



Walter Reed
National Military
Medical Center



Murtha Cancer Center

“The DoD Cancer Center of Excellence”

“Accelerating Progress against Cancer through Collaboration”

Development of Best Practices-Based Biobanking Processes

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June 23rd, 2014.



SCOPE



**Learning
Objectives**

**Biobanking
for Biomedical
Research**

Best Practices



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Best Practices



Learning Objectives

1. Understand the role of biobanks and how they support biomedical research.
2. Understand the value of implementing “best practices” to maintain standards and quality of specimens available in biobanks.



Learning
Objectives

**Biobanking
for Biomedical
Research**

Best Practices



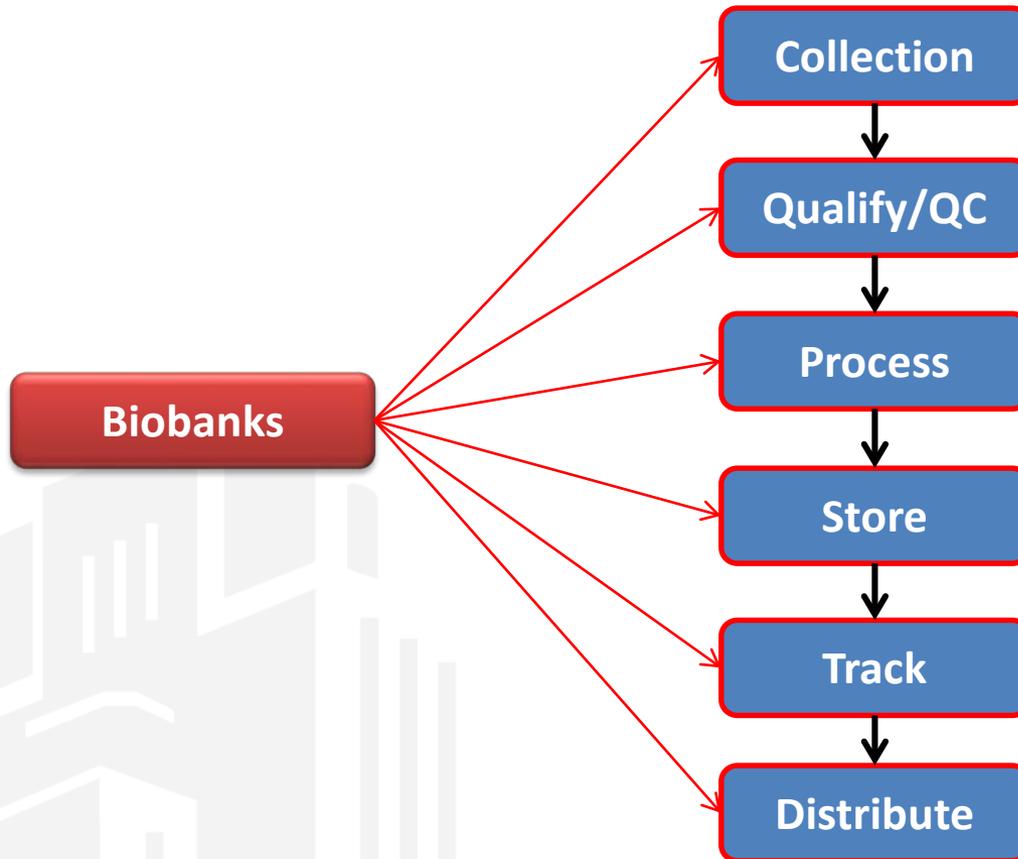


Role of Biobanks in Biomedical Research

- “**Specimen-dependent**” Biomedical research **requires** good quality human tissue specimens (body fluids and solid tissue).
- Clinics and hospitals are the source of most human tissue specimens used for research.
- Not all researchers have access to the clinics and hospitals.
- Biobanks manage and preserve the specimens so that they will be available on demand.
- Biobanks help researchers get the type and amount of tissue that is required to conduct their research.

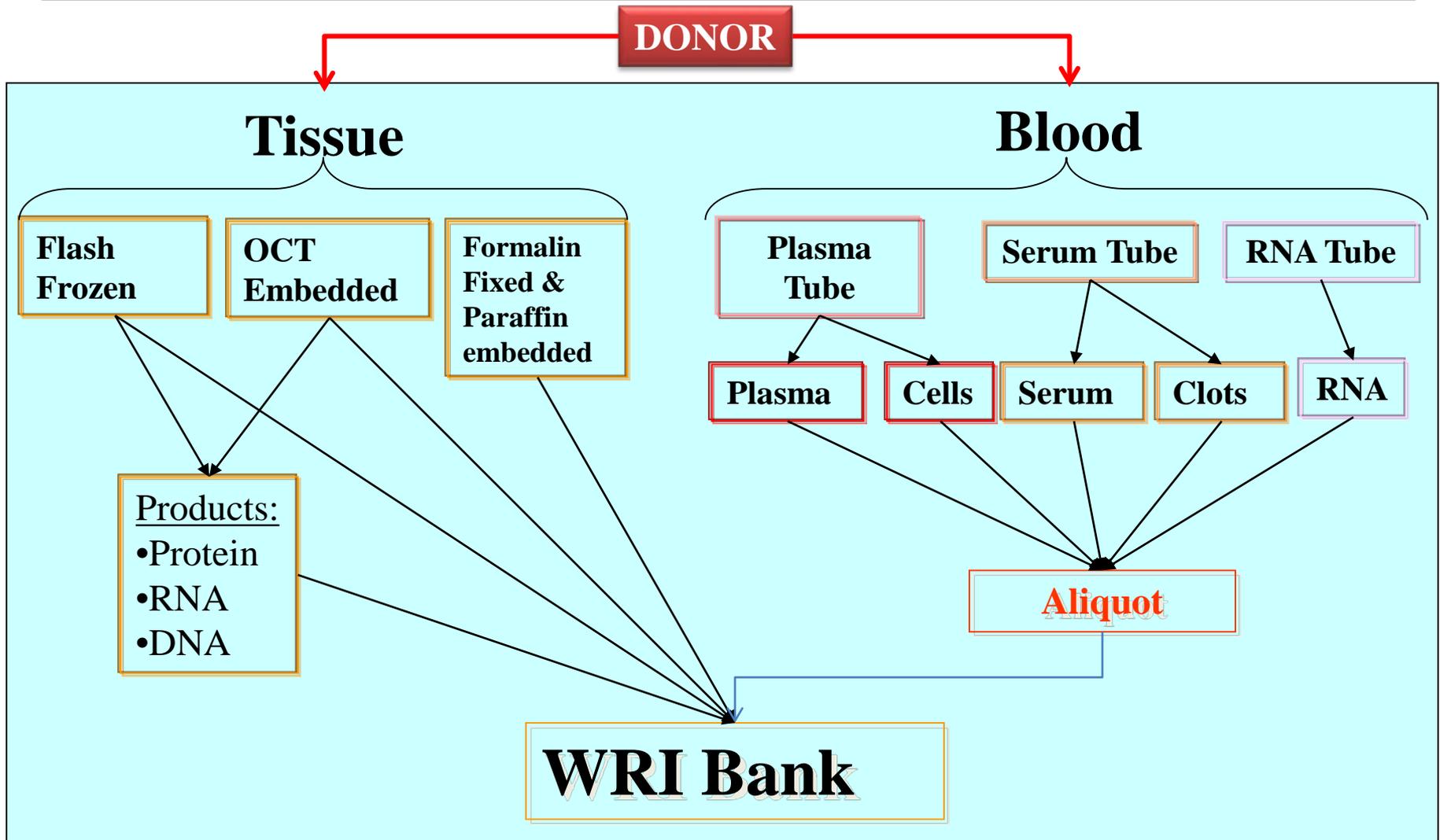


Core Functions of a Biobank



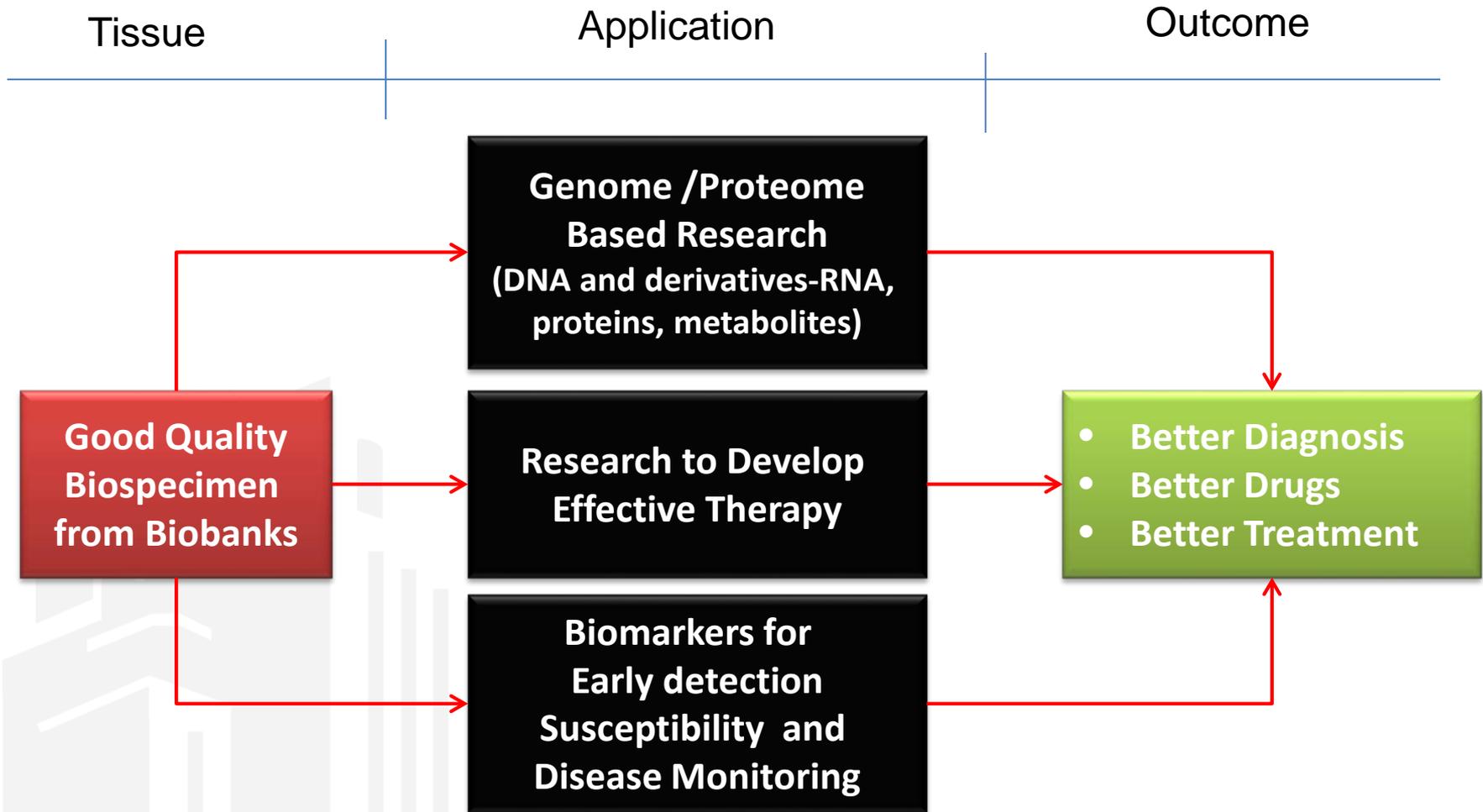


Biospecimen Types





Biobanks Support Genomics & Proteomics Age





Biobanks Support Personalized Medicine Research



- Personalized Medicine (PM) - New paradigm for practicing medicine.
- PM driven research requires good quality and well-annotated specimens (DNA, RNA, Proteins) that accurately reflect the disease state.
- By providing good quality and well annotated specimens Biobanks can impact the success of PM by helping accelerate the translation of research from “bench to the bedside”.

Windber Research Institute – Biobank



Windber Research Institute Established - 2000

Tissue collection commenced - 2001



Pittsburgh

- West Central PA
- 7 Miles from Johnstown, PA
- 70 miles East of Pittsburgh, PA



Biobanking for the Clinical Breast Care Project



Total donor tissue banked – **6,549**

Total specimens banked - **57,165**

Contributing sites to date - **7**

Current sites

- Breast Center- Walter Reed (WRNMMC)
- Breast Center- Windber (JMBCC)
- Anne Arundel Medical Center, MD



Biobanking for the Clinical Breast Care Project



Tissue Utilized – 24,346

- BRACA1
- Gene Expression
- Cytokine profiling
- Matrix modification
- MMP polymorphism
- Proteomics
- AAW
- LN Prognostics
- cSNP
- Tumor progression
- TCGA

Collaborations

- NCI
- Correlologic
- Vanderbilt
- PNNL

Biobanking for The Murtha Cancer Center



Cancer Center Biobank Shipments		Tissue Total Aliquots		Liquid Total Components		Miscellaneous		
Batch	Date Received	OCT	SF	Cryotubes	Straws	Touch Preps	Cell Scrapes	
1	10/12/2011	295	1820	418	538	0	0	
2	4/17/2012	31	0	0	0	0	0	
3	5/1/2012	10	0	28	36	4	2	
4	6/12/2012	60	6	0	0	21	4	
5	9/11/2012	28	0	12	11	0	0	
6	9/25/2012	111	0	0	0	21	14	
7	10/16/2012	74	0	70	0	1	3	
8	11/14/2012	73	1	74	0	6	4	
9	1/29/2013	108	3	66	0	13	9	
10	4/9/2013	181	6	0	0	6	2	
11	4/30/2013	54	2	167	0	0	0	
12	6/5/2013	81	2	179	0	0	0	
13	6/19/2013	33	0	111	0	1	0	
14	8/13/2013	75	4	140	0	10	0	
15	9/17/2013	84	10	103	0	2	0	
16	10/8/2013	46	1	89	0	4	0	
17	10/29/2013	61	4	103	0	3	0	
18	11/19/2013	64	3	66	0	4	0	
19	12/17/2013	81	7	76	0	2	0	
20	1/28/2014	65	3	72	0	1	0	
21	2/25/2014	65	1	117	0	1	0	
22	3/25/2014	51	4	123	0	1	0	
23	4/29/2014	71	3	179	0	0	0	
24	6/3/2014	72	1	173	0	0	0	
TOTALS		1874	1881	2366	585	101	38	6845



Learning
Objectives

Biobanking
for Biomedical
Research

Best Practices





Why do we need Best Practices for Biobanks?



- To ensure consistency in annotation and tissue quality.
- To ensure that the same standards are used in all biobanks.
- Good research outcome relies on good quality specimens. Without implementing “best practices”:
 - Tissue quality will vary within and between tissue banks.
 - Pre-analytical variables which affect the quality of biospecimens may not be detected, documented and reported.

Life cycle of a biospecimen-NCI-BBRB





Biobanking Best Practices

Biobanking Oversight

Best Practices

- Collective Experience
- Guidelines & Recommendations
 - **ISBER**-International Society for Biological and Environmental Repositories
 - 2005/2008/2012
 - **NCI**
 - 2006/2011



Biobanking Best Practices

Biobanking Oversight (ISBER)

- Self Assessment Tool (SAT)
 - Assess adherence to ISBER Best practices
- Certified Repository Technician Training Program
 - Consistency in staff training
 - Provide pool of trained staff
 - Career path
- Proficiency Testing
 - DNA Quantification
 - RNA Integrity
 - Tissue Histology



Biobanking Best Practices

Biobanking Oversight

College of American Pathologists (CAP) Accreditation

- The first formally recognized accreditation for Research Tissue Banks
- Drive adoption of standardization through consistent application of best standards
- Ensure consistent, verifiable quality of biospecimens
- Continuous oversight of biobanks



Best Practices at WRI

- Development of appropriate Standard Operating Procedures (SOPs)
- Strict adherence to the SOPs
- Staff Training
- Use of Human Subjects for Research Training
- Audits
- Quality (QA/QC)
- Corrective Measures (as needed)

Best Practices at WRI

- Design of appropriate “document controlled” Standard Operating Procedures (SOPs)
- From 5 SOPs to 88 SOPs & 72 Forms/Logs in 11 years!

Year	Total Number of SOPs
2003	5
2006	31
2008	33
2010	58
2012	62
2014	88

- Consenting, sample collection/processing, shipping, archiving
- Histology processes
- Facility related SOPs, record correction, data entry., additional lab protocols
- Administrative protocols, SOP review/modifications, ethics, record retention, QA programs, Education/Training
- Alarms/monitors, more histology (microtome, cryostat)
- More administrative policies, Record & documentation management, competency, more QA/QC



Best Practices at WRI

1. Tissue Acquisition and Processing:

Goal: Maintain biological content of donor tissue

- Design appropriate SOPs
- Monitor and track pre-analytical variables
- Monitor nucleic acid quality
- Document
- Analyze
- Initiate corrective action for Quality Improvement



Best Practices at WRI

2. Storage, Maintenance, Tracking, Distribution

Goal: Maintain uniform storage conditions

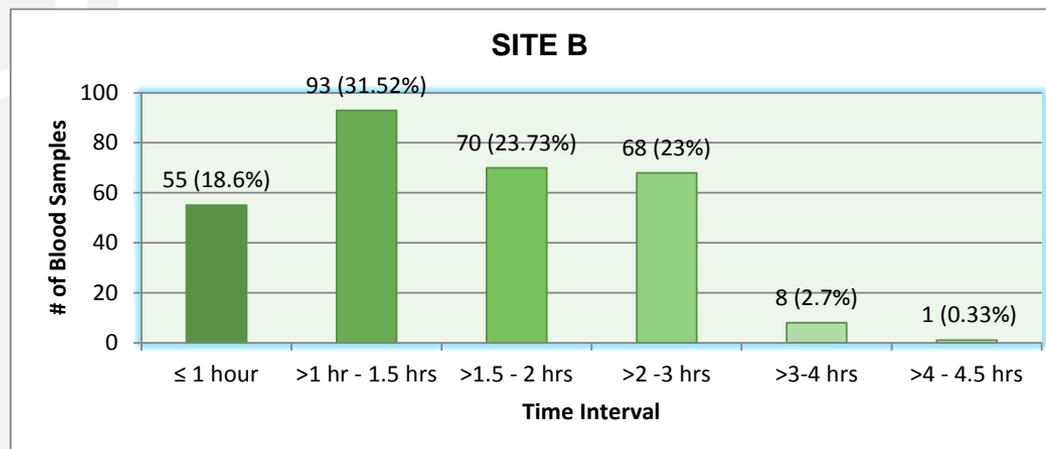
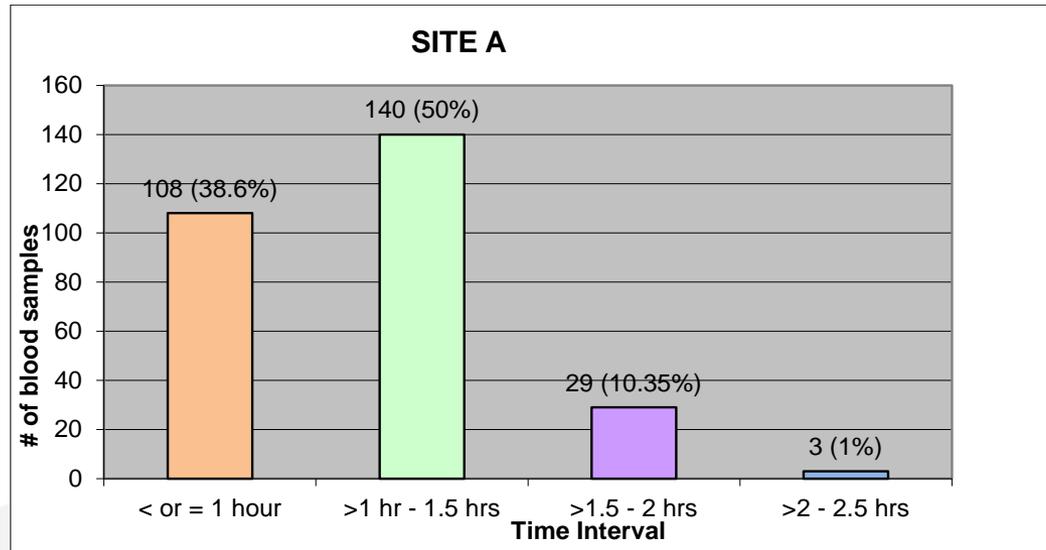
Maintain sample identity at all times

- Monitor freezer temperature/liquid nitrogen levels
- Monitor equipment
- Document
- Analyze results
- Determine corrective action if any



Monitor/Document/Analyze

Blood collection data





Monitor/Document/Analyze



RNA

Analytical Quality Control

	Number of Tissue Samples per year				
RIN #	2008	2009	2010	2011	2012
≤ 5.0	0 (0%)	5 (4%)	6 (4%)	2 (1%)	0 (0%)
5.1-5.9	0 (0%)	4 (4%)	7 (5%)	11 (5%)	0 (0%)
6.0-6.9	7 (19%)	26 (22%)	25 (17%)	36 (17%)	3 (7%)
7.0-7.9	21 (57%)	41 (35%)	67 (47%)	76 (35%)	22 (51%)
≥ 8.0	7 (19%)	17 (15%)	21 (15%)	19 (9%)	10 (23%)
NA	2 (5%)	23 (20%)	17 (12%)	72 (33%)	8 (19%)
Total # samples	37	116	143	216	43

DNA

260/280

≥ 1.8

1.5 - <1.8

< 1.5

Samples

733

14

3

%

97.7%

1.9%

0.4%



Monitor/Document/Analyze



Acceptable Ranges

Freezer Temperature (≤ -165 °C) Liquid Nitrogen Level (12-23 inches)
Please contact biorepository staff if readings fall outside acceptable ranges.

Freezer Room 1 and 2

Date - 6/12/2014

Freezer 1 Centron Monitoring System # 1

	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	19.2	-192	2010	MS
12:00 AM	18.2	-191	2357	PCY
4:00 AM	17.2	-191	0337	PCY

Freezer 2 Centron Monitoring System # 2

	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	19.4	-193	2010	MS
12:00 AM	18.3	-193	2351	PCY
4:00 AM	17.3	-192	0337	PCY

Freezer 3 Centron Monitoring System # 3

	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	18.4	-192	2010	MS
12:00 AM	17.0	-192	2351	PCY
4:00 AM	15.7	-191	0337	PCY

Freezer 4 Centron Monitoring System # 4

	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	19.7	-196	2010	MS
12:00 AM	18.7	-196	2356	PCY
4:00 AM	17.8	-196	0337	PCY

Freezer 6 Centron Monitoring System # 6

	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	21.0	-195	2010	MS
12:00 AM	20.1	-195	2350	PCY
4:00 AM	19.3	-195	0336	PCY

Freezer 7 Centron Monitoring System # 8

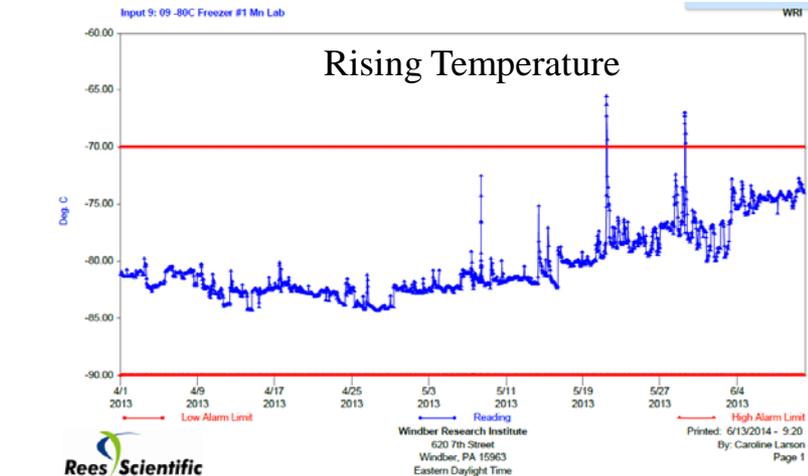
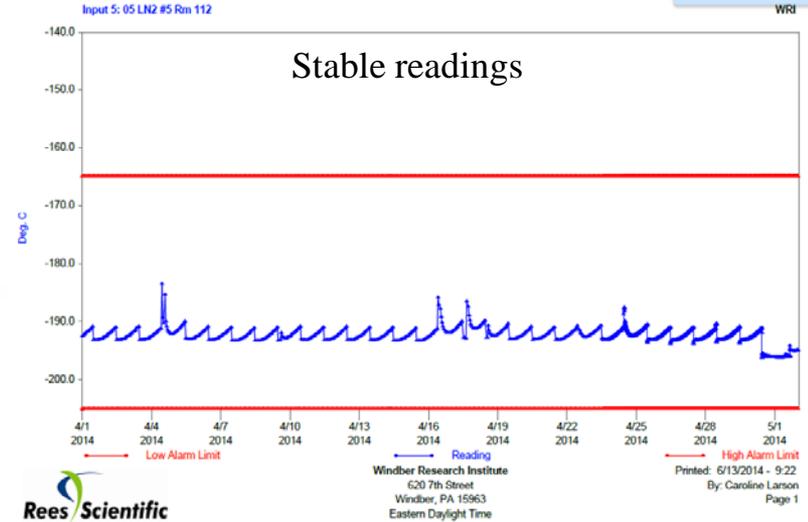
	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	21.2	-195	2010	MS
12:00 AM	20.4	-195	2350	PCY
4:00 AM	19.6	-195	0336	PCY

Freezer 8 Centron Monitoring System # 39

	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	22	-197	2010	MS
12:00 AM	21	-196	2352	PCY
4:00 AM	20	-195	0335	PCY

Freezer 9 Centron Monitoring System # 40

	Nitrogen Level	Lid Temp.	Actual Time Checked	Initials
8:00 PM	21.0	-196	2010	MS
12:00 AM	20.1	-196	2352	PCY
4:00 AM	19.3	-196	0335	PCY





Best Practices

Analytical Quality Control

- Volume/Quantity
- Concentration
- Purity/Integrity
- Evidence of Degradation



Best Practices

Functional Quality Control is needed

Quality assessment relying on nucleic acids may not provide information on:

- Downstream performance
 - Gene Expression
 - SNP
- Collection Errors
 - Sample Identification
- Contamination
 - Laboratory processing



Biospecimen Science

Design Evidence Based SOPs to address issues currently based on “experience”

- Design research in the context of observed pre-analytical variables.
- Generate data to support the design of **Evidence Based SOPs**.
- Provide new evidence based biobanking standards.



New collection/processing methods

- Number and size of solid tumors diminishing over the years.
- Alternate sources of processing and storage required to feed biomedical research in the future.
- Pilot studies confirm feasibility of adapting touch imprint preparations on glass slides and filter paper in situations where surgical specimen is limited.
- Touch imprints can also be used to prolong the availability of “rare and precious” specimens in the tissue bank.



Conclusion

- We have established protocols and workflow processes for acquisition and banking of large quantities of good quality tissue for biomedical research.
- We have processes and protocol in place to monitor our performance and take appropriate corrective action when necessary.
- Functional QC will be necessary to maximize the usefulness of the banked specimen.
- We are conducting biospecimen research to generate data to support evidence based SOPs.
- Implementing Best Practices that are backed by scientific data will allow the standardization of Biobanking processes and ensure consistency in the quality of tissue specimens stored and distributed for research.



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Thank you!



Clinical Breast
Care Project





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Questions

