

## “Giving” Tissue and Blood for Research Purposes

An advocate’s perspective

Karl Schwartz  
Patient advocate, Lymphoma

*Participant: 2005, NCI Workshop on Biospecimen Access and  
Ethical, Legal, and Policy*

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## Biospecimen ... to Biomarkers

*There’s an urgent need for practice-guiding  
biomarkers*

- To minimize unproductive toxicity that can limit subsequent options to choose the right drug for the right patient at the right dose and schedule
- To avoid under- or over-treating the patient to maximize efficacy and minimize toxicities
- **Patients want to contribute!**
  - The larger concern is the disease



*If danger can be seen in terms of a **narrowing range of choices**, Billy Tyne's choices have just ratcheted down a notch.” ~ The Perfect Storm.*

## Informing the decision to participate

- Is the biomarker study exploratory or validated?  
Informing my confidence to participate
  - Is it reliably predictive of response or prognosis?  
Informing my decision to participate
  - Is extra biopsy mandatory or optional?  
Degree of burden/risk informing my decision to participate
  - Is the study size sufficient ....  
Informing my referring physician's recommendation
  - How long will I be on treatment (over-treating?)
  - Is the capture, storage , and analysis standardized – can data be pooled?  
Informing my referring physician's recommendation
- Collaboration and standardized methods are needed to find answers that are likely to help patients.*

## Risks and Burdens

### NCI Consent elements:

- \* What **extra** tests and procedures will I have if I take part in this study?
- \* What possible risks can I expect from taking part in this study?
- \* Who will see my medical information?

Disease-specific / Unspecified future use

### Physical

Extra or different surgical / imaging procedures, blood draws and frequency of each

### Non-physical risks and side effects

- Privacy and confidentiality
- Time Travel , Financial - time off from work ...
- Genetic information – familial risk  
Future use ... third party access?  
Potential to identify stigmatizing information?
- Perception or risk? (Educational materials)

\* NCI Informed Consent Template provides sample text and guidance

## Patients' Concerns – feasibility

- Is it painful, dangerous, burdensome?
  - Travel expenses; time off from work?
  - Do other equally appropriate protocols require less of me?

*\* Curt, Chabner, 2008, The Oncologist  
One in Five Cancer Clinical Trials are Ever Published,  
most often from failure to accrue*

- Privacy and Consent– best practice\*
  - Is my privacy protected?
  - Will I be informed if the findings are validated?
  - Unspecified future uses ...

*\* NCI Best Practices for Biospecimen Resources*

## ... Future uses of “my” biospecimen?

- Will status and uses be published?
- Who “owns” my tissue ... (stewardship?)
- Privacy: Is my clinical information exposed?
- Future use (consent / value) is it:
  - Limited to disease-specific research?
  - Based on merits of the science  
(expert panel includes advocates)
  - Sold to a company for commercial uses?

### **Perspective on reporting:**

*When you communicate with the public about the uses and the status of contributed biospecimen, you are encouraging also best practices and fostering public trust in clinical research.*

*But doing this efficiently requires an informatics system - a recommended part of best practices\**

**Perspective on ownership:** *The center is the steward of the sample. The patient decides who has access to the tissue for research purposes.*

*\* NCI Best Practices for Biospecimen Resources*

## Perspectives on Appropriate use of Mandated Biospecimen

- To **select the right patients to receive the study drug**  
To limit risk to the patients most likely to benefit from the targeted agent.  
An integral biomarker study – precision medicine
- To **monitor for safety**, especially for new class of drug
  - Detect toxicity early
  - Monitor clearance, where it goes, etc.
  - Is study drug helping in sampled region?
- When findings of study are very **likely to help future patients**
  - Not exploratory. Strong supporting evidence. Could validate a biomarker that guides future practice and future studies –  
An Integrative biomarker study
- **Exploratory uses** of biospecimens may be appropriate when procedure risks are very low,. Otherwise, exploratory studies should be limited to extra samples acquired from standard procedures.

## Coercion?

When might requiring a high-risk or painful procedure to acquire biospecimen be considered coercion in a clinical trial?

- When the analysis is exploratory - not tied to primary study questions
- When the sample size is underpowered and therefore unlikely to advance the science
- When the research is siloed – does not use standard or certified (CLIA) practices
  - Particularly when there are high expectations about the efficacy of the study protocol – that harm will result if not accepted in the study.

### **Coercion:**

*“The threat of further harm may lead to the cooperation or obedience of the person being coerced.”*

## An advocate's perspective on the "ownership" of patient-derived biospecimens

- That researchers and medical institutions are **stewards** of patient biospecimens (not owners)
- That the biospecimens that patient's have taken risks to give will be maintained and protected for optimal research use.
- That requests for biospecimen transfer (e.g., tissue blocks) from one accredited institution to another should be granted when the patient gives consent

*The patient or patient advocates may help to resolve access to tissue disputes*

*The patient has no claim on IP or profits that may result from correlative research.*

## Optional Research Biospecimen?

- Consider when the procedure is worrisome ... adding to the challenge of accrual -- putting other important clinical questions in your study at risk.
- Consider the negative impact on the power of the correlative study if many participants opt out

### QUESTIONS

- Can other tests on the same sample potentially guide future choices – such as eligibility for other trials, such as NCI MATCH?
- When would offering additional uses of the same biospeciment be considered undo influence?

*Ask also patient advocates for guidance!*

## Rare Cancers and Subtypes

### Familiar Challenges / Emerging Opportunities

#### **Rare and uncommon subtypes of cancer**

are excluded from many trials due to rarity (challenge of enrolling sufficient participants) and lack of financial incentive

**Opportunity:** By adopting NCI standards for tissue collection, biomarkers-based trials can be based on mutations or biomarkers that may predict response to targeted drugs across different cancers/subtypes, such as [NCI MATCH](#)

## Biospecimen Best Practice Complementing Accrual

**Mistrust of research, low rates of participation** in clinical trials, the burden and risk of extra biopsies, siloed research – isolating instead of publishing data.

**Opportunity:** Forward thinking research centers might adopt NCI Best Practices (standardized collection, storage, and analysis) as part of routine diagnostics ... supporting enrollment in trials based on standardized tumor analysis. Providing biospecimen specimens, data and resources for pooled analysis and additional research.

... Adopting consent policy that is patient-centered and disease-specific. Guiding future choices for the patient –eligibility for biomarker-based trials.

## NCTN Biobank Resources

### Emerging Opportunities / Familiar Challenges

#### Cooperative Group Banks (CGB)

[Biorepositories for NCI-Sponsored Cancer Clinical Trials](#)

*CGB in an exciting and important advance!*

**Opportunity:** Proposing that samples also be made available for patient-directed clinical research on request of clinical researchers ... such as patient's eligibility for biomarker-based trials or tumor specific antigens (when a new biopsy is dangerous to the patient).

**However, mandated biopsies can add to the challenge of study accrual** in science-based clinical trials

## Resources

### \* Cooperative Group Banks (CGB)

[Biorepositories for NCI-Sponsored Cancer Clinical Trials](#)

### \* The Cancer HUman Biobank (caHUB)

Biospecimens.cancer.gov: <http://1.usa.gov/1r2gfrQ>

#### Consensus of the Broad Scientific Community:

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

#### Understanding the Problem:

The Siloed National Biobanking Landscape

- 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

## Resources

- JCO, 2012: Peppercorn, Shapira, Collyar, Deshields, Lin, Krop, Grunwald, Friedman, Partridge, Schilsky and Bertagnoli Ethics of Mandatory Research Biopsy for Correlative End Points Within Clinical Trials in Oncology <http://bit.ly/1s0u1vx>
- A GUIDE TO RESEARCH ETHICS UNIVERSITY OF MINNESOTA CENTER FOR BIOETHICS 2003 [http://www.ahc.umn.edu/img/assets/26104/Research\\_Ethics.pdf](http://www.ahc.umn.edu/img/assets/26104/Research_Ethics.pdf)

## Summary

When the purpose is explained ... we will often want to contribute tissue - the larger concern is the disease

... But the burden and risks of the procedures need to be considered and minimized – especially for exploratory study

Validating biomarkers is not easy, requires quality resources, standardized methods, and cooperative study.

... But the benefits can be enormous -- extending to patients outside of your study – making future trials much more efficient.

*Sincere thanks for the work you do on behalf of patients – present and future – all of us!*