Direct to Consumer Genetic Testing: An FDA Case Study

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May 21, 2015

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
  - http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm376296.htm

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^{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^{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 ≥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