

Update on GWAS Policy Implementation and ACD Recommendations

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Advisory Committee to the Director,

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NATIONAL INSTITUTES OF HEALTH



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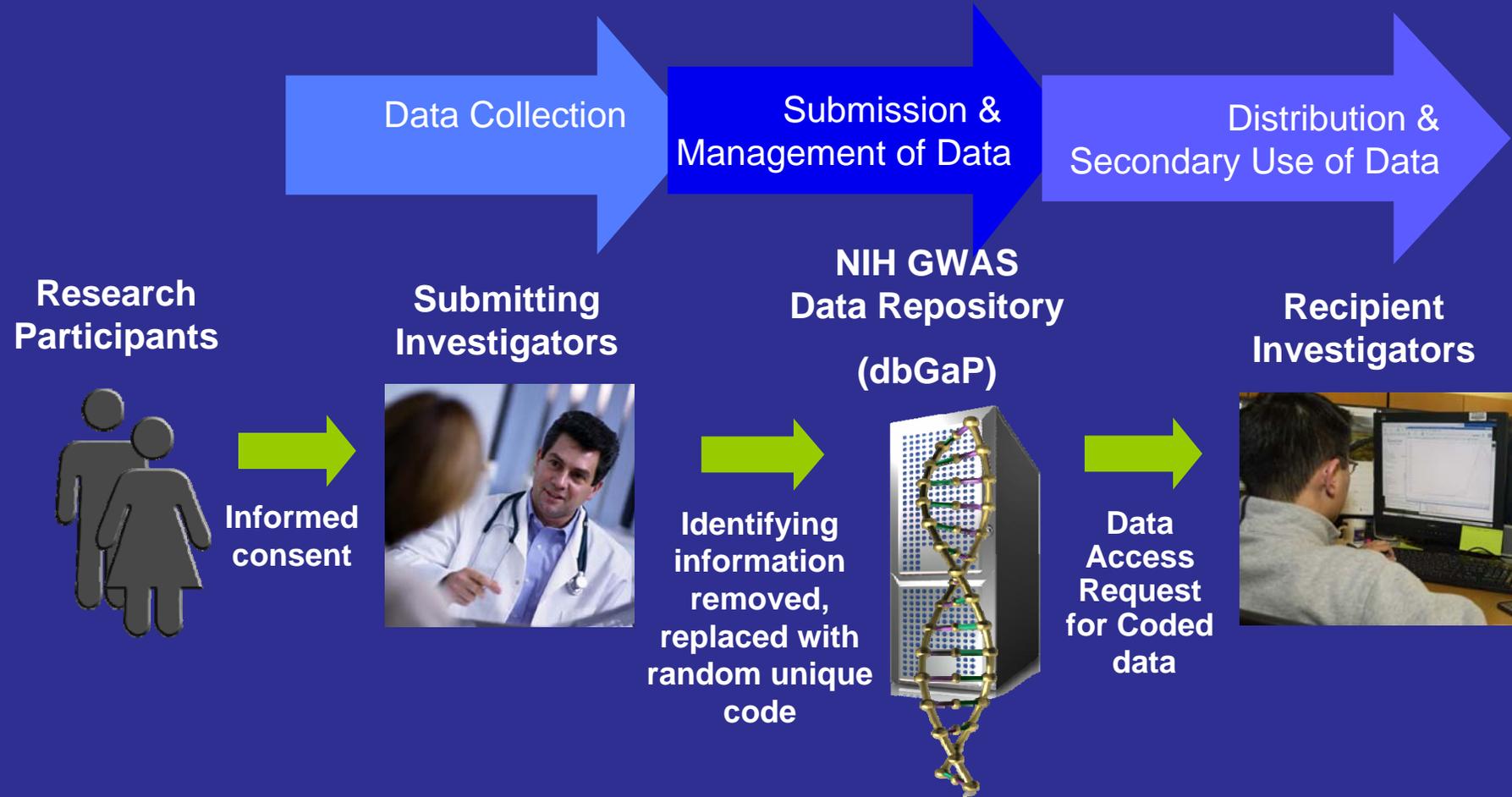
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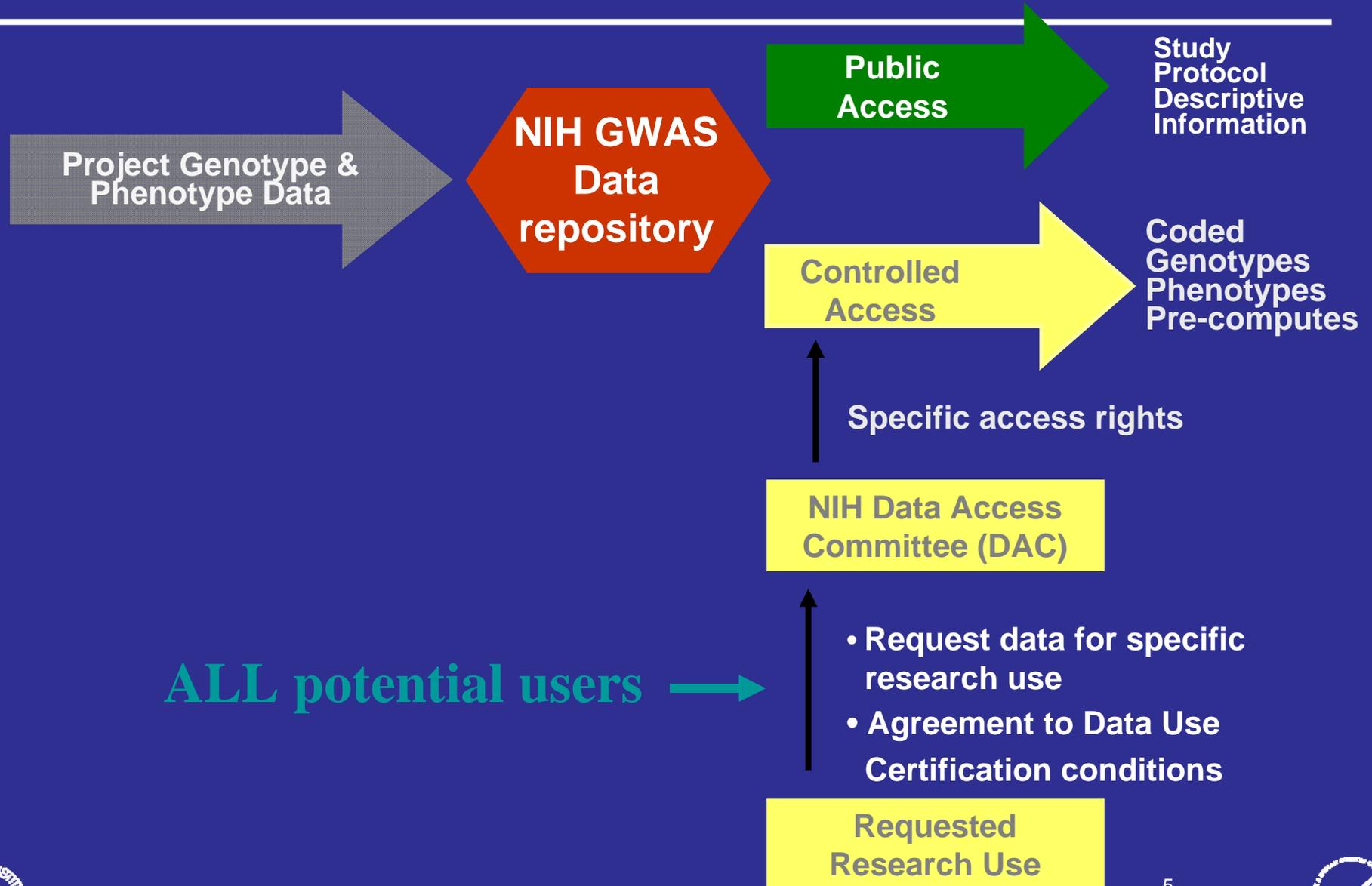
NIH GWAS Policy

- Goal is to advance genome-wide association studies (GWAS) to identify common genetic factors that influence health and disease
- Promotes the sharing of GWAS data via a central repository at the NIH (dbGaP)
- Policy outlines
 - Data submission procedures
 - Data access principles
 - Protection of research participants
 - Scientific publication
 - Intellectual property

GWAS Data Management Overview



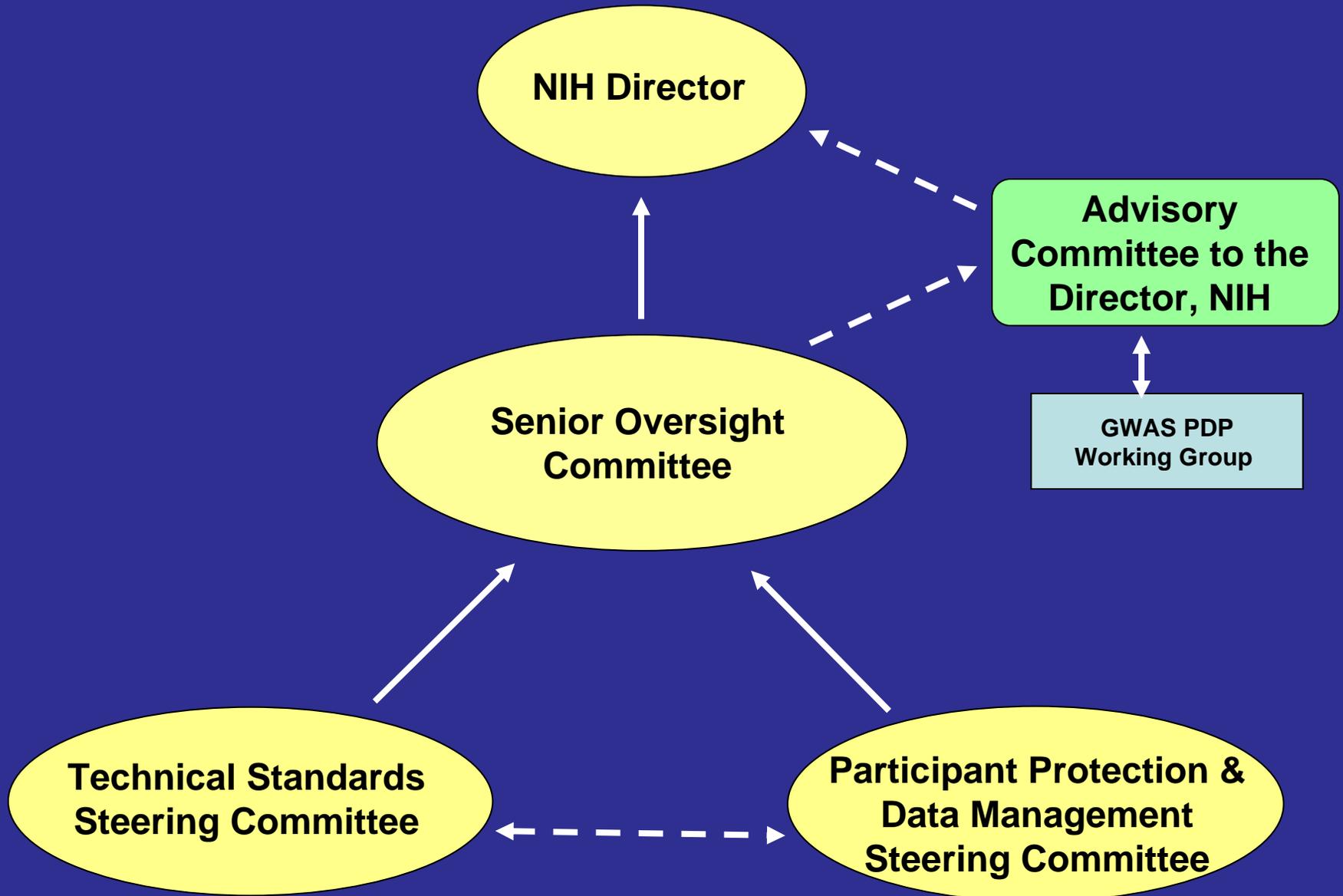
Data Access Overview



Function of DACs

- Reviews requests for GWAS data to assure appropriate use
 - By determining whether the proposed use is consistent with the uses identified by the submitting institution
- Provides ongoing monitoring via reviews of annual reports from approved data users

NIH GWAS Oversight Structure



Submissions to dbGaP as of 5/08

Studies Available in dbGaP with Individual Level Data = 15

	<i>N</i>	<i>Study Type</i>
Framingham SHARe	14261	Longitudinal, family-based cohort
GAW16 Framingham and simulated data	7130	Framingham study subset of data + simulated phenotypes
GAIN ADHD	2835	Parent-offspring trios
GAIN Psoriasis	2875	Case-control
GAIN Schizophrenia	5066	Case-control
GAIN Major Depression	3741	Case-control
GAIN Diabetic Nephropathy	1825	Case-control
GAIN Bipolar Disorder	3261	Case-control
Mayo-Perlegen LEAPS (Parkinson's Disease)	1550	Case-control
NEI Age-Related Eye Disease Study (AREDS)	600	Case-control
NINDS Parkinson's Disease	535	Case-control
NINDS Parkinsonism Study	1283	Case-set
NINDS Neurologically Normal Control Collection	2723	Control-set
GAIN HapMap genotypes (Affy 5.0, 6.0)	270	Parent-offspring trios from HapMap samples
GAIN HapMap genotypes (Perlegen 1M)	270	Parent-offspring trios from HapMap samples

Studies Available in dbGaP with Summary Measures & Analysis Only

Diabetes (FUSION) study	2335 *	Case-control – summary measures & analysis only
Systemic Lupus Erythematosus	4678 *	Case-control – summary measures & analysis only
Genome-wide Association Study of Neuroblastoma	780 *	Case-control – summary measures & analysis only

Studies in Process for Release

Irish Amyotrophic Lateral Sclerosis (SIALS)	432	Case-control (in process for release)
Ischemic Stroke Genetics Study (ISGS)	219	Case-control (in process for release)
CIDR – Parkinson's Disease	1991	Case-control (in process for release)
NINDS Cerebrovascular Disease/Stroke Study	870	Case-set (in process for release)

* No individual level data is provided for these 3 studies because of informed consent restrictions on data release



New Submissions to dbGaP expected by 12/2008

Family-Based Studies

	<i>N</i>	<i>Study Type</i>
SHARe Asthma CAMP	1000	Longitudinal, affecteds
SHARe Asthma CARE	2100	Longitudinal, trios
GEI Lung Cancer	6192	Longitudinal
EDIC/DCCT	4037	Longitudinal

Case-Control Studies

SHARe Asthma ACRN	800	Case-Control
NINDS ALS	547	Case-Control
NINDS IBD	1912	Case-Control
NINDS MS	2000	Case-Control
CIDR COGA (Alcohol Addiction)	2180	Case-Control
CIDR Age-Related Maculopathy	2750	Case-Control
CIDR Bone Fragility	1700	Population Continuous
GEI Addiction	5500	Case-Control

Investigator Interest in dbGaP Data as of 5/08

Number who have logged into at least one dataset = 410

Number who have submitted at least one data request = 251

Number with at least one DAC approved data request = 164

Number who have downloaded data = 124

Requests for dbGaP data as of 5/08

- DAC-approved projects (data downloaded) = 224
- DAC-approved projects (data not downloaded) = 184
- Projects awaiting DAC approval = 88
- Projects awaiting SO approval = 65
- Disapproved projects = 100
- Projects started but not completed = 120



Inadvertent Data Releases

- Software problems resulted in two releases:
 - GAIN Dataset
 - Approved user able to access datasets for a “consent group” for which he did not have approval
 - User directed not to use data until approval was obtained
 - Framingham SHARe Dataset
 - Disapproval decision recorded as an approval decision, enabling an unapproved user to download a dataset
 - User directed to destroy data and any derivative research work products

Inadvertent Data Releases

- Caused by software problems, not deliberate efforts to obtain unauthorized access to data.
- NCBI's response:
 - corrected problems,
 - conducted an extensive review to ensure there were no other problems, and
 - added more automated checks.
- Recipient investigators were responsive to agency directions. They both subsequently sought and were granted approval for access to the datasets.
- ACD PDP WG was briefed and concluded that NIH's response was adequate and appropriate.

NIH's Response to ACD Recommendations on GWAS Policy

- ACD Recommendations from December 2007 accepted by NIH Director
- Recommendation 1:
 - *the NIH Director should seek an Exemption 3 statute and other means to enhance legal safeguards to protect the privacy of individual genotype-phenotype data held by the Federal government*

NIH's Response to ACD Recommendations on GWAS Policy

- **Response to Recommendation 1:**
 - NIH Office of Legislative Policy and Analysis (OLPA) developing proposal for Exemption #3 statute
 - Office of General Counsel is reviewing current laws (Privacy Act, FOI and 301(d) of the Public Health Service Act)

NIH's Response to ACD Recommendations on GWAS Policy

■ Recommendation 2:

- *NIH should develop a strategy for disseminating information about GWAS to study participants, including information about the purpose of the GWAS repository, the types of genetic studies being carried out with GWAS data, the nature of the findings resulting from those studies, and the potential risks and benefits of broad data sharing. It is also important for NIH to develop a better understanding about the different ways in which such information will be received by participants and to design its dissemination strategy accordingly. In addition, the general public would also benefit from a better understanding of the value of GAIN and GWAS and their unique roles in advancing knowledge of the genetic basis of common diseases.*

NIH's Response to ACD Recommendations on GWAS Policy

■ Response to Recommendation 2:

- Participant and Data Management Steering Committee (PPDM) is developing a strategy for the provision of information to participants about NIH GWAS
- Trans-NIH Communications Group on Genetics and Common Disease is developing a communication plan to inform and educate the public about genetics of common disease

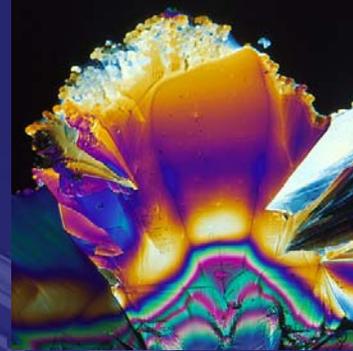
NIH's Response to ACD Recommendations on GWAS Policy

■ Recommendation 3:

- *A system should be developed to ensure that inquiries from investigators, study participants, and members of the general public about dbGaP are addressed in a thorough and timely way.*

NIH's Response to ACD Recommendations on GWAS Policy

- **Response to Recommendation 3:**
 - A mechanism has been established for responding promptly to public inquiries that uses the GWAS website mailbox as a portal



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