Realizing the Potential:

Building an ethical framework for whole genome research policy

Laura Lyman Rodriguez, Ph.D.
National Human Genome Research Institute

House of Lords Visit
June 5, 2008

http://www.sciencemag.org/cgi/content/full/318/5858/1842

Case Example: The NIH Genome-Wide Association Study (GWAS) Policy

Finding the balance between the need for robust participant protections and the desire to encourage research…

Putting the Pieces Together

- **Scientific Design**
  - Research aims and objectives
  - Program priorities
  - Relationship to individual investigators
- **Policies and Procedures**
  - Guiding principles
  - Applicable laws and regulations
  - Relationship to investigators and institutions
- **Governance & Oversight**
  - Project and program
  - Policy and ethics
  - Transparency

The NIH GWAS Policy

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

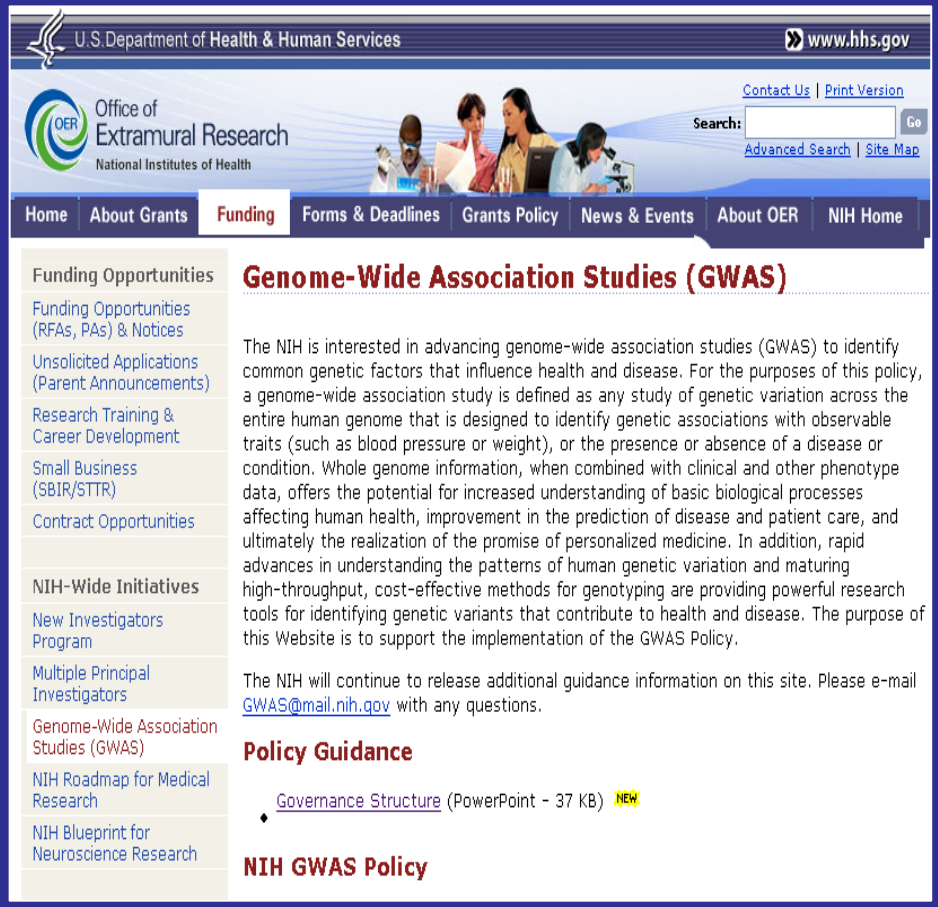
Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS)

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

Background

The NIH is interested in advancing genome-wide association studies (GWAS) to identify common genetic factors that influence health and disease. For the purposes of this policy, a genome-wide association study is defined as any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood



Policy Announced: August 28, 2007
Policy Effective: January 25, 2008

GWAS Homepage:
http://grants.nih.gov/grants/gwas/index.htm

Guiding Principle

The greatest public benefit will be realized if data from GWAS are made available, under terms and conditions consistent with the informed consent provided by individual participants, in a timely manner to the largest possible number of investigators.

- Respect for Participants
- Data Sharing
- Freedom to Operate

GWAS Design & Overview

Data Collection

Submission & Management of Data

Distribution & Secondary Use of Data

Research Participants

Submitting Investigators

GWAS Data Repository (dbGaP)

Recipient Investigators

Ethics Questions

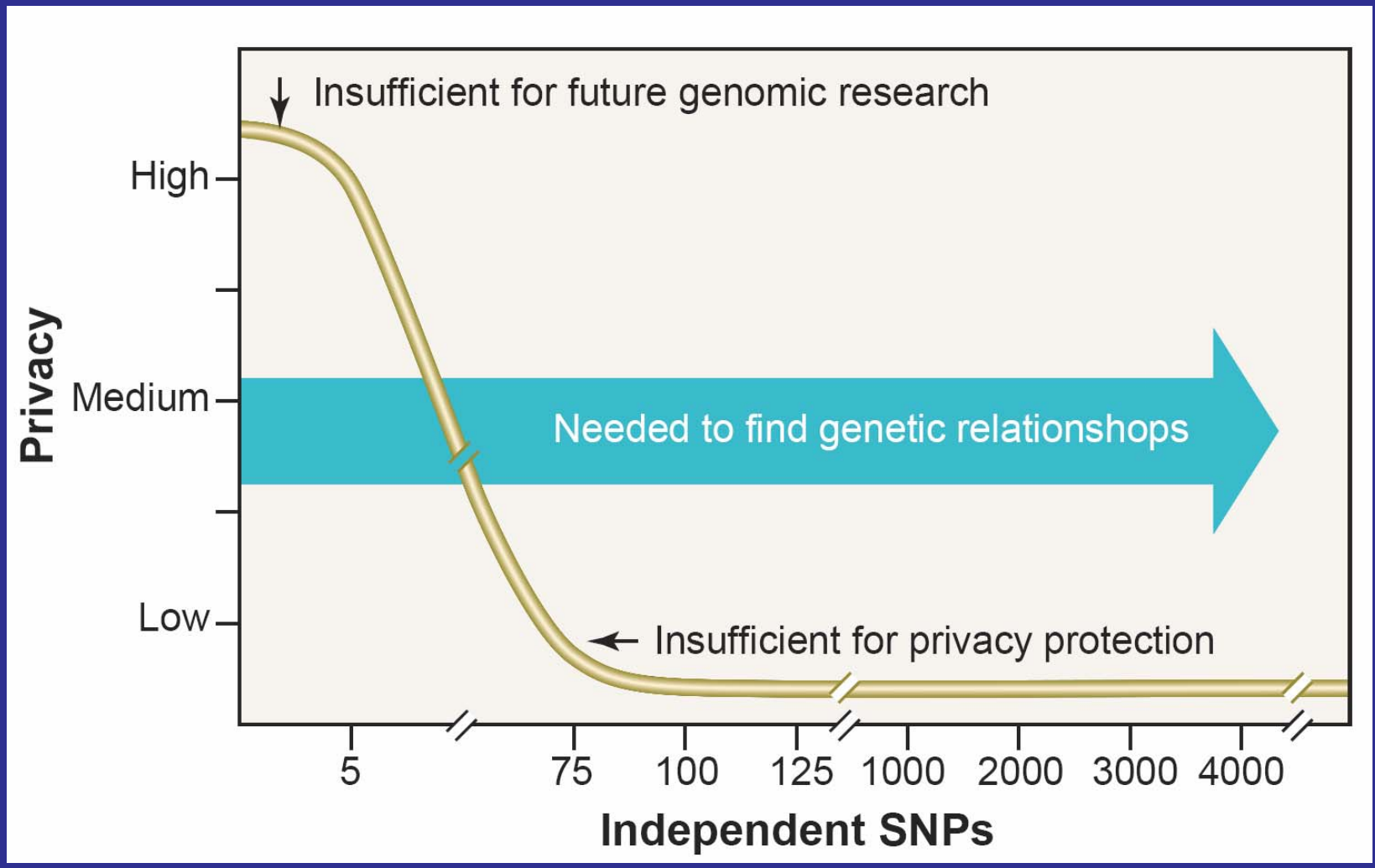
- Is whole genome data identifiable?
- How do we respect the wishes of the individual participants and sustain the public's trust?
- Should individual results from basic GWAS be returned?
- How to provide responsible stewardship of the research?

Policy Questions

- What is the optimum standard for data access for researchers? For the public?
- What level of de-identification provides “adequate” confidentiality protection to participants without damaging the science?
- What is the standard for informed consent? Is it different for prospective studies versus retrospective studies?
- If results are returned to participants, how and in what form?
- How to ensure appropriate oversight of the research?

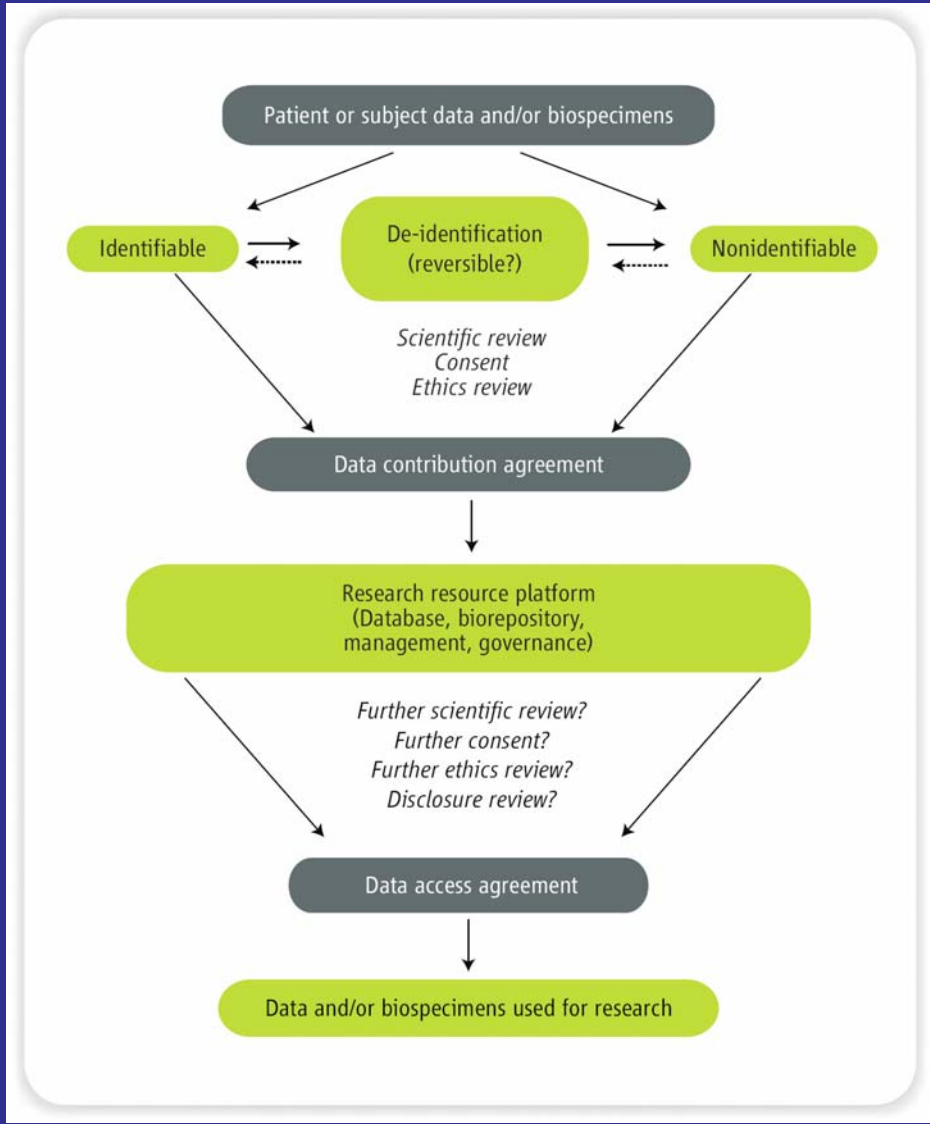
Ethics Questions

Identifiable or Just a Unique Pattern?



Source: Lin, Owen, and Altman. Science, 2004

Looking for balance …



- Different definitions of "identifiable"
- Variety of means to render data "identifiable"
- Uncertain and debatable risk calculation
- Balance scientific potential with public trust/participant protection…in the context of varied enforceability

Source: Lowrance and Collins. Science, 2007

Informed Consent

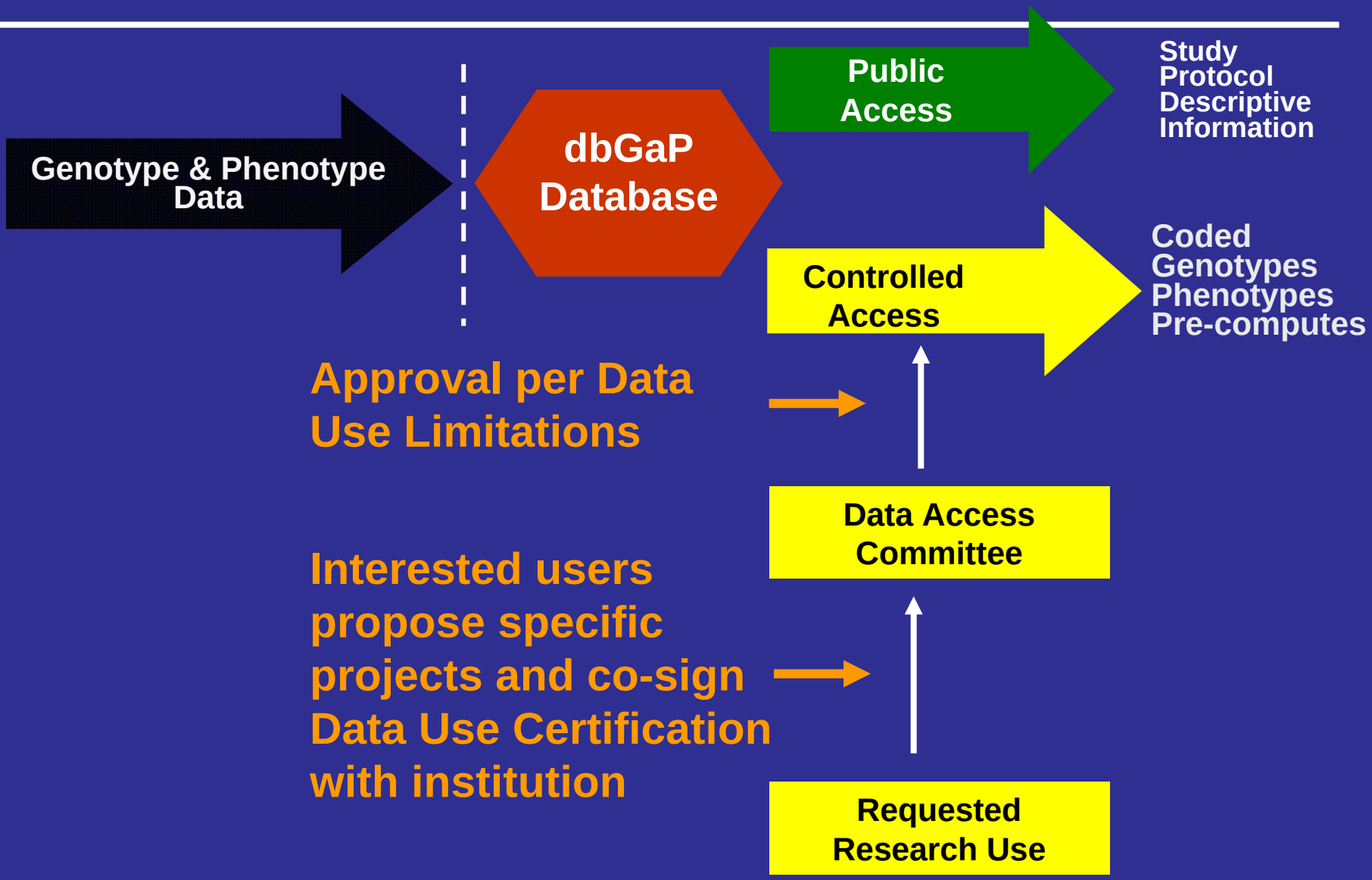
- Can consents for earlier studies ever be adequate for an open access model?
- Is re-consent really practical?
- Local IRB issue
  - Guidance in this area is not entirely clear and issues are evolving
- What if a waiver was issued for genetics research?

Policy Strategies

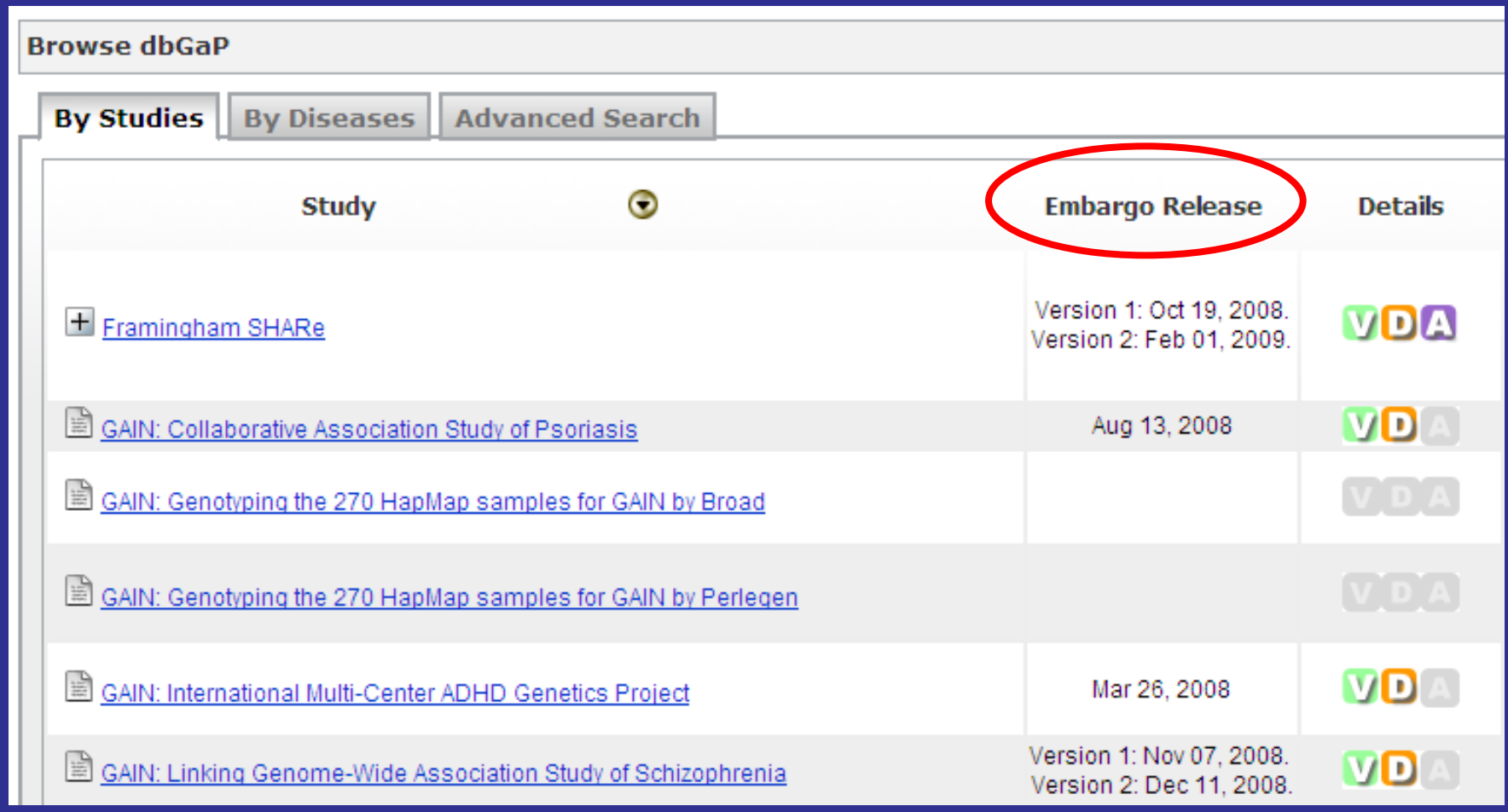
Effecting goals – Data access

- Immediate and unfettered access to all qualified users provides maximum opportunity for scientific progress
- But … should protect confidentiality of research participants and respect consent provisions
- … should recognize need of investigators for academic recognition
- and…should preserve basic knowledge for full range of downstream development possibilities

Data Access


Genotype & Phenotype Data
dbGaP Database
Public Access
Study Protocol Descriptive Information
Controlled Access
Coded Genotypes Phenotypes Pre-computes
Approval per Data Use Limitations
Data Access Committee
Interested users propose specific projects and co-sign Data Use Certification with institution
Requested Research Use

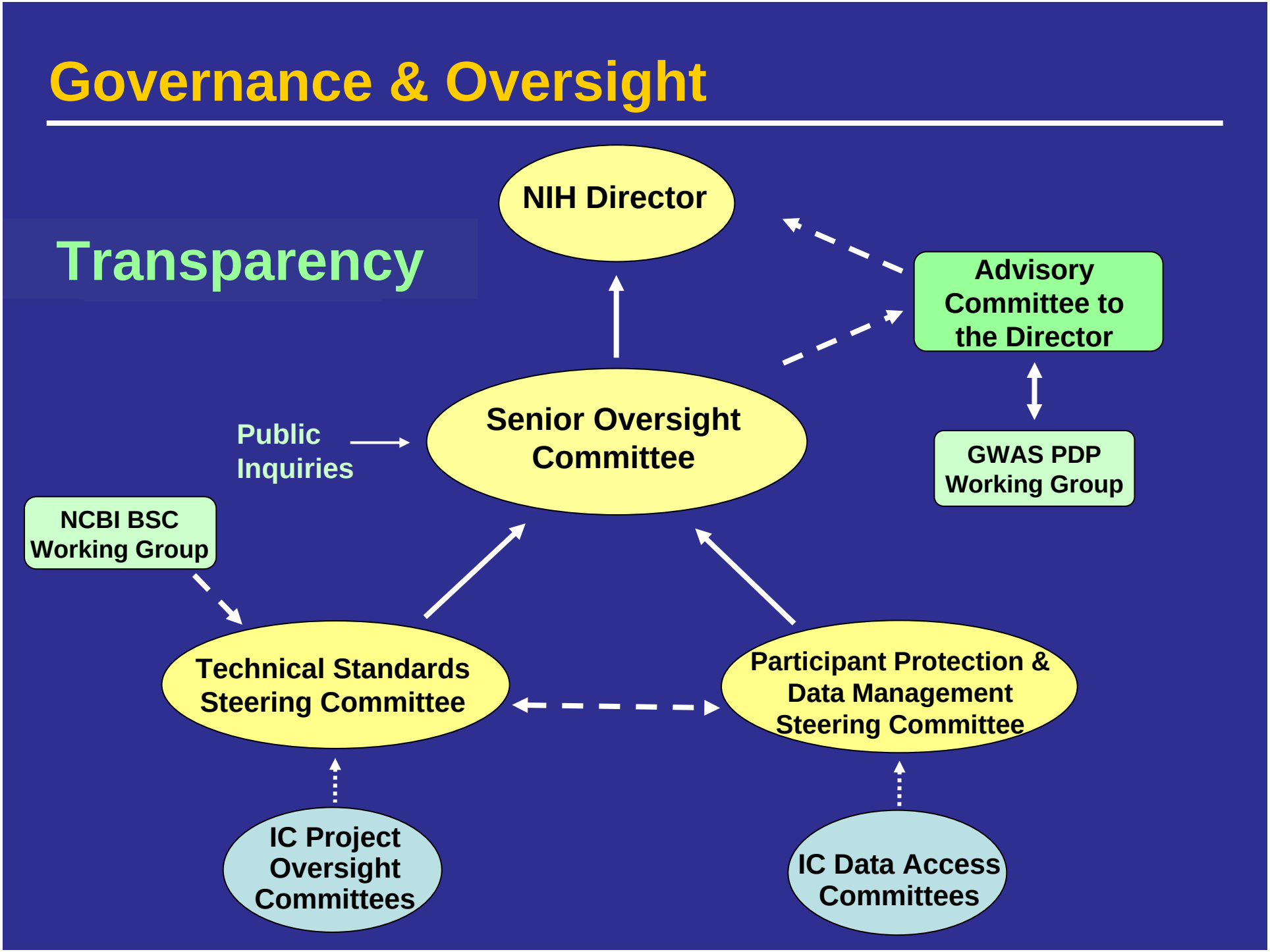
Scientific Concern: Publication



Intellectual Property

- Consensus is that GWAS data should be pre-competitive for use by all
  - Automated calculations to identify first round genetic associations are made available through dbGaP
- NIH urges that associations remain available to all investigators & discourages premature claims
  - Encourage broad use consistent with NIH's Best Practices for Licensing with Genomic Inventions.

Governance & Oversight



Acknowledgements – GWAS AdHoc Working Group

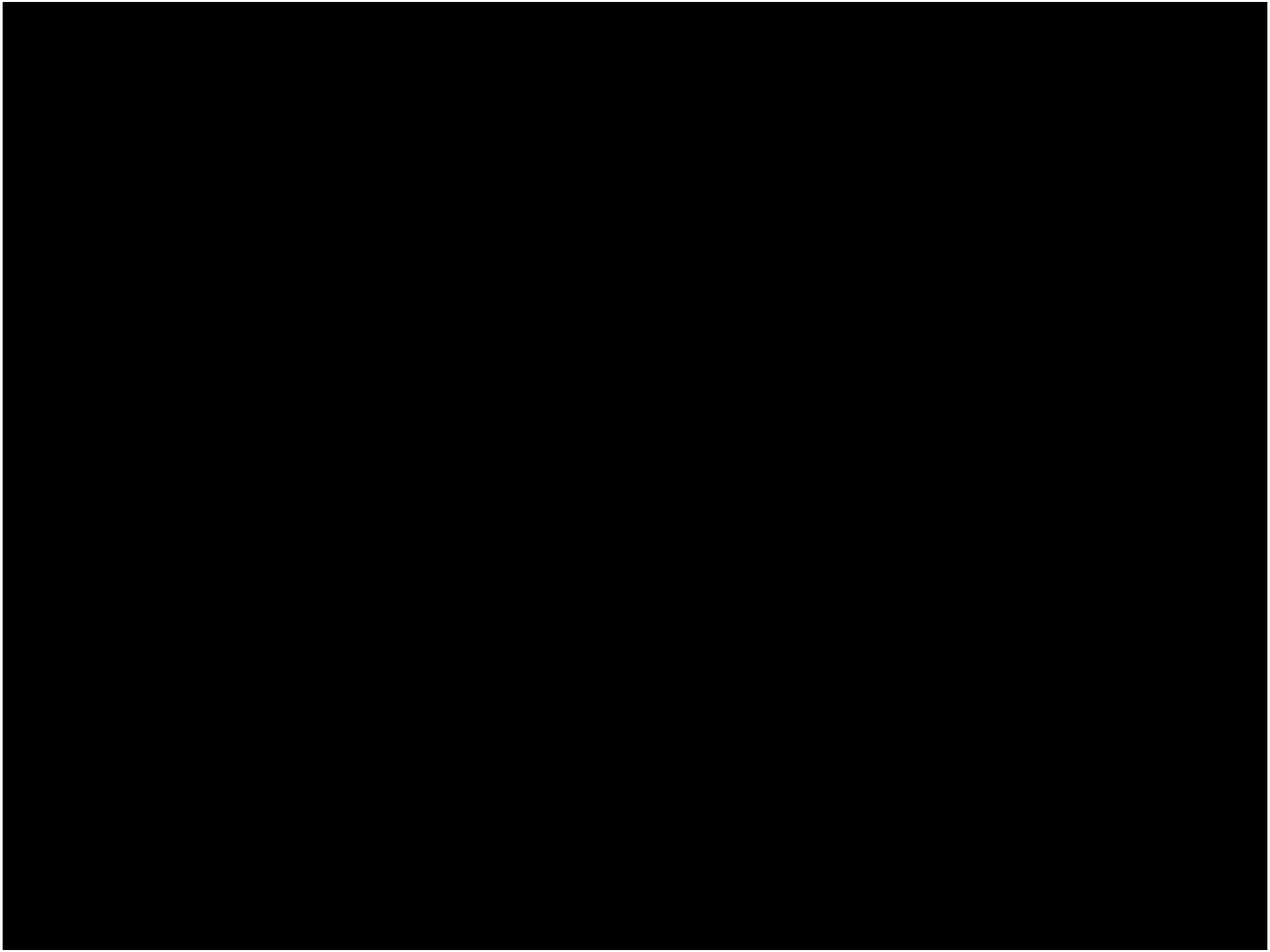
Elizabeth Nabel - Chair
Susan Shurin
Carl Roth
Christopher O'Donnell
Richard Fabsitz
Barbara McGarey
Valerie Bonham
Annette Levey
Lauren Higgins
Don Schneider
Stephen Chanock
Deborah Winn
Daniela Gerhard
Robert Hoover
Daniela Seminara
Maria Giovanni
William Sharrock
John Ilekis
Jeff Evans

Francis Collins
Laura Rodriguez
Mark Guyer
Teri Manolio
Lisa Brooks
Jean McEwen
Elizabeth Thomson
Jerome Wilson
Katrina Gwinn
Hemin Chin
James Battey
Jerome Wilson
Anthony Hayward
Elaine Collier
Zhaoxia Ren
Thomas Hart
Vivian Ota Wang
Marin Allen
Catherine McKeon

Lana Skirboll
Marianna Bledsoe
Amy Patterson
Sarah Carr
Norka Ruiz-Bravo
Valery Gordon
JP Kim
Sam Shekar
David Lipman
James Ostell
Steve Sherry
Alan Graeff
Michael Gottesman
Jerry Menikoff
Charlotte Holden
Jonathan Pollock
Steven Kleeberger
Charlene Cho
Thomas Lehner
Melinda Tinkle

GWAS Policy Implementation Committee

Sally Amero (OER)
Christopher Beisel (NIAID)
Amy Bielski (OER)
Marianna Bledsoe (OSP)
Valerie Bonham (HHS)
Carlos Caban (OER)
Sarah Carr (OSP)
Joe Ellis (OER)
Suzanne Fisher (CSR)
Ellen Gadbois (OSP)
Emily Harris (NHGRI)
Charlotte Holden (OIR)
Janelle Jobe (OER)
John (JP) Kim (OER)
Teresa Marquette (NHLBI)
David Maslow (NCI)
Jerry Menikoff (OIR)
Stephen Mockrin (NHLBI)
Jim Ostell (NCBI)
Dina Paltoo (NHLBI)
Tracy Rankin (NICHD)
Laura Rodriguez (NHGRI)
Carl Roth (NHLBI)
Denise Russo (OER)
Chuck Selden (OER)
Sam S Shekar (OER)
Susan Shurin (NHLBI)
Michael Small (NCI)
Carol Wigglesworth (OER)



Returning results -- issues

- Many research projects are predicated on never returning genetic results
- But, if samples are not irreversibly anonymized, and information of compelling clinical utility is discovered, is it ethical not to provide that?
- What should be the threshold for disclosure?
- How can CLIA standards be maintained?
- Who provides counseling?
- Who pays?

Data Use Certification Agreement

- Access requests will stipulate through DUCs that requestors:
  - are responsible for compliance with federal, state, and local policies
  - will only use the data for the specified research use
  - will not identify study participants
  - will not transfer data
  - will immediately notify the DAC if a security breach occurs
  - will submit brief annual updates on research progress and publications
  - will be identified within the dbGaP as an Approved User of dbGaP data and their approved research use statement will be posted
  - acknowledge GWAS policies on Publication and Intellectual Property

Identifiers Excluded from GWAS Datasets

- Names
- Phone numbers
- Fax numbers
- Electronic mail addresses
- Social security numbers
- Medical record numbers
- Health plan beneficiary numbers
- Account numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate numbers
- Device identifiers and serial numbers
- Web universal resource locators (URLs)
- Internet protocol (IP) address numbers
- Biometric identifiers, including finger and voice prints
- Full face photographic images and any comparable images
- Geographic subdivision
- Dates
- “Other" identifiers (e.g., outliers)

GWAS Policy Solutions

Data Collection

Submission & Management of Data

Distribution & Secondary Use of Data

Research Participants

Informed Consent

Submitting Investigators

Identifying information removed, replaced with random unique code

GAIN Database

Data Access Request for Coded data

Recipient Investigators

GWAS Timeline