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Direct-to-Consumer (DTC) Marketing of Genetic Testing

- Larger context is increased DTC marketing of medical products and services.
- Mixed reactions among consumers and among health professionals
- Advertising and direct access of genetic testing raise concerns different from those of advertising or direct access of drugs and devices.
- FDA's role is uncertain.

In Vitro Diagnostics

- Diagnostics provide information rather than treatment.
- Safety and efficacy regarded in a way different from that in which S and E are regarded for drugs and other devices. Consequences are one step removed from actual test process.
- Different regulatory approach

Promotion and Advertising of Medical Devices

- Premarket notification
- Premarket approval
- Labeling Authority
- Advertising Authority
- Intended Use
- Practice of Medicine
- Federal Trade Commission

Premarket Notification (510(k))

- Sponsor notifies FDA 90 days before marketing product.
- Products are granted marketing clearance based on substantial equivalence to already marketed device.
- Generally, Class I and II devices
- General controls and special controls

Premarket Approval (PMA)

- Sponsor submits premarket approval application
- Approved if conditions of use in proposed labeling provide reasonable assurance of safety and effectiveness if labeling is not false or misleading
- Approval order may restrict sale and distribution to extent allowed in section 520(e) of the Federal Food, Drug and Cosmetic Act

Restricted Devices

- Section 520(e) - FDA may require that sale, distribution and use of an approved device be restricted by regulation as follows:
  - Available only on written or oral authorization of licensed practitioner
  - Upon other conditions that FDA can prescribe if, because of potentiality for harmful effect or the collateral measures necessary to its use, there cannot otherwise be reasonable assurance of safety and effectiveness.

Restricted Devices

- Only three devices restricted by regulation
  - Analyte specific reagents
  - Drug of abuse test kits
  - Hearing aids
- Most restricted devices are Class III requiring PMA and restricted through approval order (previous slide)

Restricted Device Advertising

- Section 502(q) provides that a restricted device is misbranded if its advertising is false or misleading in any particular or it is sold, distributed or used in violation of regulations prescribed under section 520(e)
- Section 502(r) provides that a restricted device is misbranded if its advertising does not include “a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications…”

Device Labeling

- 502(a) provides that a device is misbranded if its labeling is false or misleading in any particular
- Applies to all devices, not only restricted devices
- Labeling is defined in section 201(m) of the Federal Food, Drug and Cosmetic Act as “all labels and other written, printed or graphic matter (1) upon any article or any of its containers or wrappers or (2)accompanying such article.

Labeling

- Interpreted broadly
- Material must textually accompany product, not necessary to physically accompany it
- Includes brochures, mailings, journal reprints if distributed by or on behalf of a company, sales materials, package inserts, immediate package label

Advertising

- Not defined in Food, Drug and Cosmetic Act
- Center for Drug Evaluation and Research has regulations referring to “advertisements in published journals, magazines, other periodicals and newspapers, and advertisements broadcast through media such as radio, television and telephone communication systems.”

FDA and FTC

- 1971 Memorandum of Understanding
- FDA has primary jurisdiction over advertising of prescription drugs and of restricted devices and over labeling of all products
- FTC has primary jurisdiction over advertising of other than restricted devices and of OTC drugs
- FDA has not clearly defined Internet promotion as labeling or advertising
- FTC more broadly defines advertising

Analyte Specific Reagents

- Restricted by regulation under authority of 520(e)
- 21 CFR 809.30 restricts sale of ASRs:
  - IVD manufacturers
  - High complexity clinical laboratories regulated under CLIA or under VHA
  - Organizations that use reagents for uses other than providing diagnostic information to patients and practitioners (i.e., forensics, academic, research etc)

Labeling for ASRs

- 21 CFR 809.10 governs IVD labeling.
- 21 CFR 809.10(e): Labeling for ASRs
  - Class I exempt: “Analyte specific reagent. Analytical and performance characteristics are not established.”
  - Class II and III ASR’s: “Analyte specific reagent. Except as a component of the approved/cleared test (Name of approved/cleared test), analytical and performance characteristics of this ASR are not established.”

Advertising and Promotion of ASRs

- 21 CFR 809.30 (d):
  - Include identity of reagent and identity of analyte
  - Include Class I exempt: “Analyte specific reagent. Analytical and performance characteristics are not established.” (Broad range of reagents)
  - Class II and III ASR’s: “Analyte specific reagent. Except as a component of the approved/cleared test (Name of approved/cleared test), analytical and performance characteristics of this ASR are not established.” (Class II - Blood bank, Class III - HIV,TB)
  - No statement regarding analytical or clinical performance

Analyte specific reagents

- Ordering in-house tests developed using analyte specific reagents is limited under section 520(e) of the act to physicians and other persons authorized by applicable State law to order such tests, unless
- Sold to IVD manufacturers or organizations using reagents to make tests for other than providing diagnostic information to patients and practitioners, e.g., forensic, academic, research, nonclinical laboratories

Regulating Home Brew

- Does the combination of ASR and lab processing become a device?
- How to limit ordering of ASR-based tests to physician ordering?
  - Is test a device
  - Internet use of physician prescribers
- Limiting access to tests would not prevent laboratories from advertising
- Does advertising a specific use for an ASR create a device requiring premarket approval?

Risk Assessment

- Risk-based review
- Validity of tests
- Consequences of False Negative or False Positive Results
- Seriousness of Disease or Condition
- Role of Genetic Counseling
- Societal Views on what to do with genetic information – does it place unwanted responsibilities on families, health care professionals,

Approved Genetic Test Kits

- FDA has cleared about 12 genetic tests kits
- The PerkinElmer Tandem Mass Spectrometry for newborn screening
- The Roche Amplichip for CYP 45O for metabolic enzyme measurements
- The TM Biosciences Multiplex test for Cystic Fibrosis

Genetic Test Claims of Concern

- Drug metabolism and drug reactions
- Nutritional counseling, vitamins, obesity
- Detecting susceptibility to
  - cardiac disease
  - cancers
  - Loss of bone mineral density, osteoporosis
  - autoimmune disease
  - fatigue syndromes
  - Infectious diseases

Current FDA/FTC activity

- Two recent telephone conferences
- FDA has collected information on laboratory websites with claims for wide range of tests
- FTC evaluating to determine whether there is sufficient basis to proceed on individual sites