Promotion and Advertising of Medical Devices

Enforcement and New Guidance

FDA Symposium

October 1, 2009

Objectives of presentation

- Convey FDA's concerns about off-label promotion and risk information communication
- Provide guidance on how to comply
- Present new guidance information

Regulation of Promotion

- Marketing claims raise issues in different spheres –
  - Patient injury
  - Practitioner liability
  - Manufacturer liability
  - Reimbursement
  - Public understanding of clearance and approval processes
  - Progress of science and medicine through new techniques and studies

Practice of Medicine

- Licensed practitioners' use of regulated products
- Practitioners' promotion of regulated products
- Section 906 of Federal Food, Drug and Cosmetic Act

Some Areas of Concern

- Unapproved Indications or Intended Use
- Comparative Claims
- Direct to Consumer: Imbalances of benefits and risk
- Live case presentations
- Specific claims but general indications
- Genetic Testing
- Combination Products

Statutory Requirements
Federal Food, Drug and Cosmetic Act

- Section 201(h) - defines device
- Section 201(m) - defines labeling
- Section 201(n) - requires material facts in advertising and labeling
- Section 501(f)(1) -adulteration for failure to have approved PMA or IDE
- Section 501(i) – adulteration for investigational devices

Statute, cont'd

- Section 502(a) – misbranding for false or misleading labeling
- Section 502(f)(1) – adequate instructions for use
- Section 502(o) – failure to submit required documentation
- Section 502(q) and (r) – restricted device advertising
- Section 510(k) – submission of premarket notification

Statute, cont'd

- Section 513(f) – Class III by operation of law – important for intended use
- Section 515 – approval for PMA claims and designation of restricted devices
- 520(e) - restricted devices
- 520(g) – investigational devices

Regulations

- 21 CFR 801.4 – intended use
- 21 CFR 801.6 – misleading reference to other FDA regulated product
- 21 CFR 801.109 – prescription device labeling
- 21 CFR 809.10 – Labeling for *in vitro* diagnostic devices

Regulations

- 21 CFR 807.81 – required premarket notification
- 21 CFR 812.7 – promotion of investigational devices
- 21 CFR 814.39 – required premarket approval application

Sources of Violative Materials

- Trade Complaints
- Inspections
- Surveillance of the Internet
- Observation (TV, radio, trade meetings…)
- Labeling

Inappropriate Promotion

- Triage and action based on risk

Process

- Attention letter
- Call to clarify
- Inspection
- Warning or untitled letter based on findings and risk
- Issues arise with how to follow-up noncompliance

Categories of Enforcement Letters

- "It has come to our attention……"
- Warning in Heading
- Otherwise untitled

Enforcement

Examples

Warning Letter

- PMA approved to “deliver beta radiation to the site of successful percutaneous coronary intervention for treatment of in-stent restenosis in native coronary arteries with discrete lesions…in a reference vessel diameter ranging from 2.7 mm to 4.0 mm.”

Journal Advertisement

- Claimed “vascular brachytherapy as adjunct therapy to PCI for patients presenting with ISR of a DES is safe and associated with low rates of recurrence. VBT appears superior in efficacy …and should be considered the therapy of choice for this difficult subset of patients.”

Changed Intended Use

- Treatment of in-stent restenosis in drug eluting stent represented different population
- Thus indication for use different from that approved in PMA
- Vascular healing times different for bare metal and drug-eluting stents
- Different health risks

H1N1

- FDA Flu Task Force
  - http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm166801.htm
  - Fraudulent products and unapproved claims for legally marketed products (masks, gloves, *in vitro* diagnostic products)
  - Ongoing efforts – anticipate 2009-2010 efforts

H1N1

- IVD tests not approved to detect the H1N1 flu virus (some detect Influenza A but not H1N1)
- electronic instrument that claimed to utilize “photobiotic energy” and “deeply penetrating mega-frequency life-force energy waves” to strengthen the immune system and prevent symptoms associated with H1N1 viral infection.

Orthopedic Device Warning Letter

- Device cleared through 510(k) for vertebral body replacement to aid in surgical correction and stabilization of the spine.
- Indicated for use in the thoracolumbar spine (T1 to L5) to replace or restore height of a …vertebral body or portion thereof, excised as a result of tumor or trauma (i.e., fracture).“
- Cleared for use with bone graft

Off Label Claims

- a hollow core to accept autograft or biologics but cleared only for bone graft (autograft or allograft) – see PHN
- surgical implantation of the device in the cervical spine but cleared for use only in the thoracolumbar spine

Public Health Notification

- This is to alert you to reports of life-threatening complications associated with recombinant human Bone Morphogenetic Protein (rhBMP) when used in the cervical spine. **Note that the safety and effectiveness of rhBMP in the cervical spine have not been demonstrated and these products are not approved by FDA for this use.**

Guidance Documents

- Presenting Risk Information in Prescription Drug and Medical Device Promotion (Draft issued May 2009)
- Good Reprint Practices for the Distribution of Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (January 2009)

Risk Information Guidance

- Applies to all classes of regulated devices
- Presents FDA's approach to reviewing promotional material
- Addresses healthcare professionals and consumer directed promotion
- Meant to guide risk information where it is required; does not address alternative sources, as did draft broadcast guidance of 1994.

Risk Communication Guidance

- Based on statutory and regulatory requirements
- “Net impression”
- General Considerations
  - Appropriate Language
  - Signals
  - Framing
  - Hierarchy of risk information

Risk Communication Guidance

- Content Considerations
  - Quantity of information
  - Materiality and Comprehensiveness
    - Target audience
    - Benefit claims
    - Accuracy and comprehensiveness of risk information
- Format Considerations
  - Print
    - Location of Risk Information (Overall and within part of piece)
    - Font size and style
    - Contrast
    - White Space

Risk Communication Guidance

- Format Considerations
  - Non-print
    - Textual Elements
    - Contrast
    - Dual Mode Considerations
    - Audi Considerations

Good Reprint Practices Guidance

- Distribution by manufacturer or representative of medical journal articles or reference publications that discuss unapproved new uses for approved or cleared medical devices marketed in United States

Background

- Section 401 of Food and Drug Administration Modernization Act (FDAMA, 2007) provided conditions under which sponsors could distribute medical and scientific information without being considered to be changing intended use
- Codified at 21 CFR Part 99

Background, cont'd.

- Section 401 ceased to be effective on September 30, 2006
- Guidance intended to provide current views on disseminated of scientific and medical information on unapproved uses of approved or cleared devices
- Federal Food, Drug and Cosmetic Act and implementing regulations generally prohibit manufacturers from distributing in interstate commerce devices not approved or determined to be substantially equivalent to legally marketed predicate

Good Reprint Practices

- FDA recognizes public health and policy justification for dissemination of truthful and non-misleading scientific and medical information
- FDA's legal authority to determine that dissemination of materials constitute promotion of new use has not changed
- Recommends good reprint practices

Good Reprint Recommendations

- Types of Reprints or reference publications that should be distributed:
  - Published by organization with editorial board that uses independent experts and that has policy of full disclosure of conflict of interest
  - Peer reviewed and published in accordance with peer-review procedures
  - Not in the form of special supplement funded wholly or in part by one or more of the manufacturers of the device that is subject of the article

Good Reprint Recommendations

- Publication should not be
  - Primarily distributed by manufacturer
  - Written, edited, excerpted or published for or at request of manufacturer
  - Edited or influenced by manufacturer or anyone with financial relationship with manufacturer

Good Reprint Guidance

- Material should
  - Address adequate and well-controlled clinical investigations
- Material should not
  - Be false or misleading
  - Pose a risk to public health
- Does not include
  - Letters to editor
  - Abstracts
  - Reference publications without substantive discussions

Good Reprint Guidance

- How to Disseminate
  - Unabridged reprint, copy or reference publication
  - Not marked or highlighted by manufacturer except as described below
  - Accompanied by approved labeling
  - Accompanied by bibliography
  - Accompanied by with representative information that provides contrary conclusions
  - Be disseminated separately from promotional material

Reprint Guidance

- Prominent Statement by Manufacturer
  - Uses described are not approved or cleared by FDA
  - The manufacturer's interest in the device
  - Any author known to the manufacturer as having financial interest in the product or who is receiving compensation, along with information on author's affiliation and amount and nature of financial interest
  - Anyone who has provided funding for study
  - Significant risks or safety concerns known to the manufacturer to be related to the unapproved use

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