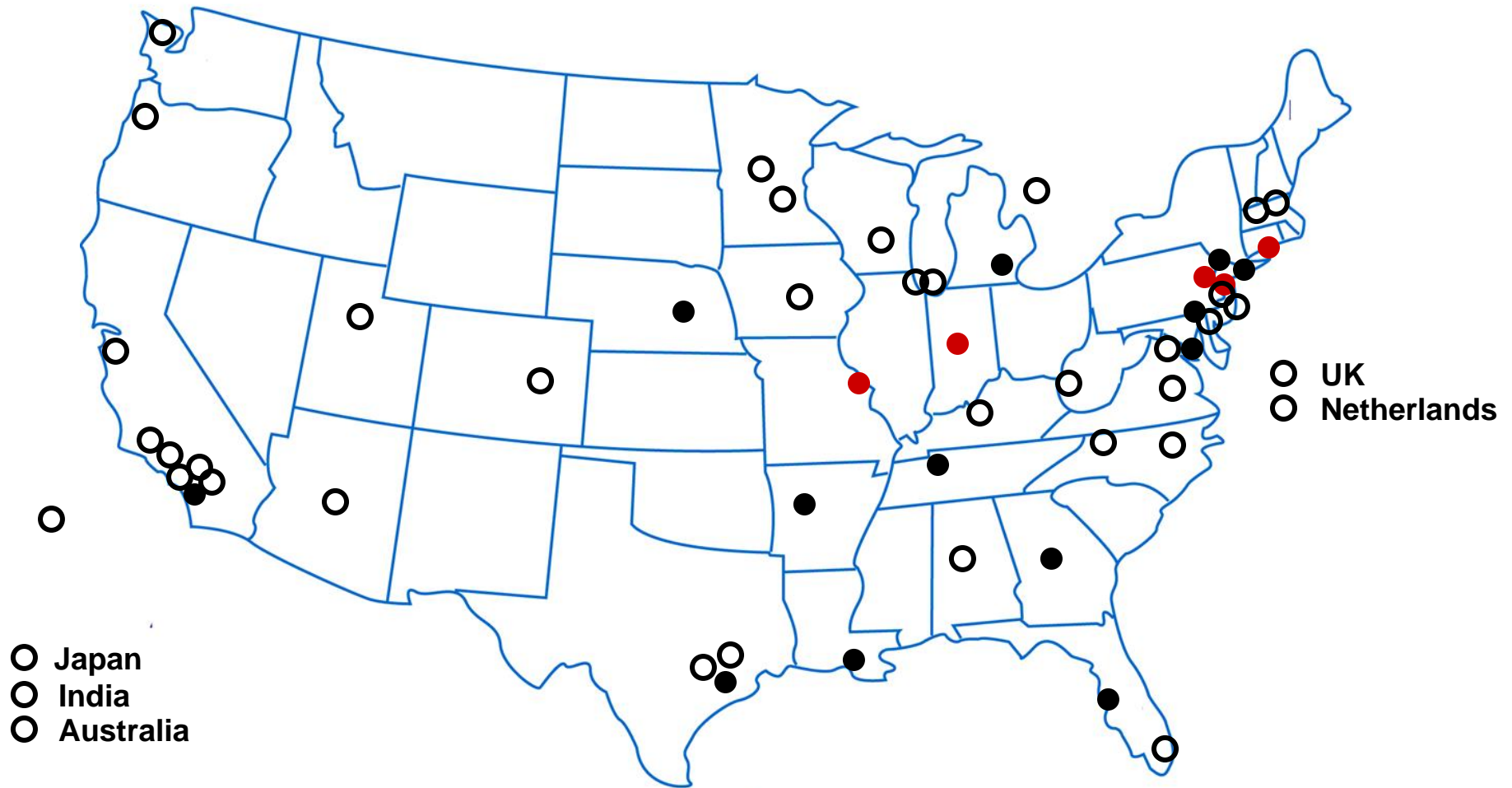
Fixed Tissue Block	45156
Frozen Tissue	39284
Fixed Tissue Slide	16493
Fixed Tissue	5050
Fresh Tissue	2032
Frozen Tissue Block	1053
Not Specified	608
Frozen Tissue Slide	410
Microdissected	243

**Total Molecular Specimens: 41050**

DNA	21171
RNA	16913
Whole Genome Amplified DNA	2576
Total Nucleic Acid	314

# The caTissue Biospecimen Network

(February 2010)



○ **Testing**

48 institutions

**10,000 specimens**

● **Production**

13 institutions

**470,000 specimens**

● **Grid-enabled Production**

5 institutions

**716,000 specimens**

# Deploying caTissue: New Challenges

- Unsuspected bugs revealed during 'real-life' use
  - Bug reporting, tracking, fixing
- Performance of web interface vs. client software
  - Code improvements
  - GUI improvements
- Necessary workflow modifications
  - Pre-printed barcodes
  - Lab reorganization (benches and webstations)
- More data + Complex data entry = More time consuming
  - More personnel
  - Revised financial model to reflect increased biospecimen cost
- Requirement to train user roles with differing expertise
  - Training program / personnel
- **Logistics of real time, remote data capture**

# Capturing SOP Data in caTissue

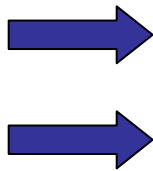
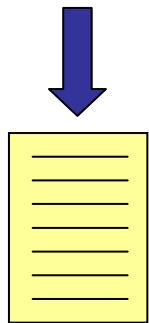
OBRR Office of Biorepositories and Biospecimen Research  
Biospecimen Research Database  
PubMed www.pubmed.gov

Search the Biospecimen Network Repository (Quick Search)

To find research studies for a biospecimen type and platform click on a cell in the table below.

Analyte	Technology Platform	Biospecimen Locations	Neoplastic Tissue
		Blood Serum Plasma Urine Saliva Normal Cancerous	
	Array CGH		2
	CGH		1 1
DNA	DNA Sequencing	1	2 2
	ESDH	1	6 2
	In situ hybridization		1
	PCR	2	10 13

BRD- Peer Reviewed Literature  
in Biospecimen Science



Abstracted  
SOP for  
Biospecimen  
Processing

1. Defining a  
Collection Protocol to  
Include Required  
Processing Events  
(Future Functionality)

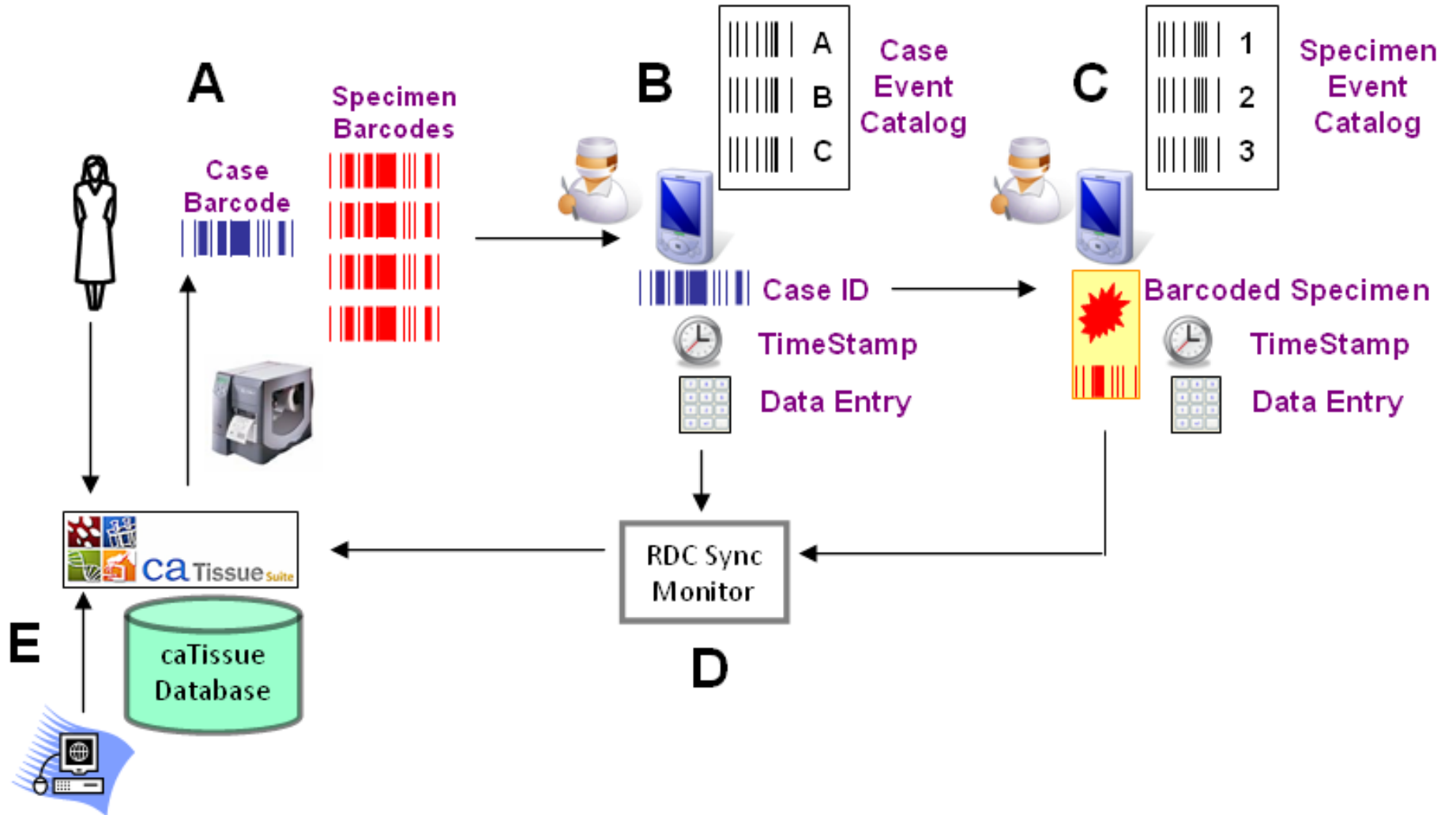


2. Recording Events in the  
Biospecimen Life Cycle



3. Search Based on Biospecimen  
Life Cycle Parameters

# Remote Data Capture using caTissue



# Remote Data Capture Challenges

- Cost of technical implementation and maintenance
- Identification / definition of desired common data attributes associated with pre-analytical variability
  - “Warm Ischemia Time”
- Training and reliable use by personnel other than biobank staff
  - Nurses / CRAs
  - Surgeons / Anesthesiologists
  - Pathologists
- Incentives for routine use
  - Improve the quality of clinical care



# caTrack- RDC by Biobank Staff



Initialization



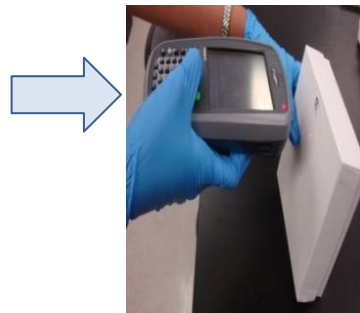
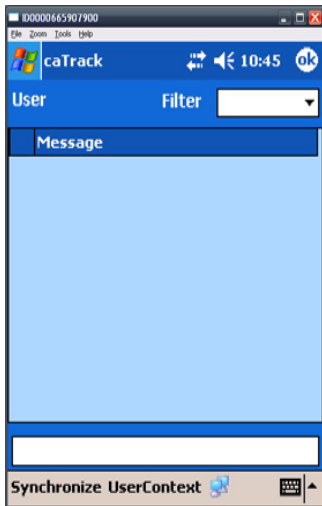
Login and Scan  
User Batch



Scan centrifuge



Scan Specimens



Scan container

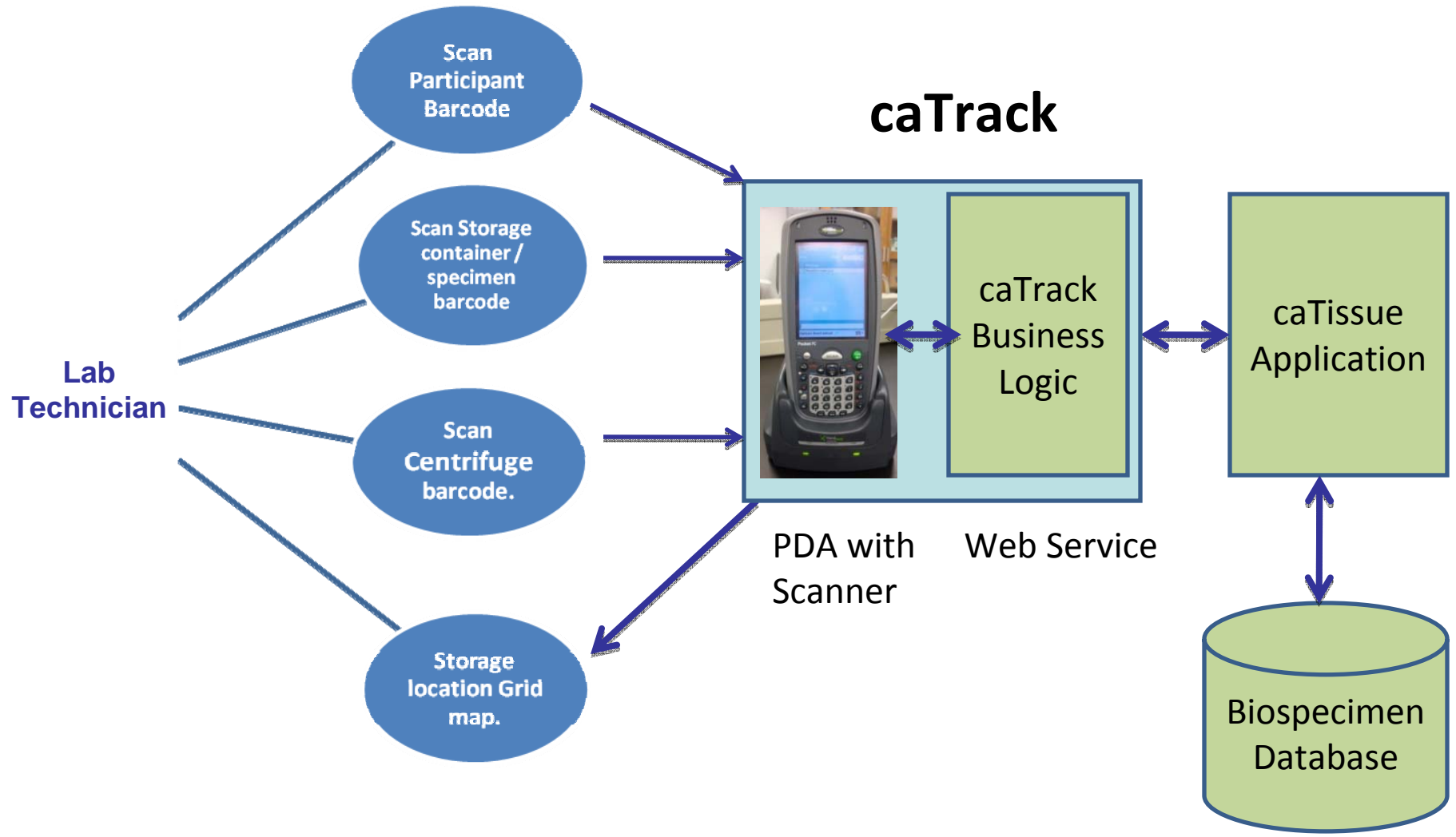


Scan Specimens

- Set the collected and received events of a specimen
- Assign a storage location to specimens
- Transfer specimens or containers within containers
- Add frozen, centrifuge events on specimens



# caTrack- RDC by Biobank Staff



# Future Directions

- Further application enhancements for performance and usability based on end-user feedback
- Remote data entry and distributed effort by multiple users / roles
- Automated data capture by 2D barcode scanning
- Integration with clinical trials and EMR systems for participant registration and annotation
  - Admission note
  - OR report
  - Anesthesia chart
  - **Pathology report**
  - **Lab Values**
  - **Vitals**
  - **Pharmacy record**
  - Radiology report

# caTissue Resources

- The TBTT KC site-

[https://cabig-kc.nci.nih.gov/Biospecimen/KC/index.php/Main\\_Page](https://cabig-kc.nci.nih.gov/Biospecimen/KC/index.php/Main_Page)

- Log on and try out the demo site for caTissue Suite v1.1-

<http://catissue.wustl.edu:8080/catissuecore>

- View a narrated video overview of the tool and installation-

[https://cabig-kc.nci.nih.gov/Biospecimen/KC/index.php/Tissue/Biospecimen\\_Banking\\_and\\_Technology\\_Tools:Current\\_events](https://cabig-kc.nci.nih.gov/Biospecimen/KC/index.php/Tissue/Biospecimen_Banking_and_Technology_Tools:Current_events)

- Practice learning how to use the tool on the E-learning portal-

<http://cabigtrainingdocs.nci.nih.gov/caTissue/index.html>

- Browse through the on-line manual-

[https://cabig-kc.nci.nih.gov/Biospecimen/KC/index.php/CaTissue\\_1.1\\_User\\_Manual](https://cabig-kc.nci.nih.gov/Biospecimen/KC/index.php/CaTissue_1.1_User_Manual)

- For additional questions, post them to the TBTT KC Forum-

<https://cabig-kc.nci.nih.gov/Biospecimen/forums/>



# Acknowledgements



**Rakesh Nagarajan MD, PhD**

**Mark A. Watson MD, PhD**

**Dave Mulvihill**

**Vicky Holtschlag**

**Amy Brink**



Aniket Pandit  
Ganesh Naikwade  
Prafull Kadam  
Supriya Dankh  
Vijay Pande  
Rajesh Patil  
Madhumita Shrikhande

Ashish Gupta  
Komal Gulati  
Sachin Lale  
**Srikanth Adiga**  
Virender Mehta  
Kalpana Thakur  
Abhishek Mehta

Deepti Shellar  
**Poornima Govindrao**  
Sayali Salodkar  
Vaishali Khandelwal  
Rushikesh Subedar  
Snehil Gupta  
Preeti Munot



**INDIANA UNIVERSITY**

