

Regulatory Guidance for Genetic Testing

Three Specific Areas

- Laboratory tests
- Results of genetic testing
 - Clinical
 - Research
- GenomeWide Association Studies (GWAS)

FDA Guidance – Laboratory Tests

- Non-binding guidance for pharmacogenetic tests and genetic tests for heritable markers issued by
 - Center for Devices and Radiological Health (CDRH)
 - Center for Drug Evaluation and Research (CDER)
 - Center for Biologics Evaluation and Research (CBER)

Why Regulate Tests?

- Unregulated tests may
 - identify stigmatizing diseases
 - substantially affect family members
 - identify disorder for which there is no treatment or action
 - be difficult or impossible for clinician to interpret
 - provide misleading information (much controversy over direct-to-consumer genetic testing)

Applications to FDA for Pre-market approval and pre-market notification 510(k)

- Intended use
- Indications for use (predictive, prognostic, Rx response, drug sensitivity)
- Methodology
- Technical interpretation of results (e.g., variant allele)
- Quality control
- Clinical validity
- Clinical interpretation
- Benefits and risks
- Claims of effectiveness

Oversight of Genetic Testing

- Centers for Medicare and Medicaid Services (CMS) - Clinical lab oversight
 - Education requirements for technicians
 - Quality control of lab processes and proficiency testing
- FDA
 - Test kit approval
- Federal Trade Commission
 - False and misleading advertising

Types of Genetic Tests

- Newborn Screening
- Diagnostic
- Carrier
- Prenatal diagnosis
- Pre-implantation screening
- **Predictive and Pre-symptomatic**
- Forensic

Predictive and Pre-symptomatic Tests

- Pharmacogenetic
- Disease-associated genes or arrays of genes

IRB evaluation of the information to be shared and with whom. No requirement for investigator to provide counseling or delve into any downstream areas such as notification of relatives of treating physician.

Consent should indicate results strictly related to the research and that results have no impact on diagnosis or clinical care.

GenomeWide Association Studies (GWAS)

- 2008 NIH policy established database of genotypes and phenotypes in order to identify gene associations with diseases or other observable traits.
- Open access to public – for submission of data
- Controlled access available to researchers with NIH grants for study of genome-wide analysis of specimens – typically studies looking at 100,000 or more SNP markers that are being analyzed.

GWAS – IRB Considerations

- For submission of information to GWAS
 - Specimens and data were or will be collected in compliance with 45 CFR 46 (human subjects protection regulations)
 - All the information to be submitted meets the HIPAA standard for de-identification which requires minimizing risks to study participants by removing the 18 identifiers (HIPAA) and coding using a random, unique code
 - GWAS studies of these data do not pose any risks (e.g., stigmatization) to particular populations or groups

GWAS – submitting samples collected in previously IRB-approved studies

- Do any of the consent forms contain statements such as “your data/specimens will not be shared” or “will only be seen by the research team?”
- Were any of the specimen donors minors?
- Did the original consent forms limit future use to specific projects or disease states, or to non-commercial research?
- Were any of the data (e.g., medical record information) collected under a waiver of consent?

If any of the above may need re-consent or new consent.

The Genetic Information Nondiscrimination Act (GINA, 2009)

- makes it illegal to
 - make decisions about health insurance coverage or eligibility
 - make decisions about hiring, promoting, and other terms of employment