Incidental Findings & Direct-to-Consumer Genetic Testing

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Overview

- Defining DTC Genetic Testing
- Current Regulatory Landscape
- Incidental Findings in DTC Genetic Testing
DTC Genetic Testing: Breaking It Down

• Direct to Consumer:
  - Consumer decides whether/what to order, requests the test, and receives results directly. Physician may or may not “order” the test as a formal matter.
  - Counseling may or may not be provided.

• Genetic:
  - May be single gene, multiples genes, SNPs, or sequencing

• Testing:
  - Laboratory analysis

- DTC = alternative means of marketing genetic testing services
- Any test that can be performed on blood spot or saliva sample can be provided DTC
Personal Genome Services

- Analyze 500,000-1,000,000 SNPs
- Identify variants associated with disease
- Calculate a set of disease risks based on variants present in customer’s DNA
- Provide individualized report of customer’s risk of developing specific diseases
Spectrum of DTC Genetic Testing

- Fetal Gender
- Inherited
- Pharma
- Complex Disorders
- Preconception/Carrier
- Paternity
- Nutrition
- Athletic perf.
- Complex Conditions
- Ancestry
- Skin care
- Recreational
- Infidelity
- Infidelity
DTC: Is There Oversight?

- Oversight of What?
- By Whom?
- For What Purpose?
Clinical laboratory certification (CLIA)

Regulation of in vitro diagnostic devices & laboratory reagents

Unfair/deceptive trade practices incl. false/misleading advertising

Regulation of whether HCP required for test ordering and return of results
# Key FDA Events Re: LDTs/DTC Tests

<table>
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<tr>
<th>Date</th>
<th>Event</th>
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<tr>
<td>November 21, 1997</td>
<td>FDA articulates “enforcement discretion” policy for laboratory-developed tests</td>
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<td>April 7, 2000</td>
<td>FDA asserts authority over LDTs for drugs-of-abuse testing</td>
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<td>September 7, 2006-2007</td>
<td>In draft guidance, FDA asserts authority over specific subset of LDTs (IVDMIA) used in disease prognosis – holds public meeting – ultimately abandons approach</td>
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<td>September 14, 2007</td>
<td>FDA issues guidance document on ASR frequently asked questions</td>
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<td>September 29, 2008</td>
<td>FDA issues Warning Letter to LabCorp asserting that OvaSure is a device subject to FDA regulation</td>
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<td>May-June 2010</td>
<td>FDA issues Untitled Letters to companies offering DTC testing informing them that their tests are medical devices subject to FDA regulation</td>
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<td>June 17, 2010</td>
<td>FDA announces public meeting and requests comments regarding its approach toward regulating LDTs</td>
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<td>July 19-20, 2010</td>
<td>FDA holds public meeting on regulation of LDTs</td>
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<td>March 8-10, 2011</td>
<td>FDA convenes expert advisory panel to make recommendations on scientific issues concerning DTC genetic tests that make medical claims</td>
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<td>September-October 2011</td>
<td>FDA states it intends to exercise enforcement discretion with respect to all LDTs except those offered DTC pending the issuance of guidance outlining FDA’s approach to LDT regulation</td>
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<td>January 2012</td>
<td>CDRH’s 2012 guidance agenda lists three planned draft guidances on LDTs</td>
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<td>July 9, 2012</td>
<td>Congress requires FDA to notify Congress at least 60 days before issuing guidance on FDA regulation of LDTs</td>
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<td>January 2013</td>
<td>CDRH’s 2013 guidance agenda does not include any planned LDT guidances/draft guidances; does list a planned draft guidance regarding DTC Genetic Testing</td>
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Where are we now?

• FDA regulatory landscape largely remains unchanged
  – No new regulations
  – FDA has stated that it plans to issue guidance this year
    • Not clear whether the Agency has sufficient authority or will follow appropriate administrative procedures

BUT

• FDA’s public statements and individual enforcement actions have led some DTC companies to involve a physician (at least to submit test order and receive results)
DTC: Why Worry?

- Test Accuracy/Validity
- Laboratory Quality
- Lack of Counseling
- Misinterpretation
- Misrepresentation
- Inappropriate test selection
- Privacy
- Discrimination
- Surreptitious Testing
- Consequences for other family members
Impact on Consumers

• Consumers can’t understand genetic information; it is complicated.

• Consumers vulnerable to exaggerated claims.

• Consumers may get tested without adequately considering consequences to themselves and family.

• Consumers may forego standard treatments or make dietary or lifestyle changes without proven benefit.

• Consumers may seek and receive unneeded and costly care.
What does “incidental” mean in the context of DTC testing

Have a seat Kermit. What I’m about to tell you might come as big shock...
What does “incidental” mean in the context of DTC testing

• Learning something you did not expect?
  – “I thought I was at high/low risk of X, but my results say otherwise”
  – May lead to positive/negative/no actions by recipient
Collins hits the gym following genetic testing - October 26, 2009

“Collins discovered that he carries two copies of the most common risk factor of type II diabetes. Collins, whose laboratory investigates the underlying genetic basis of adult-onset diabetes, said he was "surprised" by these findings since his family has no history of the disease. Upon learning the test results, Collins got off his Harley-Davidson and instigated a regular exercise regime. The svelter NIH director said he has now lost 20 pounds.”
What does “incidental” mean in the context of DTC testing

• Receiving information you did not request?
  – Example: Patient requests information on genes related to male-pattern baldness, but Company tests for and reports information on cancer risk
  • Has company committed legal violation? Ethical violation?
What does “incidental” mean in the context of DTC testing

• **Not** receiving information you would have expected?
  
  – Company reports no increased risk for disease, but fails to disclose limitations of test
  
  • E.g., carrier screening for Tay Sachs Disease
    
    – 23andme tests for only the most common mutations; misses those more common in non-AJ population
    
    – Does not include enzyme test for HexA – which is recommended as *primary* method to screen for TS
  
  – Consumer may **think** s/he is “not at risk” when in fact s/he is