

Clearing a Path for DTC Oversight

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

Daniel Vorhaus
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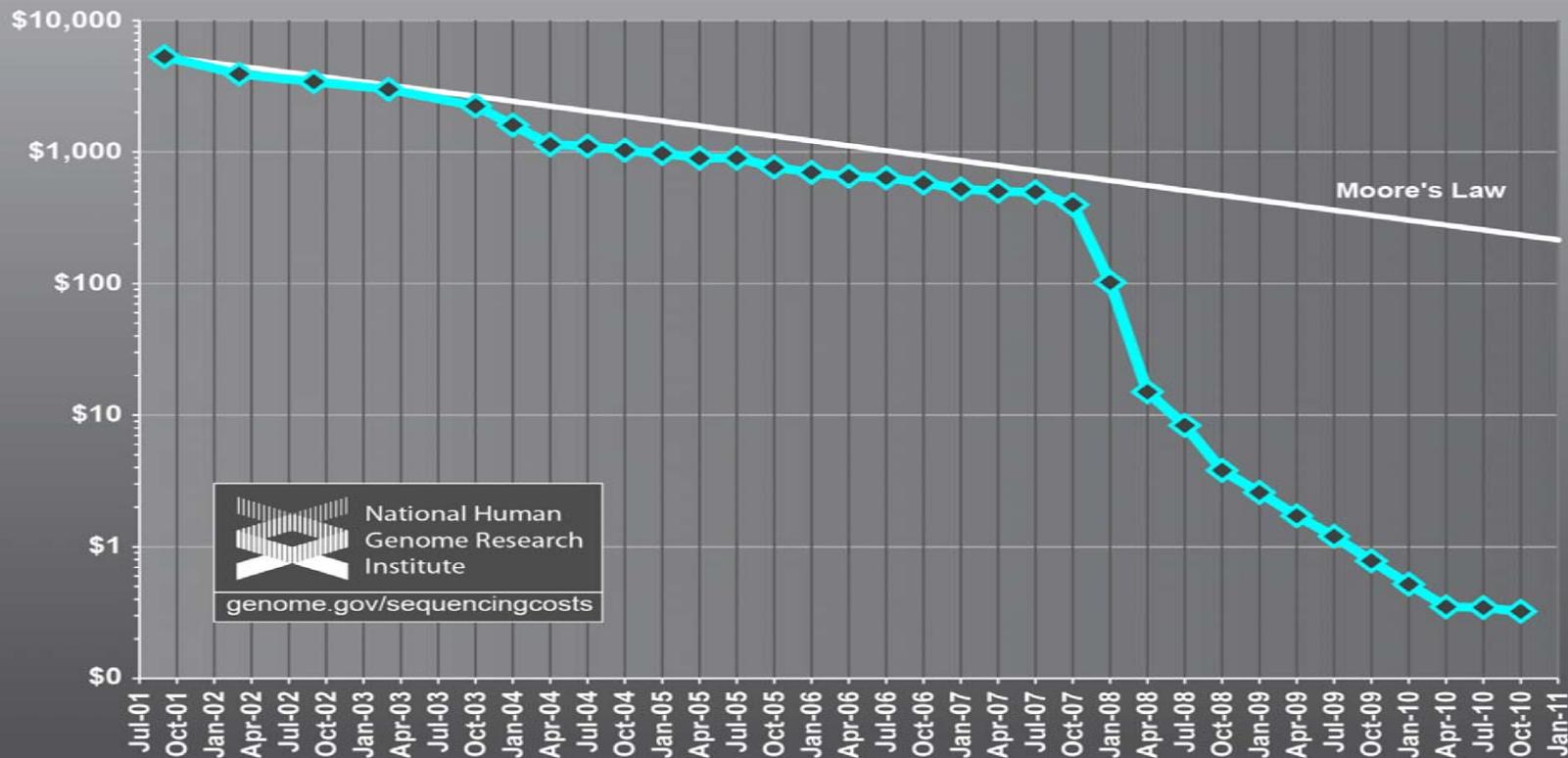
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**Robinson
Bradshaw**

Why we are here: data

Cost per Megabase of DNA Sequence



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



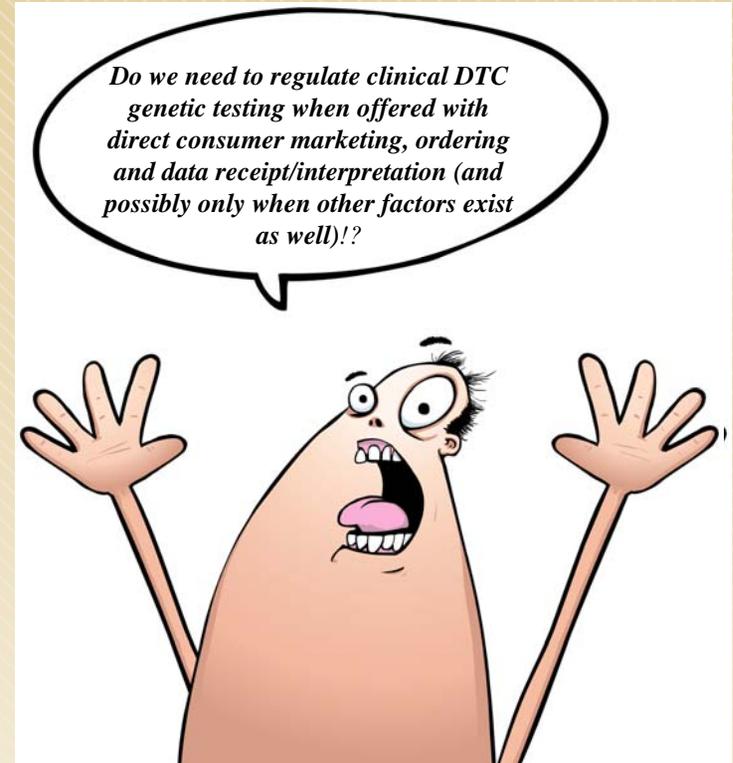
Genetic Testing



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-world 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](https://twitter.com/genomicslawyer)

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