# Clearing a Path for DTC Oversight

*DTC Advisory Meeting of the FDA's Molecular and Clinical Genetics Panel*

Daniel Vorhaus
March 8, 2011

# Permissions / Disclosures

**You are free to**:

Copy, share, adapt, or re-mix;

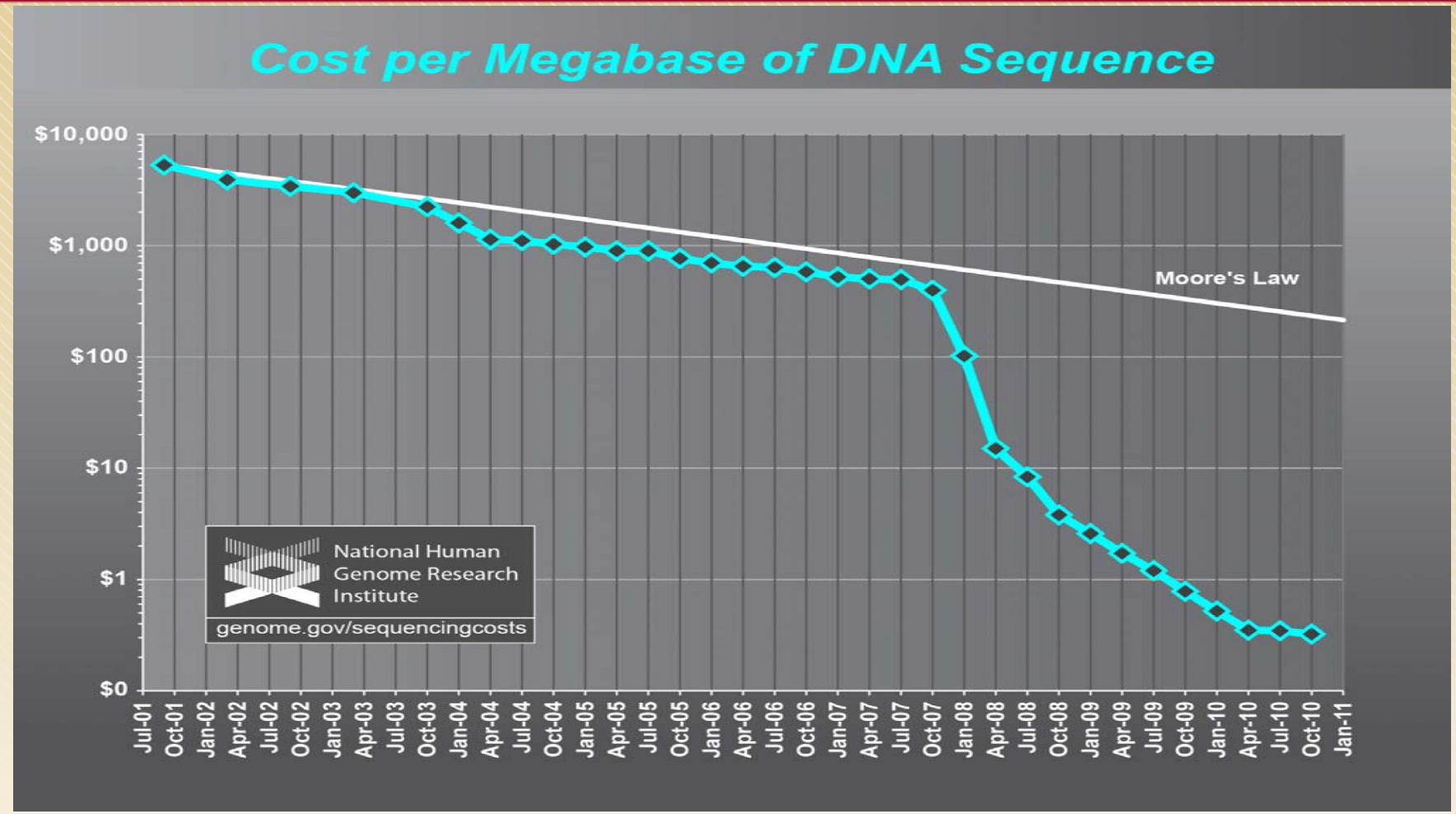
Photograph, film, or broadcast;


Blog, live-blog, or post video of;

**This presentation. Provided that**:

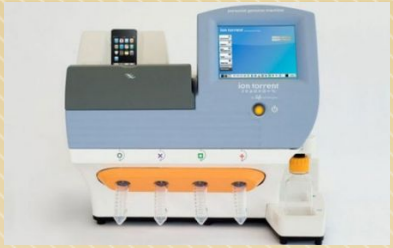
You attribute the work to its author and respect the rights and licenses associated with its components.

# Why we are here: data




Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Large-Scale Genome Sequencing Program Avail. at: www.genome.gov/sequencingcosts. Accessed 3/5/11.

# Why we are *really* here: personal genomics



# Focusing our discussion: FDA + DTC

- **A Narrow Charge**: *"FDA is convening this two-day meeting to seek the Panel's expert opinion and input on scientific issues concerning Direct to Consumer (DTC) genetic tests that make medical claims.*


*This meeting is focused specifically on issues regarding clinical genetic tests that are marketed directly to consumers (DTC clinical genetic tests), where a consumer can order tests and receive test results without the involvement of a clinician." **

- **Simple Math**: clinical genetic test + DTC marketing + no clinician involvement = "issues"

* FDA Executive Summary: Molecular and Clinical Genetics Panel. March 8 & 9, 2011. Available here.

# What could “DTC” mean?

- **Terminological Distractions**: “direct access” vs. “direct-to-consumer” vs. “over-the-counter” vs. “patient-authorized” vs. “home use” ...
- **Substantive Distinctions: for this genetic test, is there “direct”…**
  - Marketing: advertising directed at clinicians, laboratories vs. individual
  - Ordering: initiated by clinician (prescription) vs. individual
  - Payment: out-of-pocket by individual vs. reimbursement (whole or part)
  - Data Interpretation:
    - Provided by: nobody (raw data) vs. software vs. software + clinician (MD or GC?)
    - Included: no (raw data) vs. optional (add’l fee?) vs. mandatory (i.e., gatekeeper)
  - Data Receipt:
    - Type of data: all available data vs. subset (e.g., “clinically actionable”)
    - Recipient: direct to individual vs. by way of clinician (medical record inclusion?)
- **Additional Factors**:
  - Purpose of Testing: clinical vs. research vs. *commercial*
  - Mechanism of Ordering, Data Return: in-person/-store vs. online

# What does "DTC" mean to the FDA?

- **Recall Our Narrow Charge**: *"This meeting is focused specifically on issues regarding **clinical** genetic tests that are (1) **marketed** directly to consumers (DTC clinical genetic tests), where a consumer can (2) **order** tests and (5) **receive** test results **without** the **involvement** of a **clinician**."*

- **Key Additional Factor**: Test *must* be ***clinical*** ("this meeting will not address…DTC genetic tests that do not carry medical claims.")
- **Intentionally excluded?**
  - Identity of *(3) payer*
  - Availability and/or manner of test *(4) interpretation* (or is it merged with data receipt?)
  - *Mechanism* of ordering, data return

| **Test: Start-to-Finish** | **DTC?** |
|---|---|
| (1) Marketing | ✓ |
| (2) Ordering | ✓ |
| (3) Payment | ? |
| (4) Data Interpretation | ? |
| (5) Data Receipt | ✓ |

# The question of the day

## Personal Genomics

⬇

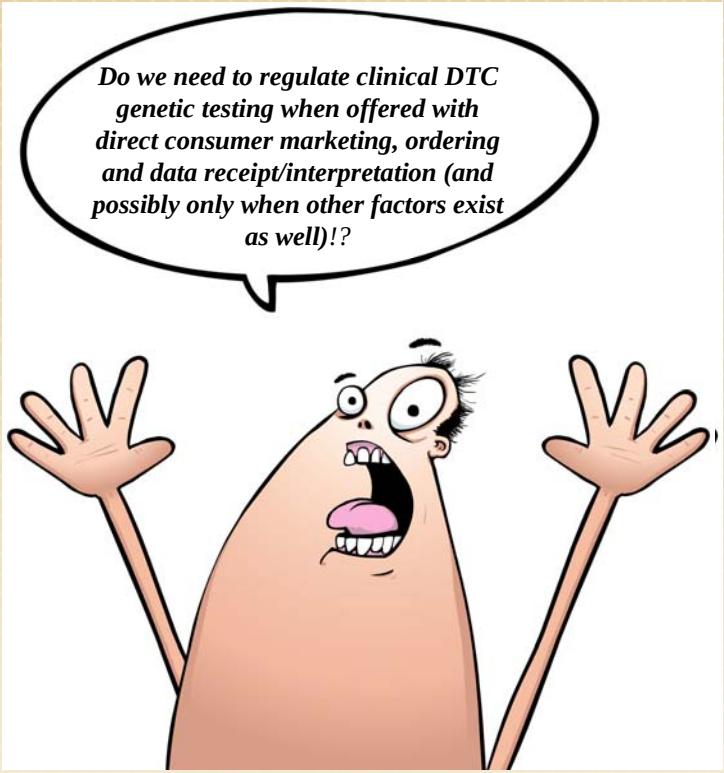
## Genetic Testing

⬇

## *DTC* Genetic Testing

⬇

***Clinical* DTC genetic testing when offered with *direct consumer marketing*, *ordering* and *data receipt/interpretation* (and possibly only when other factors exist as well)**



# Not the questions (at least not today)

- The regulation of any genetic test that's not **both clinical & DTC**, including:
  - Laboratory Developed Tests (LDTs), generally (do DTC count as LDT?)
  - Non-clinical DTC tests (e.g., genealogy, paternity, myredhairgene.com, etc.)

- ELSI issues relevant but not unique to clinical DTC genetic tests, including:
  - Genetic privacy (e.g., DTC privacy policies; de-identification for research)
  - Acceptable uses of genetic data (e.g., PGD or newborn screening; return of research results, incidental or otherwise; patenting genes)
  - Unacceptable uses of genetic data (e.g., GINA/discrimination; surreptitious testing; genetic profiling)
  - Fundamental genetic rights (e.g., the Massachusetts Genetic Bill of Rights; commercial value of a genome)

# The big non-question

- *Does clinical DTC genetic testing need **some** additional oversight?*
- That question has been affirmatively answered, again and again and again, including:
  - 1994: IOM Committee on Assessing Genetic Risks
  - 1997: Joint NIH-DOE HGP ELSI Working Group
  - 2000: SACGT ("Enhancing the Oversight of Genetic Tests")
  - 2006: GAO report, FTC/FDA/CDC consumer fact sheet
  - 2008: SACGHS ("U.S. System of Oversight of Genetic Testing")
  - 2009: DTC self-regulation efforts (PMC, S.B. 482)
  - 2010: Genetic Testing Registry, GAO report
- *Innovation Tension: how do we enhance oversight to ensure public health and safety without stifling innovation in personal genomics and personalized medicine?*

# Questioning today's (and tomorrow's) DTC

- Risks and benefits of current clinical DTC genetic testing model(s). FDA requests "input on the following issues":
  - Pros/cons of testing without clinician involvement (FDA Issue #1)
  - Risks/mitigations for incorrect, misunderstood test results (FDA Issue #2)
  - Appropriate scientific evidentiary standards for testing (FDA Issue #3)

- The *future* of DTC genetic testing model(s) in a climate of pervasive and inexpensive whole-genome sequencing (WGS):
  - Obliterates clinical/non-clinical distinction within a single test (if it is not already gone in current multiplex tests)
  - Divorces data acquisition from interpretation. Spit once and, after that, a browser (and maybe a credit card) is all you need to run a DTC genetic test
  - Geographic barriers significantly reduced, enforcement more difficult

# Common ground in DTC oversight

- Clearer scientific evidentiary standards (FDA issue #3)
  - Clarify standards for demonstrating analytical & clinical validity
- Access to raw genetic / genomic data
  - "Free and open access to genome data has had a profoundly positive effect on progress." (Francis Collins, *Nature*, April 2010)
- Greater transparency
  - GAO highlights "deceptive marketing and other questionable practices"
  - NIH Genetic Testing Registry, joint FTC/FDA oversight of advertising claims widely supported (e.g., GPPC/ASHG: 70%)
- Oversight, not proscription
  - Sensible oversight provides greater (but not perfect) clarity and assurance of quality to consumers, clinicians, companies and their investors

# Contested ground in DTC oversight

Clinical DTC testing without clinician involvement (FDA issue #1)

- Concern: "[DTC] will have a significant adverse impact on consumers and undermine the physician-patient relationship." (AMA)
- Key questions:
  - is a mandatory clinical consult for DTC a realistic possibility (today)?
  - who should decide when and whether a clinical consult is required – regulators, clinicians or consumers?
- Data:
  - "…several studies have reported that physicians find it difficult to keep up with the pace of genetic technology." (AMA public comments)
  - Ex: Medco/AMA survey of PGx and MDs: 10,000 MDs, 26% had some PGx education; 10% believe they have sufficient education/training (presented ASHG, 2010)

# Contested ground in DTC oversight

Danger of incorrect, misunderstood test results (FDA issue #2)

- Concern: consumers will undertake harmful or expensive self-directed actions as a result (e.g., unnecessary testing, worry/stress, detrimental changes in treatment, lifestyle, etc.)
- Key question: regulate in advance of demonstrated harms or continue gathering data?
- Data:
  - **GPPC** (n=1048): results easy to understand (88%) vs. vague (38%); 4-7% misinterpretation
  - **Scripps** (n=3639/2037): "…no indication of test-related distress in 90.3% of the subjects and no evidence of increased use of screening tests." No physician, genetic counselor impact. (But 44% non-complete rate)
  - **Genomes Unzipped** (n=252): 166 DTC genetic tests, 1 direct negative experience
  - Other Items:
    - **REVEAL**: APOE genotyping does "not result in significant short-term psychological risks"
    - **23andMe "Sample Swap"**: Wrong data to 96 customers due to lab error. Evidence of risk or benefit of DTC model?

# Additional issues for FDA consideration

- Role of utility (clinical vs. personal) in evaluating benefits/harms
- Source of clinician, consumer information & education (DTC vs. gov't)
- Multiplex / WGS tests:
  - Regulation without constant resubmission (impossible FDA & industry burden)
  - Regulation of secondary interpretation-only "genetic tests"
- Coordination:
  - Other ongoing FDA efforts (particularly LDT, CMS/CLIA coordination)
  - Goal: integrate clinical DTC genetic testing oversight into personal genomics regulatory landscape given other potential federal (GPMA, Hatch), state (NY, MA, VT, CA) & int'l efforts.
  - **Avoid the band-aid approach.**

# Next step: transparency, regulation or both?

- What don't we know about clinical DTC genetic tests?
  - How many there are & who offers them
  - How they are intended to be used vs. how they are actually used
- How could we collect this information?
  - Informational registry: voluntary (NIH) or mandatory (SACGHS, previous GPMA)
  - Via regulatory submissions (CDRH for devices or CADER for APDx)
  - Either way: cont. consumer/clinician engagement, monitor real-word use, outcomes
- How could we balance the innovation tension in clinical DTC genetic testing?
  - Pre-test: FDA regulatory approval/clearance, gatekeeper model
  - Post-test: oversight of marketing, interpretation, use/outcomes by regulators (FTC) and community (e.g., 23andMe sample swap)
- Fundamental Tensions:
  - Public health precautions vs. innovation
  - Clinical guidance vs. individual autonomy

# Questions or Comments?

**Email:** dvorhaus@rbh.com

**Twitter:** @genomicslawyer

**Genomics Law Report:** http://www.genomicslawreport.com/