REGULATORY POLICY CONSIDERATIONS PRESENTED BY NUTRIGENOMICS IN THE COMMERCIAL CONTEXT

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2. Overview

- Legal Framework
  - Genetic Testing
  - Health Benefit Claims for Food
- Key Legal & Regulatory Developments
- Regulatory Policy Considerations

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3. CMS Regulation of Genetic Tests

- CMS regulates clinical laboratories under the Clinical Laboratory Improvement Amendments (CLIA), and enforces requirements including in the following areas:
  - Quality Control
  - Personnel Qualifications
  - Proficiency Testing
- CLIA standards are designed to ensure the analytical validity of genetic tests. They do not address the clinical validity or clinical utility of the tests.

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4. FDA Regulation of Genetic Tests

- FDA regulates genetic testing kits & components that are sold to clinical laboratories or other persons under the Federal Food, Drug & Cosmetic Act (FDCA). FDA exercises enforcement discretion for Laboratory Developed Tests (LDTs).
- "Device" - "means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals . . ., and which does not achieve its primary intended purposes through chemical action within or on the body of man . . . ."

21 U.S.C. § 321(h).

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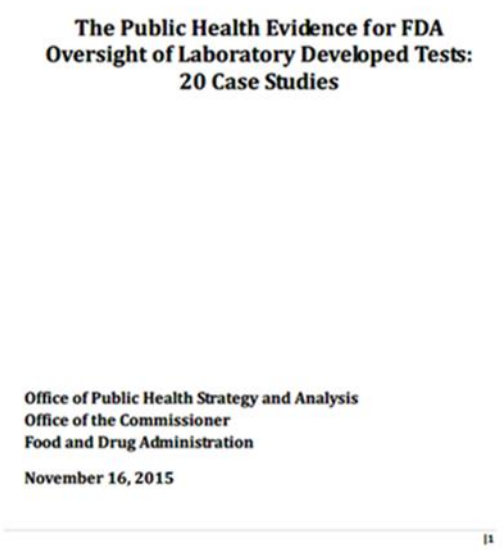
5. 2015 FDA Report on LDTs



The Public Health Evidence for FDA Oversight of Laboratory Developed Tests: 20 Case Studies

Office of Public Health Strategy and Analysis
Office of the Commissioner
Food and Drug Administration

November 16, 2015

- FDA report identified key issues, including:
  - Lack of evidence supporting clinical validity
  - No premarket review of performance data
  - Threats to scientific integrity of clinical studies
  - Inadequate product labeling
  - Unsupported manufacturer claims

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6. Genetic Tests Offered for Other Purposes

Personalized Socks
by Dot One

Entertainment

You're a fun person and your DNA can be fun, too. From finding your next bottle of wine, to wearing a scarf customized by your DNA, turn the building blocks of you into interesting and playful insights.

Wine Explorer
by Vinome

Metabolism
by Insitome

Neanderthal
by Insitome

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7. FDA Clearance of 23andMe Personal Genome Service Genetic Health Risk (GHR) Tests (2017)

- First direct-to-consumer (DTC) genetic test cleared by FDA that provides information on an individual's genetic predisposition to particular diseases/health-related conditions.
  - Intended provide information which may help individuals to make decisions about lifestyle choices or inform discussions with a health care professional.
  - Isolates DNA from a saliva sample, which is then tested for more than 500,000 genetic variants:
    - Parkinson's disease
    - Late-onset Alzheimer's disease
    - Celiac Disease
    - Alpha-1 antitrypsin deficiency
    - Early-onset primary dystonia
    - Factor XI deficiency
    - Gaucher disease type 1
    - Glucose-6-Phosphate Dehydrogenase deficiency
    - Hereditary hemochromatosis
    - Hereditary thrombophilia

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8. FDA Clearance of 23andMe Personal Genome Service Genetic Health Risk (GHR) Tests (2017)

- Cleared through de novo premarket review pathway
  - Available for devices that are novel, low-to-moderate-risk devices that are not substantially equivalent to an already legally marketed device.
  - Conditions of approval are designed to provide reasonable assurance of safety and effectiveness of these and similar GHR tests.
  - Clearance excludes diagnostic tests
- Exemptions from FDA premarket review additional 23andMe GHR tests, and GHR tests from other makers may be exempt after submitting their first premarket notification.

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9. FDA Regulation of Foods

- Under the FDCA, FDA regulates the safety and labeling of food, including food products that are consumed to manage a disease, health-related condition, or otherwise address a nutritional need that has been determined through genetic testing.
- "Food" means "articles used for food or drink," "chewing gum," and "components" of these articles. 21 USC § 321(f).
- "Food" includes:
  - Conventional foods and beverages
  - Dietary Supplements
  - Foods for Special Dietary Use & Medical Foods

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10. "Food" may also be "Drug"

FDCA Drug Definition

"Drug" means . . . (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals*; and (C) articles *(other than food)* intended to affect the structure or any function of the body of man or other animals; and [components] . . . ." 21 USC 321(g)(1).

*Excludes FDA-cleared "health claims"

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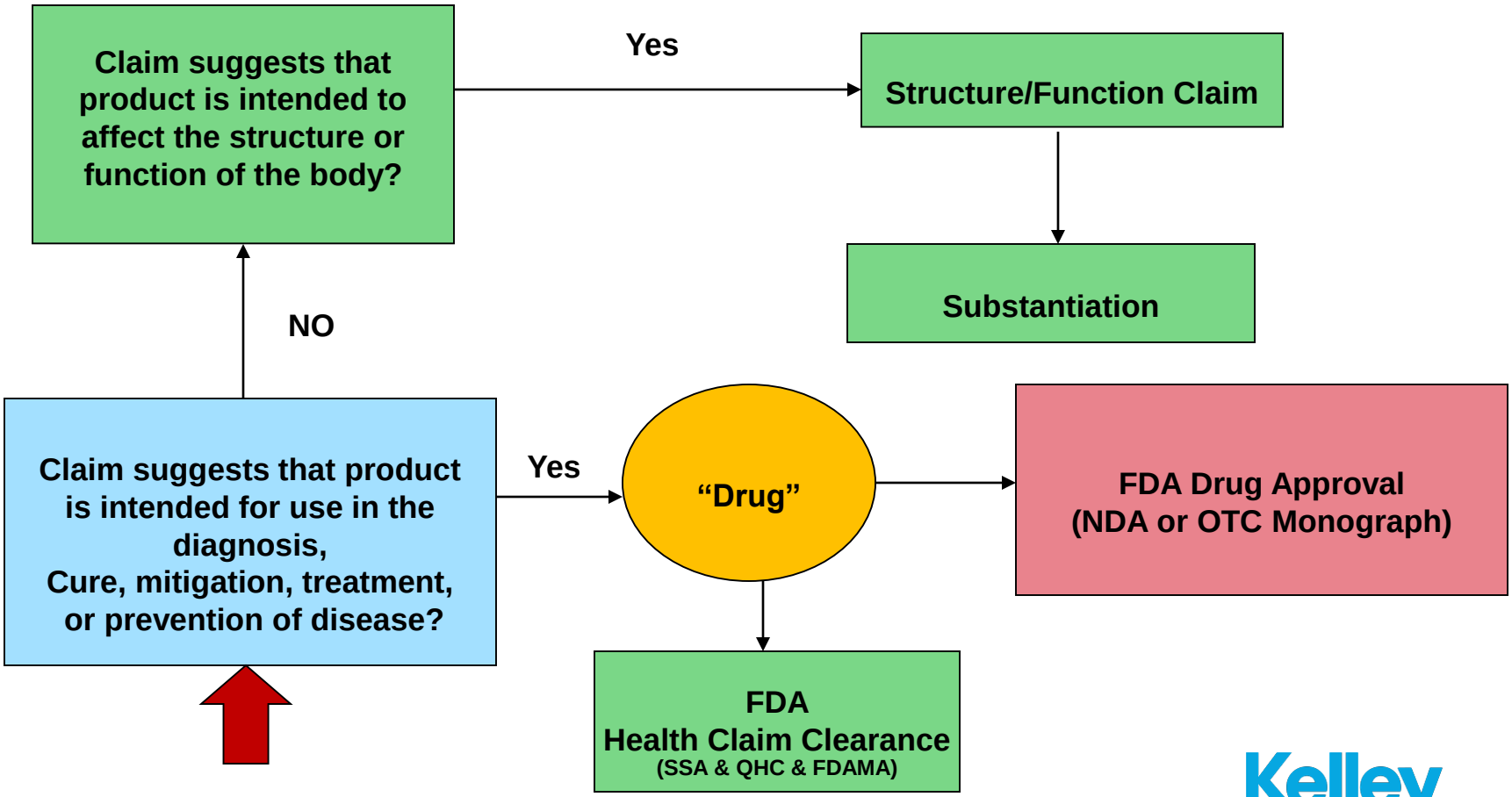
11. Health Benefit Claims for Food



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12. FDA Has Broad Authority to Interpret & Enforce the Statute & Regulations in a Flexible Manner

- Enforcement Discretion Policy Examples:
  - "Healthy" claims for higher fat foods containing healthy fatty acid profile (responds in part to current Dietary Guidelines).
  - Qualified "health claims" which are truthful and substantiated by credible evidence that does not meet the "significant scientific agreement" evidence standard (responds to First Amendment case law).
  - Non-enforcement of medical device requirements for certain health IT applications:
    - Medical Device Data Systems (MDDS)
    - Medical Apps

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13. Federal Trade Commission (FTC) Authority

- Federal Trade Commission Act (FTCA) -- Prohibits unfair & deceptive acts & practices, including false advertising. 15 USC § 45
- Scope of authority encompasses
  - Advertising claims for genetic testing products and services
  - Advertising claims for foods
  - Data security practices concerning genetic test results and other personal consumer information

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14. Claim Substantiation – Reasonable Basis Standard

- Express and implied claims must be accurate and substantiated before they are used.
- Claims must be supported by evidence providing a "reasonable basis." Amount & type of evidence depends on several factors:
  - Type of Product & Claim
  - Benefits of a truthful claim & consequences of a false claim
  - Cost/feasibility of developing claim substantiation
  - The amount of substantiation that experts in the field believe is reasonable.

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15. Claim Substantiation – Competent & Reliable Scientific Evidence

- "Competent and reliable scientific evidence" generally is required for health related claims.
  - Studies must be -
    - Conducted in an objective manner
    - Conducted by qualified persons
    - Conducted using procedures generally accepted in the relevant scientific community (e.g., RCT)

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16. Amount and Type of Evidence

"When no specific claim about the level of support is made, the evidence needed depends on the nature of the claim. A guiding principle for determining the amount and type of evidence that will be sufficient is what experts in the relevant area of study would generally consider to be adequate. The FTC will consider all forms of competent and reliable scientific research when evaluating substantiation. As a general rule, well-controlled human clinical studies are the most reliable form of evidence. Results obtained in animal and in vitro studies will also be examined, particularly where they are widely considered to be acceptable substitutes for human research, or where human research is infeasible. . . ."

FTC, Dietary Supplements: An Advertising Guide for Industry.

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17. Amount and Type of Evidence

"**. . . Although there is no requirement that a . . . claim be supported by an specific number of studies, the replication of research results in an independently-conducted study adds to the weight of the evidence. In most situations, the quality of studies will be more important than quantity. When a clinical trial is not possible (e.g., in the case of a relationship between a nutrient and a condition that may take decades to develop), epidemiologic evidence may be an acceptable substitute for clinical data, especially when supported by other evidence, such as research explaining the biological mechanism underlying the claimed effect.**"

FTC, Dietary Supplements: An Advertising Guide for Industry.

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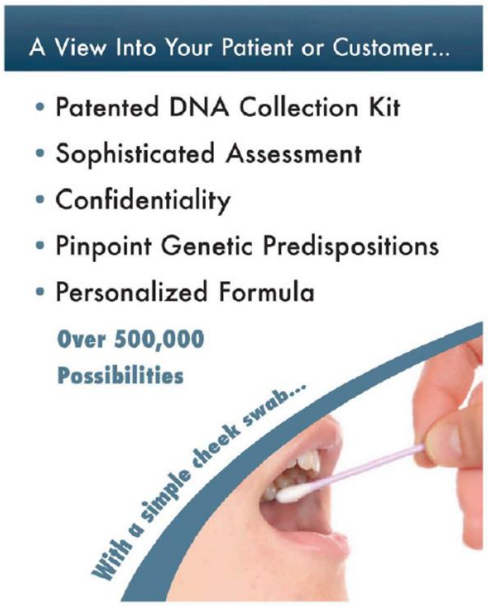
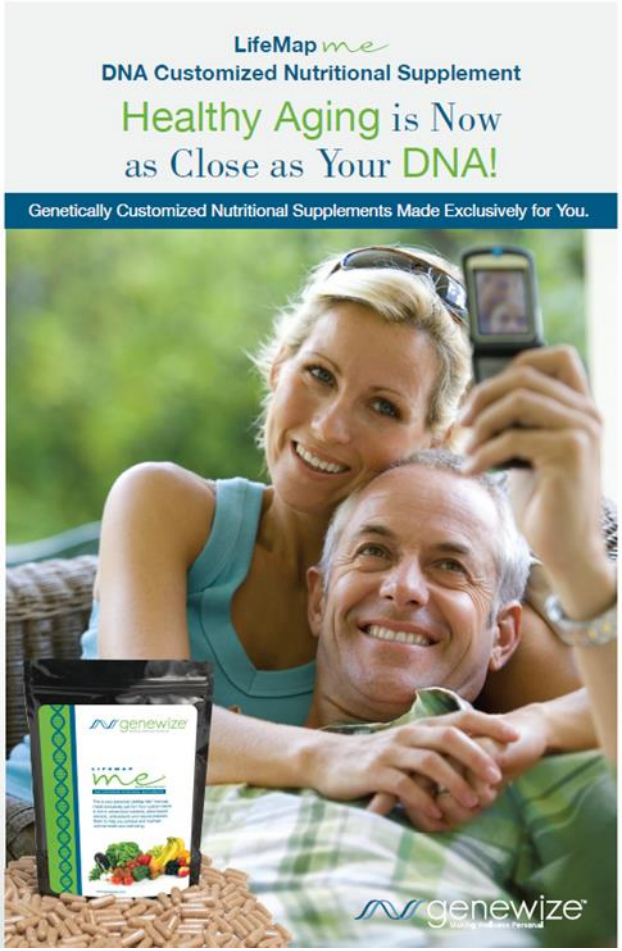
18. FTC Enforcement (2014): Genelink & foru™ Int'l Cases





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19. FTC Enforcement (2014): Genelink & foru™ Int'l Cases

- FTC allegations in the case included:
  - Inadequate claim substantiation both for claims promoting genetic testing and dietary supplement benefits.
  - Misrepresentation characterizing the nature/amount of substantiation possessed by marketers
  - Inadequate data security practices to protect personal consumer data including genetic test results and social security numbers.
- Cases were settled in 2014

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20. Consumer Class Action Litigation Under State Consumer Protection Laws

- In the aftermath of an FDA warning letter that was issued to 23andMe in 2013 (FDA closing letter issued in 2014), a number of consumer class action lawsuits referencing the FDA warning letter were filed under state consumer protection laws, and were subsequently settled. The complaints that were filed in these cases alleged state law violations relating to the following types of issues:
  - Marketing DTC genetic testing products without FDA pre-market clearance
  - Inadequate claim substantiation
  - Inadequate data security practices
  - Inadequate disclosures concerning how personal genetic information would be used (e.g., research, commercial applications).

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21. Regulatory Policy Considerations

- Adequacy of existing CMS and FDA frameworks for regulating genetic tests, including those relating to DTC products and services.
- Adequacy of existing FDA regulatory framework to accommodate nutrigenomics claims for foods without triggering "drug" status for foods.
- Adequacy of existing claim substantiation guidance with respect to claims for genetic tests and foods in the context of nutrigenomics.
- Adequacy of consumer privacy and data security safeguards with respect to the storage and uses of consumers' genetic information.

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Thank you

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