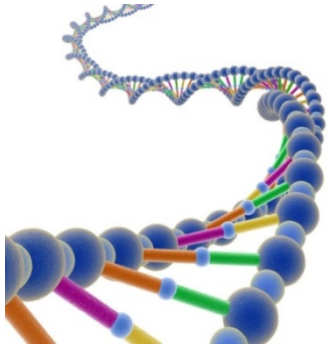

Advertising and Marketing Genetic Tests – New Pathways or Old Roads?

Kathleen M. Sanzo, Morgan Lewis

FDLI Advertising & Promotion Conference
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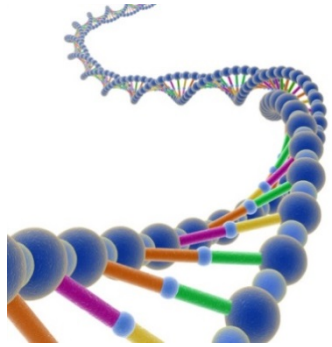

Context for Use of Genetic Tests

- Standalone tests, either sourced directly by consumers (nutritional, athletic, general wellness, lineage), through consumers' physicians (standard Rx), or through physicians who work for the test provider.
- Tests used in combination with a drug, either "essentially" (i.e., patient can't use the drug without the information from the test) or merely "informative," (i.e., may help to predict drug effect, adverse events, resistance, etc.) but not necessarily critical to the use of the drug.
- Tests used during the investigation of a drug (e.g., helps measure safety or effectiveness, assist in exclusion/inclusion criteria, etc.) but is not intended to be used independently in connection with the drug once approved.

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Historical Federal Concern about Promotion of Genetic Tests

- 2006 GAO Report found certain DTC Genetic Test manufacturers engaged in false and misleading advertising. See General Accounting Office, Direct to Consumer Genetic Tests are Further Complicated by Deceptive Marketing and Other Questionable Practices, 2006.
- FDA November 2015 report on 20 case studies of test deficiencies—false negatives and positives of serious disease conditions. See The Public Health Evidence for FDA Oversight of Laboratory-Developed Tests: 20 case studies, at http://www.fda.gov/aboutfda/reportsmanualsforms/reports/ucm472773.htm.

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Current FDA Position on Genetic Tests Used in Precision Medicine

- Precision Medicine is the key to future effective treatments and good health.
- LDTs and IVDs are important to the progress of Precision Medicine Initiative.
- We will figure out how to identify and regulate these tests at some point but will likely opt for more rather than less regulation.
- Any marketing of these tests or services directly to consumers makes them automatically regulated devices requiring FDA clearance or approval.

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Stakeholders Pushing Back on FDA Regulation

- American Clinical Laboratory Association hired two of the most well-known constitutional lawyers in the US—Lawrence Tribe and Paul Clement—to debate why LDTs are medical services providing clinical information, part of the practice of medicine, and **not** medical devices, therefore asserting that FDA has no jurisdiction over LDTs, how they are used, or provided to HCPs or consumers.
- Association of American Medical Colleges in August 2016 stated that "the FDA's regulation of LDTs as proposed would interfere with delivering innovative, cutting edge medical care, negatively impact patients, or mire the development of critical new tests in a costly and laborious process."
- Not clear where FDA will end up in its regulatory model for LDTs—based on NGS IVD Test Guidance, it appears it will use a "standards-based" approach for at least some subset of LDTs.

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The Problem??

- Unless you know how a test is regulated, you can't figure out how to legally market and promote it.
- What should companies and laboratories do in the meantime?
- What should companies/laboratories do once new Guidance issues?

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Other Considerations to Marketing and Advertising

- CLIA regulates laboratory services, and imposes quality standards and processes on how testing services are conducted and delivered.
- The ACA mandated that consumers have direct access to their CLIA-certified lab test results. See 42 C.F.R. § 493.1291(l).
- As of 2015, 37 states and DC permit consumers to order some or all of their laboratory tests directly, without a physician's involvement.
- CA, NY and FL have significant clinical laboratory certification and inspection regulatory requirements.
- Consequently, there are other federal and state regulators involved in actively policing LDTs and their marketing.

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It's a breakthrough in prostate cancer care that will change men's lives forever. And it's called Systems Pathology. Mount Sinai has developed an advanced algorithm that integrates new imaging technologies, genetic data, biomarkers, and the patient's clinical history. It then takes these dissimilar data sets and compares them to hundreds of thousands of other cases in a powerful supercomputer. The result? A more personalized view of the patient's tumor, which enables the surgeons at Mount Sinai's Department of Urology to know just how aggressive or slow-growing the tumor actually is. Which means doctors and patients can make more informed treatment decisions. Systems Pathology. Another way Mount Sinai is changing the face of medicine...again. For you. For life.
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BEFORE
YOUR DOCTOR RECOMMENDS
PROSTATE CANCER SURGERY,
MAYBE YOUR DOCTOR SHOULD RECOMMEND
A BETTER TEST.

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What standards apply to advertising and promotion of genetic tests?

- Depends on whether they are regulated by FDA as medical devices, and if so, whether FDA exempts them from active regulation as LDTs, or if they are not FDA regulated.
  - As non-devices promoted to consumers, they would be subject to Federal Trade Commission (FTC) and state regulation.
  - As FDA-regulated products, they would be prohibited from containing in their labels and labeling (e.g., websites, brochures) claims which are false or misleading in any particular; advertising likely would also be subject to FDA standards.
  - As regulated but exempt products, they likely are potentially subject to all standards (FDA, FTC, State).

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FTC Standards

- Advertising must be truthful, not deceptive or unfair.
- The advertiser must have proper substantiation for all establishment claims prior to making them.
  - Scientific claims (e.g., CLIA or other certification, precision and reliability of tests, clinical utility claims) will require higher level of substantiation/data/studies than more general claims.
  - Note in 2006 FTC issued a notice entitled “FTC Facts for Consumers, At-home Genetic Tests: A Healthy Dose of Skepticism May be the Best Prescription” (July 2006), advising consumers to speak with their doctor before and after home testing to understand results and to ensure protection of the privacy of the results. Note, however, FTC did not preclude marketing.

FTC Advertising Regulation

- FTC has taken enforcement action against health-related products and services (e.g., Zika tests, eyeglass prescribers, weight loss clinics, etc.).
- FTC has established general advertising guidelines for novel classes of claims (e.g., Green Guides for environmental claims, Social Media Guidelines, Endorsement Guidelines).
- FTC also works with voluntary industry self-regulating advertising body—BBB/NAD—to investigate and take enforcement action against non-complying companies.

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FDA Standards

- Medical device claims cannot be false or misleading in any particular and must be promoted consistent with their intended use and cleared/approved label.
- Existing guidelines for providing benefit/risk information for drugs and devices require significant risk disclosure and balance, and no unapproved label claims.
- Social media use is likely difficult because of risk disclosure burden.
- There are significant differences in disclosures and content between promotion/advertising for HCPs and consumers.
- FDA's legal authority to prohibit accurate and non-misleading information about products has been limited by decisions in off-label cases, including *Amarin Pharma Inc., et al. v. U.S. Food & Drug Admin., et al., 119 F. Supp. 3d 196 (S.D.N.Y., 2015),* and *Pacira, Pacira Complaint, Pacira Pharmaceuticals, Inc. v. FDA, No. 15-7055 (Sept. 8, 2015),* and *U.S. Vascular Solutions, Inc., Criminal No. 5:14-CR-00926, Final Jury Instructions (W.D. Tex. Filed Feb. 25, 2016).*

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FDA Enforcement Action

- FDA has issued many “it has come to our attention” and Warning Letters to testing companies asserting that their products are unapproved devices and not eligible for enforcement discretion as LDTs. See Letters to InterLeukin Genetics, Pathway Genomics, Genomics Express, DNA4Life, 23andMe.
- FDA has complained among other issues that the promotion of the products to consumers for disease states or conditions such as periodontitis, osteoarthritis, warfarin and tamoxifen response, and other disease predispositions, make the products regulated diagnostics and not LDTs.

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LDT claims that could prompt legal issues

- Efficacy claims about the test itself—its accuracy, precision, reliability, reproducibility, etc., e.g., "All DNA sequencing is not equal."
- Inaccurate or exaggerated claims about the risk of disease and need for test; what the genetic information tells you.
- Claims relating to the clinical relevance of the test to treatment success or clinical outcomes (this could also invoke complaints from drug manufacturers).
- Lab certification or similar comments that suggest test superiority.
- Inaccurate claims about medical acceptance of test, payments, insurance coverage, etc.
- Claims that physicians are not necessary for the test order.

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Considerations for Marketing and Advertising LDTs

- For Laboratories (stand alone, hospital, etc.)
  - Advertising/marketing should include accurate, well substantiated statements about the test service, its precision, reliability, and the scope of information it provides to test subjects and HCPs.
  - Disclose that the test is not FDA approved or cleared.
  - Whether the tests can be marketed directly to consumers will depend on whether the test is for disease or diagnostic purposes (vs. general wellness, “know thyself” or other conditions) and thus whether regulated by FTC, FDA, or both
    - Query – if the distributor disclaims use for “diagnostic use” and “FDA clearance” can it be advertised to consumers?
    - Is there some benefit to also stating that there is no interpretation of DNA information?

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Considerations for Marketing and Advertising LDTs

- For Drug Manufacturers
  - Unless the test is approved as a companion device, it cannot be promoted by the drug manufacturer without risk of off-label claims.
  - LDTs can be recommended to sites for investigational use during drug clinical trials; however, once the drug product is approved:
    - must be approved or cleared by FDA for the test itself to be commercially distributed outside the laboratory

    OR
    - to maintain its status as an LDT, must be manufactured and used only within a single laboratory.

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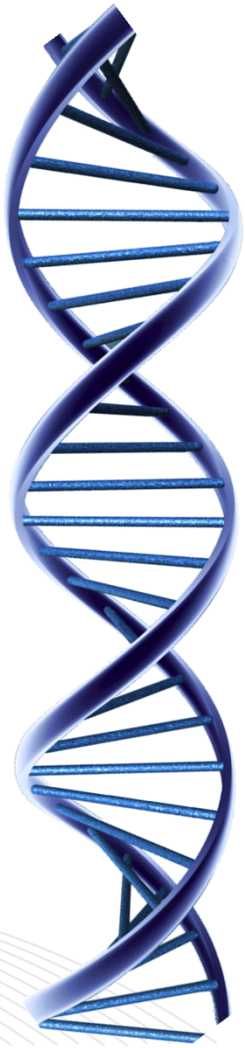
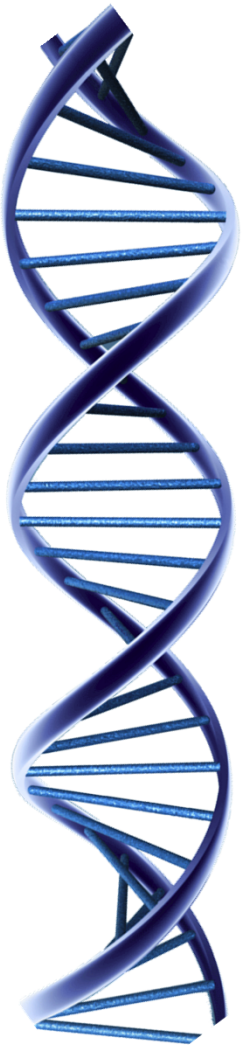
Considerations for Marketing and Advertising LDTs

- For Device Manufacturers
  - Tests which are commercially marketed and advertised must be cleared/approved as IVDs, either alone or in combination with a drug therapy.
  - FDA has approved over 25 IVDs for use with specific drugs, i.e., companion diagnostic IVDs, and these products must be promoted and advertised according to their approved uses, and by the drug companies as described in the appropriate drug label referencing the test.

    See http://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm301431.htm.



Questions



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