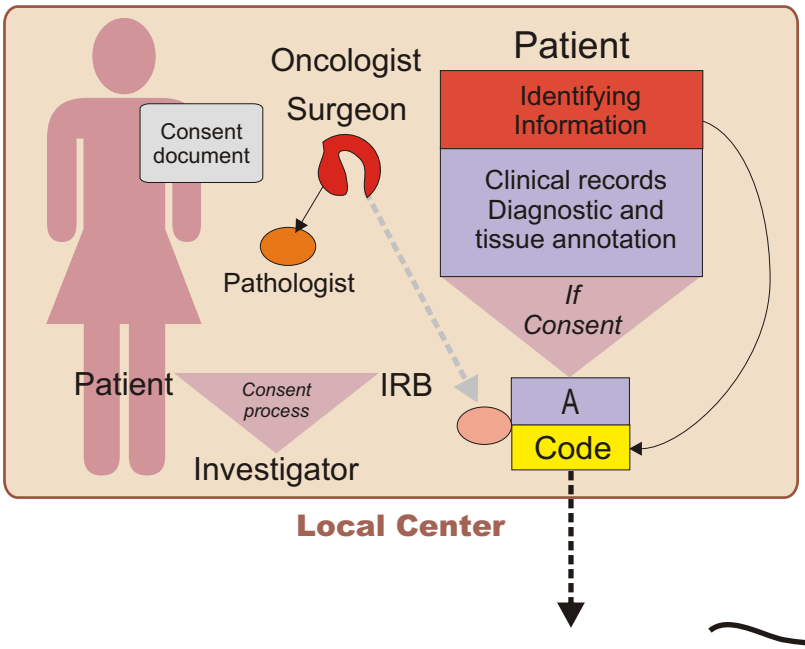
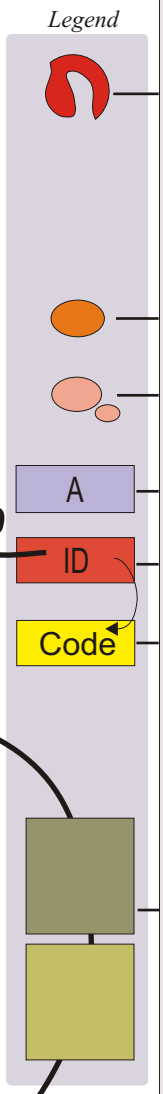
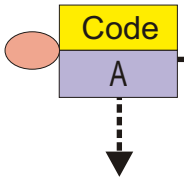
Modernizing Cancer Research



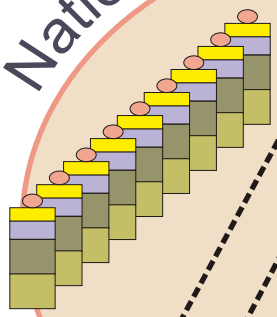


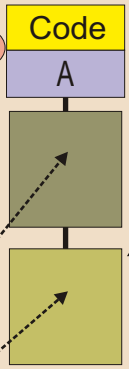


Bio-record:
* Unidentifiable Code
* Clinical annotation
* Tissue sample
* Tissue analysis, and clinical outcomes from research data (green boxes)

NBN

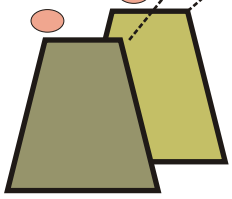
National Biospecimen Network





Other bio-records (unidentifiable)

Targeted drugs



Research Groups

Research groups awarded use of tissue will receive tissue of the same diagnostic type from the NBN.

The research done will produce data, such as from gene expression analysis of the tissue, to identify new drug targets, and bio-markers - specific biological traits that predict the clinical course, toxicity and responses to different therapies.

NBN will further accelerate clinical research by providing open access to this valuable data.

1 You have been referred to an oncologist because a lump is thought to be suspicious.

It may or may not be a cancer.

2 Your oncologist refers you to a surgeon to have a biopsy to obtain a **specimen** of the suspicious tissue.

You are asked to participate in the **NBN** research project; and informed that declining or participating will not affect the quality of your care.

3 A **sample** (part of the specimen) is sent to the pathologist for diagnosis.

4 If you give *consent* to participate in NBN, an **extra sample** is stored in a **bio-record** for research purposes.

5 Clinical and specimen detail (annotation) is added to the bio-record.

6 Identifying information (**ID**) is stripped from the bio-record ...

... and replaced with a unique **Code** that is not identifiable to help protect your *privacy*.

7 Access to the tissue samples is based on the *merits of the research* as judged by an independent stakeholder panel that will include patient representatives.

8 Data, such as molecular profiling and clinical trial results, are published to the NBN. ...

... This enables all researches to correlate the characteristics of the tumor and patient with clinical outcomes - so called "*data mining*."

KEYS TO DISCOVERY OF TARGETED DRUGS

Standardized capture, storage, and analysis of large numbers of annotated bio-specimens so that research findings are comparable and the results are statistically powered.

Bio-Informatics software that can store the considerable amounts of clinical and molecular data, linked to the tissue.

Common data elements, so that each research group is reporting and describing data using the same terminology.

Data sharing, including publishing of failed research, so discovery and validation of bio-markers can be accelerated and resources can be deployed efficiently.

Privacy protection and *consent* - to inspire trust, participation and continued public funding.

DRAFT

Karl Schwartz, Patients Against Lymphoma

DID YOU KNOW?

Virtually every family will be affected by a serious cancer

one in three women, and
one in two men

1,372,910 men and women will be diagnosed and 570,280 men and women will die of cancer of all sites in 2005.[2]

[2] *SEER.cancer.gov*

The number of new cancer drug applications is in decline

FDA 2004 *– The "Innovation/Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products."*

http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html

The vast majority of cancer drugs fail to win marketing approval

"...the vast majority of investigational products that enter clinical trials fail. Often, product development programs must be abandoned after extensive investment of time and resources. This high failure rate drives up costs, and developers are forced to use the profits from a decreasing number of successful products to subsidize a growing number of expensive failures. Finally, the path to market, even for successful candidates, is long, costly, and inefficient, due in large part to the current reliance on suboptimal assessment methods."

~ Harnessing Science: Advancing Care By Accelerating The Rate Of Cancer Clinical Trial Participation" ***FDA 2004***

Only 5% of cancer patients participate in clinical trials

Providing incentives and finding better ways to recruit patients will not fix an underlying problem: the appeal of the clinical trial to the patient – and his or her physician – as a treatment decision.

~ Karl Schwartz

Cancers with the same name are not the same

"The trick with molecular targeting is that you have to be able to match the drug to the patient. And until you understand how the drugs work, why they work, and for whom they work, your results might not be as remarkable as you would like for them to be. Once we understand how to match the drug to the patient, I think we will see many, many examples like imatinib [Gleevec]."

~ Dr. Brian Druker, Howard Hughes Medical Institute

Research analogy - The cost of trial and error medicine:

In order to compare how well different detergents clean you must account for the **type of cloth** and the **type of stain**. If you use a new detergent on the entire batch, it may clean 20% of the items better than the rest. But if you don't know what type of cloth and stain it cleaned best you haven't learned anything useful. And when it's time to clean your next shirt you're back to **trial and error**, and the chance you'll get it wrong 80% of time.

Similarly, **clinical cancer research** does not often account for the underlying differences in the patients and tumors, and the cost is often tragic:

> *The majority of patients can suffer toxicity for no benefit; expensive failures gives pause for drug sponsors to try again; potentially useful new drugs (for some patients) are not approved; the wariness of patients to participate in this kind of trial-and-error research delays evaluations . . .*

Enter the National Bio-specimen Network (NBN):

To identify the differences in the tumors and the patients, the tumor, blood, and other bio-specimens are collected in a controlled way. Bio-specimens are fragile and can change based on how long it takes to remove them, the temperature at which they're stored, and the methods used to freeze them, etc.

Standardization provides the foundation for a reliable analysis to discover what the defects are in the cells – how they are different from normal cells and other tumor cells of the same cell type using **molecular profiling**.

One important goal of molecular profiling is to better characterize the patient and the tumor – to identify the genetic signatures that predict response to treatment, prognosis, or the toxicity of a drug in specific patients. That is, it will accelerate the discovery and validation of **bio-markers that will drive research and personalized medicine.**

NBN will provide:

- **Standardized storage of bio-specimens** and **associated data**
- **High-quality bio-specimens for cancer research**
- **Advanced bio-informatics software to store, analyze, and share the tissue-associated data**

Importantly, the information stored in each **bio-record** will be stripped of identifying information and replaced with a unique code in order to **protect the privacy of the participants**.

The NBN system will provide **access to the quality bio-specimens** based on the merits of the science. All scientists can "mine" the published findings to discover correlations (patterns) between clinical outcomes and patient and tumor characteristics, **dramatically accelerating productive research**.

Notably, NBN will require investigators to **publish ALL research findings** based on NBN-acquired specimens (including failures) so that resources can be applied to the most promising directions and not wasted on less promising research paths.

Importantly, access to large numbers of quality, annotated bio-specimens will make the research results comparable and **statistically powered***, and help identify sub-populations that can benefit from targeted drugs, making **personalized medicine** possible.

> * *Statistically powered findings require large numbers of tissue to ensure that the findings are not due to chance. For example, you might need to flip a coin 100 times to see the true outcome odds are 50:50. Only ten coin flips can mislead.*

Standards is the cornerstone of NBN. Medical research is severely restrained today because we do not yet have standards for collecting, assessing, analyzing, and describing bio-specimens.

> *Consider how inefficient and dangerous it would be to travel by air if each airport and pilot used different signals and procedures.*

The success of NBN is dependent on the participation of patients, requiring awareness of the urgency, the crisis in clinical research, and how NBN can address it.

Success also depends on **trust** in the NBN system – which will provide stewardship of our tissue, which contains our DNA, the "recipes" for cell behavior and also for who we are as individuals and groups.

Given the sensitive nature of genetic information, the designers of NBN have incorporated strong consent procedures and privacy safeguards, including patient representation and oversight within NBN.

To further protect participants, we propose:

(1) a policy asking or requiring those who implement the NBN system to also contribute bio-specimens as controls;

(2) laws, carrying strong penalties, which prohibit discrimination based on genetic characteristics.

Karl Schwartz
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