Oversight of Genetic Testing

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Statement of Director Kathy Hudson regarding announced resignation of NHGRI's Francis Collins
It is no coincidence that Francis Collins's tenure at the National Human Genome Research Institute marked one of the most extraordinary periods in modern science.

President Bush signs long-awaited Genetic Information Nondiscrimination Act
Signed into law today, GINA provides vital protection for Americans against the misuse of genetic test results by health insurers and employers.

Center to hold personal genomics seminar June 10
The seminar, "The Molecular Full Monty: Personal Genomes, Personal Health," will take place at the National Press Club at...
Mission

• The Center works to help policy leaders, decision makers, and the public better understand the rapidly evolving field of human genetics and its application to healthcare. . . . To inform genetic policy decisions, the Center surveys public attitudes about genetics issues, conducts analyses of the existing regulatory landscape, monitors the transition of genetic applications into clinical practice, and posits options and likely outcomes of key genetics policies.
Goals of Regulation

- Protect the public
- Foster innovation
- Create uniform rules to prevent market inequalities ("level playing field")
Mechanisms of Regulation

• Many “tools” in the toolbox
• The right “tool” depends on the problem one is trying to fix or prevent, or the good one is trying to maintain or achieve
Tools of Regulation

- Statute
- Regulation
- Incentives/Penalties (e.g., taxes, subsidies)
- Tort law
- Private mechanisms (e.g., professional societies)
Goals of Genetic Testing Oversight

1. High quality laboratory testing
2. Clinically valid tests
3. Truthful, non-misleading claims about test benefits and limitations
4. Continued development of new tests
5. Appropriate and timely translation into clinical practice

Public confidence
Challenges to Oversight of Genetic Tests

• Rapidly moving technology
  - tests for more than 1500 diseases
Challenges to Oversight of Genetic Tests

• Old laws, new situations
  • need for continued updating of regulations to respond to new technologies
  • the laws may not “fit” the new context neatly
Challenges to Oversight of Genetic Tests

- Prospective v. reactive
- Many government actors potentially involved
Federal Oversight

Department of Health & Human Services

- Food & Drug Administration: Regulates drugs, devices, biological products, human tissue
- Centers for Disease Control & Prevention
- Centers for Medicare & Medicaid Services: Certification of clinical laboratories, personnel standards, QA/QC, proficiency testing

Advice
CLIA

Definition of a Clinical Laboratory:

A laboratory that examines materials "derived from the human body" in order to provide "information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings."
Components of Laboratory Oversight

- Certification
- Inspection
- General requirements relating to QC, personnel, documentation, etc.
- More specific and tailored requirements for laboratories performing “high complexity” tests are set forth through the creation of “specialty areas”
CLIA and Genetic Tests

- Law passed in 1988, regulations implemented in 1992
- Not specific to genetic tests
- Need to ensure that laboratory requirements appropriately include genetic testing laboratories
  - Proficiency testing
- Need to ensure that public has necessary information about laboratory quality
FD&C Act

• Gives FDA authority to approve pharmaceuticals and medical devices before they are marketed
FDA and Genetic Tests

• Regulatory status of genetic tests depends on how the laboratory develops and performs the test
  • Test kit/test system = regulation as medical device
  • Laboratory-developed = no FDA regulation

• Most genetic tests are laboratory developed

• Most genetic tests not required to demonstrate clinical validation
IVDMIA Draft Guidance
(July 2007)

- Defines new category of laboratory test -- “in vitro diagnostic multivariate index assays”
- Hallmarks of IVDMIAs
  - measure multiple analytes simultaneously (e.g., multiple gene or gene expression products)
  - use proprietary algorithm to calculate patient-specific result
  - provide result that cannot be independently interpreted by physician
- Require premarket clearance/premarket review by FDA
- Must demonstrate analytic and clinical performance of test
Challenges to Oversight of Genetic Tests
Meanwhile, on the Internet…

- Fetal Gender
- Inherited Complex Disorders
- Pharma
- Complex Disorders
- Paternity
- Nutrition
- Athletic perf.
- Complex Conditions
- Ancestry
- Skin care
- Recreational
- Infidelity
- Infertility
## Companies offering health-related tests DTC

| Genetic Testing Company | Personal Genome Service | Addiction | Alzheimer | Asthma | Cystic Fibrosis | Celiac Disease | Bipolar/Depression | Cardiovascular Disease | Cancer | Fetal Gender | Fragile X Syndrome | Gaucher Disease | General Nutrition | Glaucoma/AMD | Gynecological Diseases | Hair Loss | Hemochromatosis | HIV/Herpes | Inflation | Metabolic Health | Nephropathy | Neurofibromatosis | Osteoporosis | Perinatal Disease | Recurrent Pregnancy Loss | Scoliosis | Sleep Apnea | Food Intolerance | Type 1/2 Diabetes | Thrombosis |
|-------------------------|-------------------------|-----------|-----------|--------|----------------|----------------|-------------------|----------------------|--------|--------------|----------------------|----------------|------------------|-------------|------------------------|--------------|-----------------|-------------|---------------|------------------|----------------|----------------|-----------------|----------------|----------------|------------------|-----------------|----------------|
| 23andMe                 | X                       | X         |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Acu-gen Diolabs        |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Consumer Genetics      |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Cygine Direct          |                         | X         |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| DeCODE                | X                        | X         | X         |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Dermogenetics          |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| DNA Direct             | X                        | X         | X         |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| DNA Tracts             |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| G-nostics              |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| GATC Fintech           |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Genenex                |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Genetwist              |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Graceful Earth         |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Hair DX                |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Health Check USA       |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Health Tests Direct    |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Holistic Heal          |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Knome                  |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| MediCheckers           |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Medigenomics           |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| My Genome              |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Navigenics             |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Preventive Genomics    |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Pysonomics             |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Quasar - Interleukin Genetics |                 |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Saugener - DNA Services of America |   |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Scientific Match       |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Score                  |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| SaugWright             |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Sesorpost              |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| Smart Genetics         |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
| &nacell                |                         |           |           |        |                |                |                   |                      |        |              |                      |                |                  |             |                         |              |                 |             |              |                  |              |                |                |                |                |                  |                |              |                |                |              |              |
July 27, 2006:

Senate Hearing, Special Committee on Aging, “At Home DNA Tests: Marketing Scam or Medical Breakthrough”

GAO Highlights

Tests Purchased from Four Web Sites Mislead Consumers

Why GAO Did This Study

Scientists increasingly believe that most, if not all, diseases have a genetic component. Consequently, genetic testing is becoming an integral part of health care with great potential for future test development and use. Some genetic tests are sold directly to the consumer via the Internet or retail stores, and purported to use genetic information to deliver personalized medical advice.

What GAO Found

The results from all the tests GAO purchased mislead consumers by making predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers. Although there are numerous disclaimers indicating that the tests are not intended to diagnose disease, all 14 results predict that the fictitious consumers are at risk for developing a range of conditions, as shown in the figure below. However, although some types of diseases, such as cystic fibrosis, can be definitively diagnosed by looking at certain genes, the experts GAO spoke with said that the medical predictions in the tests results can not be medically proven at this time.
“The results from all the tests GAO purchased mislead consumers by making predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers.”

“…some of these tests lack scientific validity, and others provide medical results that are meaningful only in the context of a full medical evaluation.”
State DTC Testing Statutes and Regulations

DTC Permitted
Limited
DTC Not Permitted

ACMG Statement on DTC

April 7. 2008

– A knowledgeable professional should be involved in the process of ordering and interpreting a genetic test.

– The consumer should be fully informed regarding what the test can and cannot say about his or her health.

– The scientific evidence on which a test is based should be clearly stated.

– The clinical laboratory must be accredited by CLIA, the state and/or other applicable accrediting agencies.

– Privacy concerns must be addressed.
1. DTC companies should provide accurate information

2. Government actors should provide adequate oversight

3. Not all tests the same – DTC may be appropriate for some but not others

Pharmacogenetics: The Promise

↑Safety
↑Effectiveness
↓Cost
= Better patient care
Pharmacogenetics: The reality

A few examples:

• Her2/neu and Herceptin
  - Only “co-developed” drug and test
• UGT1A1 and Irinotecan
• EGFR and Iressa
• HLA B and Abacavir
• CYP450 and Warfarin???????
Prerequisites for Pgx Success

1. Robust and responsive research enterprise
2. Regulatory system that encourages development of safe and effective tests
3. Mechanism for evidence development and translation to clinical practice
4. Fair reimbursement
5. Safeguards for genetic information

Public confidence
• Policy development is still evolving
• Legislation pending
• Recent recommendations by the SACGHS provide direction for future government activities
The Pew Charitable Trusts