



VANDERBILT UNIVERSITY
MEDICAL CENTER

Opt Out Biobanking: Lessons Learned from BioVU and Future Opportunities and Challenges

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The Common Rule – The Policy

45 CFR, Part 46, Section 102

“*Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains

- (1) Data through intervention or interaction with the individual, or
- (2) Identifiable private information.”



The Common Rule – The Policy

- *Private information* includes information which is:
 - “provided... by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).”
 - “individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information)”



**Office for Human Research Protections (OHRP)
Department of Health and Human Services (HHS)**

Guidance on Research Involving Coded Private Information or Biological Specimens

This guidance represents OHRP's current thinking on this topic and should be viewed as recommendations unless specific regulatory requirements are cited. The use of the word *must* in OHRP guidance means that something is required under HHS regulations at 45 CFR part 46. The use of the word *should* in OHRP guidance means that something is recommended or suggested, but not required. An institution may use an alternative approach if the approach satisfies the requirements of the HHS regulations at 45 CFR part 46. OHRP is available to discuss alternative approaches at 240-453-6900 or 866-447-4777.

Date: October 16, 2008

Scope: This document applies to research involving coded private information or human biological specimens (hereafter referred to as "specimens") that is conducted or supported by HHS. This document does the following:

(1) Provides guidance as to when research involving coded private information or specimens is or is not research involving human subjects, as defined under HHS regulations for the protection of human research subjects (45 CFR part 46).

(2) Reaffirms OHRP policy (see OHRP guidance on [repository activities](http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm) <http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm> and [research on human](http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm)

that, under certain limited conditions, research involving **only** coded private information or specimens is not human subjects research.



Impact of the Common Rule

- Federal Office for Human Research Protections (OHRP) guidelines allow use to de-identified previously collected medical records and biological samples in research
 - Formally reviewed twice by OHRP who concluded that “human subjects” are not involved
 - Creation of synthetic derivative of electronic medical records of > 1.7 million patients
 - Use of such records is consistent with decades of practice

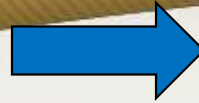


The major issue has been collection of DNA from residual blood samples

- Collected only from outpatient areas
 - Ads have been placed in local newspapers
 - Stories in university publicity
 - Ongoing efforts at publicity
 - Large posters in phlebotomy areas
 - Brochures at all patient check-in areas
- > 80, 000 samples have been collected to date
and research is already underway



JANE DOE



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Military
grade
one
way
encryption



Identifying information
removed; assigned new,
unique code



Electronic medical record is **essential** for this

Updated frequently



Vanderbilt permits patients to opt out of having their DNA included

VI. USE, RETENTION AND DISPOSAL OF TISSUE AND BLOOD

I understand and agree that any specimens or tissues normally removed from my body by VUMC in the course of any diagnostic procedures, surgery, or medical treatment that would otherwise be disposed of may be retained, used for educational purposes or research, including research on the genetic material (DNA) or other information contained in those tissues or specimens.

I acknowledge that such research by VUMC may result in new inventions that may have commercial value and I understand that there are no plans to compensate me should this occur, regardless of the value of any such invention.

I understand that any research using these leftover specimens or tissues will be done in a way that will not identify me or my medical information.

I also understand that if I do not want DNA research to be done using my leftover blood, I need to check the box shown below. If you have questions, please call 1-866-436-4710.

Do not use my leftover blood for the DNA Databank

PLEASE READ THIS ENTIRE AUTHORIZATION PRIOR TO SIGNING.

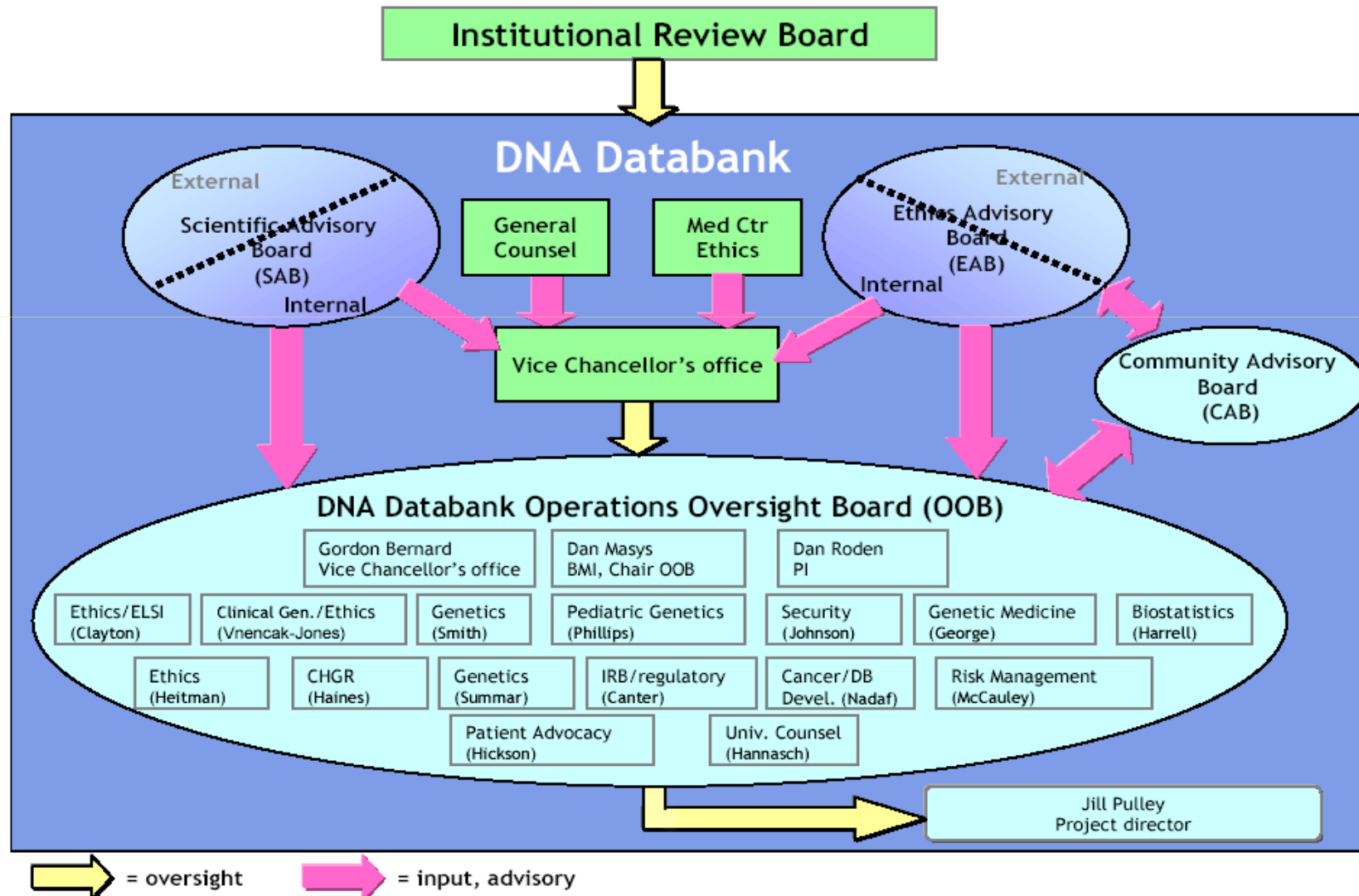
Patient/
Legal Representative _____ Date _____ Time _____ A.M. P.M.

(Relationship to Patient) _____

This document for consent to treat is signed yearly

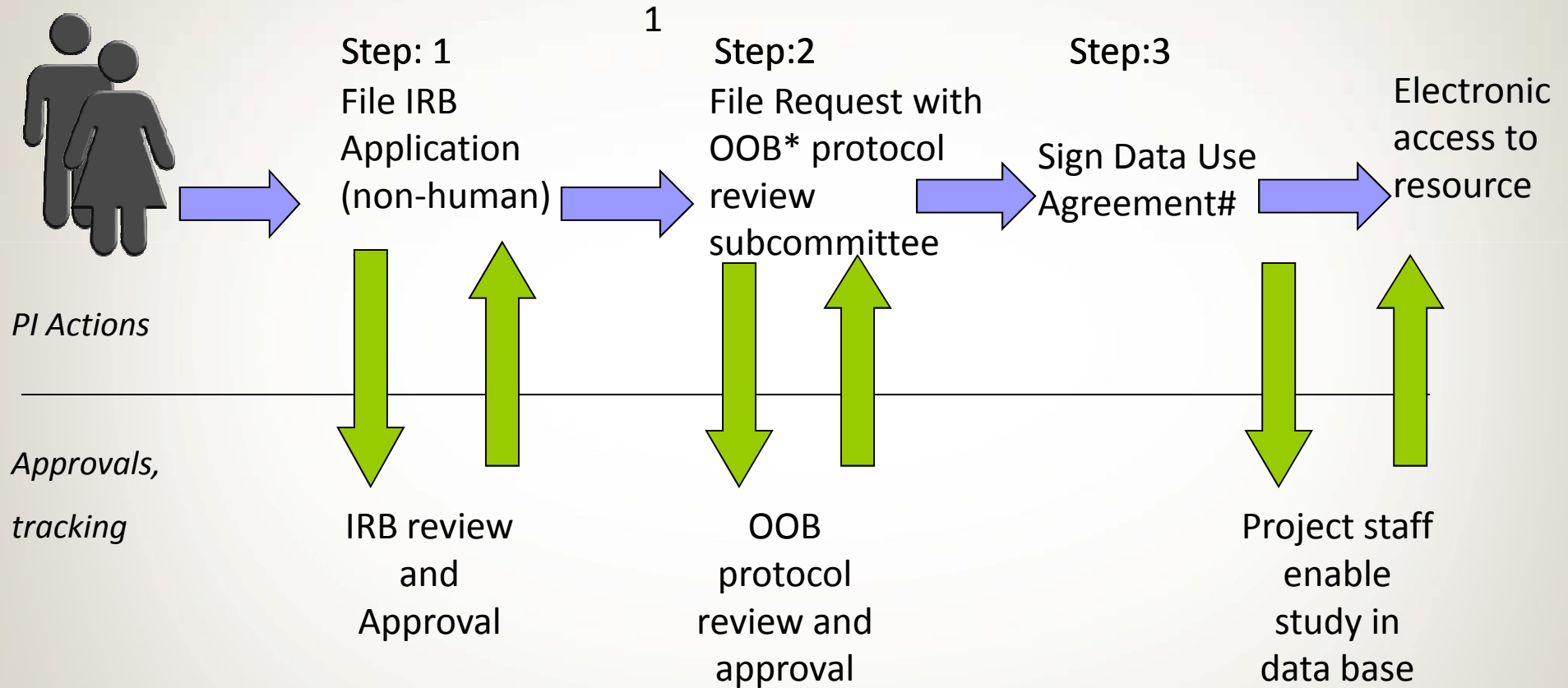


Project Oversight and Governance





BioVU Access Request Process for Local Investigators



*OOB = operations oversight board 10 # this is a contract



Preliminary studies

- Suggested majority of patients would support under the conditions we proposed
- Informed development of the overall approach (e.g. opt out)
- Helped resolve ‘kinks’ in the clinical operations implementation
- Helped Community Advisory Board (CAB) and Operations Oversight Board and Ethics make decisions and provide input
- Informed development of communication materials
- Revealed basic reasons for opting out and preliminary reactions to opt out process
- Uncovered areas of concern and/or misinformation needing further research and response



What do people think?

- Results of survey of ~4000 Vanderbilt faculty and staff

	% Somewhat or strongly agree
DNA databanks are fine as long as all identifying information is removed	93%
DNA databanks with all identifying information removed are fine as long as people can choose to opt of having their DNA included	94%
DNA databanks with all identifying information removed are fine as long as written permission from patients is required for their DNA to be included	88%
DNA databanks with all identifying information removed are fine as long as an ethics review panel approved research with DNA in the databank	91%



Nashville Community Health Survey

- Approve biobank if opt-out available

93.5%

- Approve biobank if conducted “without getting written permission”

39.1%



Interviews with 77 patients in Summer of

2009

- Slightly more than half had heard of BioVU, citing
 - Opt-out forms (n=5)
 - Brochures (n=5)
 - Posters in the clinic (n=6)
 - Other sources of information (n=19)
- Although only ~1/3 knew that residual samples could be used for research, almost 90% supported the idea of BioVU.
 - Those who supported BioVU generally cited the importance of research.
- Concerns expressed about BioVU included:
 - Not knowing how DNA would be used
 - Worries about anonymity
 - Religious beliefs.
 - Only one interviewee subsequently opted out of BioVU.



Expansion into pediatric populations

- Why?
 - Children often have diseases that do not affect adults or that affect adults differently
 - Growing evidence that events during children's lives may affect their health as adults
- Challenges
 - Children do not have blood drawn as frequently as adults do
 - The amount of blood drawn at any one time is typically smaller
 - Potential public response



Interviews with 66 parents of children seeking care at Monroe Carell Jr. Children's Hospital at Vanderbilt

	% agree or strongly agree
Support medical research generally	99%
Support medical research in children	86%
Would permit own child to participate in minimal risk research	83%
Would permit own child's information to be in BioVU	91%

- In response to open-ended questions about possible benefits of BioVU, parents volunteered:
 - Helping others (73%)
 - Not throwing blood away (15%).
- The majority identified no concerns about BioVU, even when probed specifically.



Challenges -- Preventing Re-Identification

- Internal threats – comparison with EMR
 - IRB Review
 - Review Committee
 - Replication Studies
 - Data Use Agreement
 - Ongoing monitoring of access to EMR
- External threats – comparison with public data
 - VDART
 - Empirically assessing re-identification risks



Challenges –

The debate about returning research results

- Arguments that research findings should be returned
 - People say they want them
- Returning research results raises questions about
 - The concept and acceptability of “non-human subjects” research
 - The understanding of research enterprise
 - Therapeutic misconception
 - Investigator-participant relationship
- General consensus that return of results should be included in informed consent process



Challenges --What about autonomy?

- Patients are informed and given the opportunity to opt out
 - How fully can they be informed?
- Analogy to epidemiology?
- Increasing importance of risk reduction, transparency, and governance
- Lessons from the Havasupai