NHANES Genetics Program Status and BSC Assistance

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Health Statistics

Presentation Objectives

- Recap NHANES Genetics Program Issues
- Updates
  - NHANES Genetics Program Changes - ERB approval received
  - Program Timelines for Issues to Address
  - Binning Milestones/Framework for Moving Forward
- Recap Charge to BSC from September 2011

NHANES Genetic Consent 2009-2010

- **The NHANES program will not contact you or your family with results from these future studies. We will describe the completed studies on our website. If you are interested in your results from any of these studies, you may call our toll-free number to request your specific results as they become available.**
- **Check a box:**
  - I agree that my blood may be kept for future studies using my genes to help understand genetic links to medical conditions, and that I will not be contacted with the results from these studies.
  - I disagree

Summary of NHANES Genetic Consent Parameters

NHANES consent for collection of DNA specimens varied slightly between surveys

	Age	Separate DNA consent	Opt-out later	Notice of DNA studies	Plan to contact with results
NH III	**12+**	**no**	**no**	**none**	_
99-02	**20+**	**yes**	**yes**	**Newsletter phone**	**no**
07-08	**20+**	**yes**	**yes**	**website**	**no**
09-10	**20+**	**yes**	**yes**	**website**	**no**
11-12	**20+**	**yes**	**yes**	**website**	**no**

All consent forms state

All health data will be kept strictly private

No identifying information may be released

Under penalty of law [Section 308(d) of the Public Health Service Act (42USC242m) and the Privacy Act of 1974]

Relevant Advances in Genetics

- With genetic technology advances, and analytic changes from candidate gene approaches to multiple SNP arrays, there is an increased potential for identifying incidental clinically relevant findings.

- These advances have led to changes in medical ethics guidance on reporting results of genetic tests on bio-banked specimens (blanket non-disclosure is not appropriate).

NHANES Genetics Program Main Issues

- ETHICAL considerations (Report of Findings) linked to
- CONSENT and stored specimens

NHANES must now address Report of Findings from genetic testing in the context of NHANES genetic consents (previously stating no plan to re-contact with genetic results), and stored specimens going back 20 years

May 2011 NHANES Genetics Program Workshop Highlights

- **Panel of experts**
  - intra/extra mural experts
  - geneticists/bioethicists
- **What results should be reported back – are standards or guidelines available?**
- **How to determine and operationalize criteria for clinically relevant genetic findings with a dire duty to warn threshold?**
- **Who determines ROF threshold?**
- **How/When to report back?**

What results should be reported back

Dire duty to warn =

clinical utility (clinically valid (relevant) + actionable)

+ serious condition ('significant implications'; 'very important to health'; 'substantial')

Supported by several current genetics research best practices and publications

How to determine and operationalize criteria for clinically relevant genetic findings with a dire duty to warn threshold?

Categorizing Potential Genetic Results

Binning by Loci - Berg. *Genetics in Medicine* (2011)

Bin 3 - genes of unknown clinical implication

Bin 2 - variants within genes that are clinically valid but not directly actionable

Bin 1 - variants within genes that have direct clinical utility based on professional organization diagnosis and treatment guidelines

Only Bin 1 variants should be considered for reporting

Who Makes the Call on Binning the Genome?

Proposed mechanism - the Evaluation of Genomic Applications in Practice and Prevention (EGAPP)
www.egappreviews.org

Independent, nonfederal multidisciplinary expert panel charged with developing systematic, evidence-based processes for evaluating genetic tests and other applications of genomic technology

Iterative, centralized, consensus driven process

Unclear whether all Bin 1 will be reportable in NHANES dire duty to warn context

Who Makes the Call on Dire Duty to Warn?

- Medically actionable Bin1 variants that rise to the level of dire duty to warn
- Proposed Advisory Board Composition
  - Genetic clinicians
  - Research scientists
  - Bioethicists
  - Genetic epidemiologists

How/When to Disclose

One-time re-contact to inform of consent changes re: reporting back results

- anticipate low likelihood of need to report back

- Opt-out option for future re-contact

- Opt-in participants

  - encouraged to keep NHANES informed of their current contact info

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NHANES Genetics Program Updates

NHANES Genetics Program protocol changes made incorporating these options to address report of findings (ROF) issues

- ERB approval received December 2011
- Genetics Program protocol ‘unsuspended’,

However, until Binning and Dire Duty to Warn plan implemented

- New multiple SNP array proposals cannot be accepted (Fed Register Notice through 12/2012), AND
- Analyses using Affymetrix Genome–Wide Human SNP Array 6.0 chip on hold

Program Timelines for Addressing ROF Issues

Spring 2012

- One-time re-contact to inform participants of consent changes re: reporting back results
- QA/QC of Affymetrix Genome –Wide Human SNP Array 6.0 chip data

June 2012

- 2013 Genetics Consent changes finalized

Then, dependent on implementation of Binning and Dire Duty to Warn plan:

September 2012

- Develop 2013 Genetics Program Federal Register Notice allowing clinically relevant research on genetic specimens
- NHANES runs initial Bin 1 list against Affymetrix Genome –Wide Human SNP Array 6.0 chip data

Binning Milestones/Framework for Moving Forward

December 2011

- NHGRI U01 grants awarded based on *Binning by Loci:* Berg. *Genetics in Medicine* (2011)

May 2012

- Need BSC Recommendations for any 2013 NHANES Genetics Consent changes
- EGAPP draft report describing methods for binning

Summer 2012

- BSC subcommittee review of initial Bin 1 list

Recap Charge to BSC from 9/2011

- Moving forward, should DHANES change genetics consent to report back genetics results?
- Is binning the genome a good response for NHANES re: initial guidelines for what to report back?
- Who should make the determination of which Bin 1 findings meet dire duty to warn criteria for NHANES setting
  - ? subcommittee of BSC as FACA;
  - ? NCHS technical working group (cannot serve in advisory capacity);
  - ? other
- Can we apply this model to all surplus biologic specimen projects (re: reporting back dire duty to warn findings)?

Thank You

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