Direct to Consumer Genetic Testing: An FDA Case Study

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Notice

• I will discuss particular regulatory actions pertaining to 23andMe
  – Not an endorsement or a criticism of 23andMe, just publicly available facts
  – No other company has received marketing authorization for DTC genetic testing to date
Overview

• History of DTC test oversight/issues
• Policy for oversight of DTC genetic tests
• DTC genetic test submissions
• Authorization of first DTC genetic test
DTC Genetic Test History

• 2006: GAO report on DTC testing cautions that tests may make “medically unproven” claims
  – Mostly concerning nutrition claims
• 2007: with several DTC genetic tests on the market, FDA begins meetings with sponsors
• 2010:
  – FDA sent letters to DTC genetic testing companies informing them it believed their tests were medical devices
  – FDA held a public meeting to discuss how it should regulate DTC tests
More DTC History

• 2010: US Congress holds a hearing on DTC genetic tests
  – GAO describes serious problems with
    • Who can order a test
    • Different results from different test manufacturers
    • Interpretation of results
  – FDA testimony and commitment to “do something”
FDA Policy on Oversight of DTC Genetic Testing

• DTC genetic tests are medical devices subject to FDA oversight

• Even if offered as a test designed, manufactured, and used by a single lab (LDT), FDA will not exercise enforcement discretion
  – Not a type of test suitable for enforcement discretion
  – If ordered by a physician, enforcement discretion may be exercised
FDA Policy Consequences

• Several test companies began to require physician prescription for their tests
• Ultimately, most tests companies left the market—regulation or low demand?
• One company chose to maintain direct consumer ordering
23andMe Submissions

- 2012: 23andMe makes two submissions to FDA for a portion of the tests they offered as the “Personal Genome Service”
- 2013: FDA sends a warning letter to 23andMe due to continued non-compliance
23andMe continued

• 2015: FDA authorizes marketing of 23andMe BLM (Bloom Syndrome) carrier screening test for ordering and use directly by consumers
  – De novo down-classification pathway
  – Class II
  – Exemption still pending
23andMe BLM Test

• Indications for Use:
  – The 23andMe PGS Carrier Screening Test for Bloom Syndrome is indicated for the detection of the BLM$^{\text{Ash}}$ variant in the BLM gene from saliva collected using an FDA cleared collection device (Oragene DX model OGD-500.001). This test can be used to determine carrier status for Bloom syndrome in adults of reproductive age, but cannot determine if a person has two copies of the BLM$^{\text{Ash}}$ variant. The test is most relevant for people of Ashkenazi Jewish descent.
Special Conditions for Use (condensed) (1)

• For over-the-counter (OTC) use
• Not intended to diagnose disease, tell you anything about the health of your fetus, or your risk or your newborn child’s risk of developing a particular disease later in life
• Not a substitute for visits to a healthcare provider
• Does not detect all variants associated with Bloom syndrome
Special Conditions for Use (condensed) (2)

- Only for use in adults of reproductive age
- Does not diagnose any health conditions
- The laboratory may not be able to process your sample
- User’s ethnicity may affect interpretation
- Must meet established Special Controls
Regulatory Special Controls

• Special controls: regulatory requirements for some class II devices.

• Special controls can include:
  – Performance standards
  – Postmarket surveillance
  – Patient registries
  – Special labeling requirements
  – Premarket data requirements
  – Guidelines
Special Controls: Autosomal Recessive Carrier Screening Tests

(Condensed—see FDA decision summary for complete details)

- Provide information on how to access pre- and post-test genetic counseling (if OTC/DTC)
- Use FDA authorized collection device
- Labeling—publicly available performance information
More Special Controls (3)

• User comprehension studies for appropriate for OTC/DTC
  – > 90% user comprehension
• Education module for recipients
  – Defines terms and explain significance of carrier status
More Special Controls (2)

• Performance
  – PPA and NPA against reference must be $\geq 99\%$ with lower bound of 95% CI presented
  – Number of specimens required to test
    • Common and rare variants
  – Predictive value and cautionary statements
  – Others
Conclusions

• Long, unusual history in regulatory area
• DTC tests must have demonstrated safety and effectiveness for the intended user
• First DTC genetic test authorized
  – Pathway established
  – More to come?
• FDA supports DTC genetic testing when performance is established and users can understand results