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How to Implement A System for Review of Product Promotion

Judith E. O'Grady, RN, MSN, RAC
Sr. Vice President
Regulatory, Quality and Clinical Affairs
Integra LifeSciences Corporation

Advertising and Promotion of Medical Devices

- Advertising and Promotion Policies require monitoring on a consistent basis
- Current Environment - Highly competitive and information intense
- Current environment – provides more media venues to advertise and promote products

Federal Food Drug and Cosmetic Act

Label:

- Display of written, printed, or graphic matter upon the immediate container of any article

Section 201(m) defines "labeling" 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" at any time while a device is held for sale after shipment in interstate commerce.

The term "accompanying" is interpreted liberally to mean more than physical association with the product. It extends to posters, tags, pamphlets, circulars, booklets, brochures, instruction books, direction sheets, fillers, etc. "Accompanying" also includes labeling that is brought together with the device after shipment or delivery for shipment in interstate commerce.

Federal Food Drug and Cosmetic Act

Advertising:

- According to an appellate court decision: "most, if not all advertising, is labeling. The term "labeling" is defined in the FFDCA as including all printed matter accompanying any article. Congress did not, and we cannot, exclude from the definition printed matter which constitutes advertising."

What Constitutes Labeling of a Device

- Product Label
- Package Label
- Package Insert
- Directions for Use
- Device Manual
- Product Brochures
- Company Website
- Press Releases
- Video Releases (CD's)
- Information/posters in company exhibits at professional meetings
- Letters to doctors discussing the product claims
- Direct to consumer advertising
- Essentially all information presented on the device

Medical Device – Intended Use

- Under the FFDCA, a medical device may be sold only for intended uses FDA has cleared (510 k) or approved (PMA)
- If firm promotes for a new or expanded intended use, FDA may allege **adulteration/misbranding** for failure to obtain new 510(k) clearance or PMA approval

Determination of Intended Use

- All statements by company, written or oral, labeling or advertising, or website, or other media
  (21 CFR § 801.4)
- Company-generated labeling and advertising may not promote a device for off-label indications
- Includes selective quotations or summaries of “third party” material such as published literature

Determination of Intended Use

- Physicians may use a medical device for an "off-label" use in practice of medicine
- Companies have the incentive to encourage "off-label" use
  - Increase sales
  - Avoid supplemental marketing applications

Continuing Medical Education (CME)

- Sponsoring “independent” CME programs featuring unapproved/off-label uses
- Distributing peer reviewed journal articles with off-label/unapproved use information

Dissemination of Articles for Off-Label Use

- Is it ever permissible to distribute journal articles, textbooks or sponsor CME if off-label information is presented?

Three Safe Harbors

- Unsolicited requests
- Section 401 (21 C.F.R. Part 99 procedures)
- FDA's CME guidance

Unsolicited Requests

- FDA policy that responses to unsolicited requests are excepted from agency regulation as “labeling”
- Scientist/medical officer from the company providing balanced information to health care professional who inquires
- There are limitations and precautions that companies should know

Unsolicited Requests

- Cannot be prompted by the company
- Companies should track number of requests, location to detect “prompting”

Dissemination of Articles for "Off-Label", Unapproved Use

Food Drug and Administration Act Section 401

- Section 401 of FDAMA (1997) allows dissemination of off-label, unapproved use articles/documents
  - Imposes strict requirements
  - If requirements met, allows distribution of journal articles or reference texts discussing unapproved uses

Dissemination of Articles for "Off-Label" Unapproved Use

- Target audience limited to health care practitioners, pharmacy benefit managers, health insurance issuers, group health plans, or a federal or state agency
- FDA must be provided material and summaries of other available clinical data prior to dissemination

Dissemination of Articles for "Off-Label" Use

- The following information must be included:
  - Information relates to an unapproved use
  - Firm/author financial involvement
  - Any other products already approved for the use
  - Bibliography of literature on the new use
  - Existing approved labeling
  - Other disclosures FDA requires for objectivity and balance

Dissemination of Articles for "Off-Label" Use

- The company must commit to either of the following
  - Prior to dissemination, a PMA supplement/510(k) for the use will be submitted;
  - Certify that the studies are complete and a PMA supplement/510(k) will be filed in 6 months;
  - Submit proposed study protocol and schedule for conducting studies and promise to file PMA supplement/510(k) within 36 months
    - FDA must review proposed protocol and schedule and deem them adequate/reasonable
- FDA will review the information and approve/disapprove dissemination of the articles

Procedures by the Company

- Develop Standard Operating Procedure (SOP) for Dissemination of Articles for Unapproved Use
- Procedures for application to FDA
- Procedures for record keeping required by FDA
- Log of who/what/when articles were sent to

Continuing Medical Educations (CME)

- "Final Guidance on Industry Supported Scientific and Educational Activities," 62 Fed. Reg. 64074 (Dec 3, 1997)
- FDA's position is that a program will be deemed "independent of its corporate sponsor" based upon consideration of certain factors as part of an overall evaluation of an activity

Continuing Medical Educations (CME)

- Does company maintain full control over the content, planning of the content, and selection of speakers and moderators?
  - Is there scripting, targeting points for emphasis, or other actions designed to influence the program's content?

Continuing Medical Educations (CME)

- Is there disclosure to the audience at the time of the program of:
  - the company's funding of the program,
  - significant financial relationships between the company, provider, and/or individual speakers, and
  - whether any unapproved uses will be discussed?

CME Sponsorship

- Is the focus of the program educational and free from commercial content or bias, and are all reasonable and relevant treatment option discussed (as compared to focus on a single product)?
- Are there legal, business, or other relationships between the company and provider that could place the company in a position to exert influence over the content of the activity;
- Has the CME provider been involved in the sale or marketing of the company's product?

CME Sponsorship

- Does the provider have a history of conducting programs not meeting standards of independence, balance, objectivity or scientific rigor when putting on ostensibly independent educational programs?

CME Sponsorship

- Other factors
  - Are there multiple presentations of the same program
  - Is the audience selected by the company's sales and marketing department or reflects sales or marketing goals
  - Does live presentation include an opportunity for scientific debate or questioning?
  - Information about the company's product is disseminated by or at the behest of the company
  - Ancillary promotional activities take place in the meeting room
  - Complaints are raised by the providers, presenters, or attendees regarding attempts by the company to influence content

Develop Standard Operating Procedures (SOP's)

- Labeling of products
  - Product labeling
  - Information for Use
  - Product manuals
- Promotional literature
  - Advertisements in professional journals
  - Brochures
- Internet
  - Company web-site
  - Link to other web-sites
- CME education
- Dissemination of articles for unapproved use

Standard Operating Procedures

Label Review and Approval

- Compliance with FDA-Quality System Regulations (QSR) 820.120
- European Medical Device Directive (93/42/EEC)
- EN 980
- Compliance with Regulatory Approval ad Claims received and approved by FDA
- Compliance with company procedures and policies
- Compliance patent, trademark, intellectual property

Standard Operating Procedures

Promotional Material:

Any written, graphical communication that makes or implies any statement about the products

- Intended use
- Physical specifications
- Performance characteristics
- Expected outcome

Standard Operating Procedures

Develop a Review and Approval Matrix

- New Product Package Labels
- New Product Directions for use
- Revised product package labels or directions for use
  - Minor changes
  - Significant changes
- Promotional Materials

Standard Operating Procedures

Review Departments – Promotional Materials:

- Legal
- Regulatory
- Medical Director
- Clinical Department
- Product Managers

Standard Operating Procedures

- Develop Comprehensive SOP's/Procedures
- Develop a system and procedures for tracking the review and approval process
- Develop metrics on the review process
- Training-all departments on regulations and company procedures
- Train all sales and marketing associates
- Train associates on the "cost" of non-compliance

Procedures for CME Educational Programs

- CME educational programs are **important** for **dissemination of information** of on-label indication
- Procedures developed by the company to be in compliance with FDA regulations
- Procedures developed with company Regulatory, Legal, Regulatory, Clinical, Sales and Marketing groups!
- Company should utilize a reputable Third Party Provider who can organize and produce the CME Program.

Unsolicited Requests - Procedures

- Procedures by the company
  - Develop Standard Operating Procedure (SOP)
  - Specify procedures for responding to requests for articles/documents regarding “off-label”, unapproved use
  - Specify who receives requests (Medical Director, Chief Scientific Officer, etc.)
  - How requests are handled
  - Procedures for documenting requests

Corporate Code of Conduct

- Company should develop policies/procedures for a Corporate Code of Conduct

  - Overview of Laws and Codes
  - Advamed Code
  - Anti-Kickback law
  - Educational and Healthcare Practice – related items
  - Consultant meetings
  - Speaker Training
  - Attendance at Speakers Bureau Programs
  - Educational Grant
  - Research Grant
  - False Claims and Privacy Laws Regulations and Policies
  - Violations and Penalties

Corporate Code of Conduct

- Every employee should be trained on Standards of Conduct and the Corporate Code
  - New employee training – including all sales representatives
  - Training annually
  - Training at Sales training and National Sales Meeting
  - All employees sign Code of Conduct
- Penalties of non-compliance with Regulations:
  - Untitled letters
  - Warning Letters
  - Fines and Penalties
  - Criminal penalties

Develop Standard Operating Procedures (SOP's)

- Review by Legal, Regulatory, Sales and Marketing, Clinical departments
- Training – imperative that all involved departments are trained:
  - Sales Representatives
  - Marketing
  - Legal
  - Regulatory
  - Quality
  - Clinical
  - Senior Management
- Senior management must be supportive of procedures and compliance initiatives

References

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  http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch?CFRPart=99
  21 CFR section 812.7
  http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch?cfm?FR=812.7
- **Commercial Distribution with Regard to Premarket Notification (Section 510(k)**
  CPG 300.600 (formerly Compliance Policy Guide No. 7124.19).
  http://www.fda.gov/ora/compliance_ref/cpg/cpgdev/cpg300-600.htm
- **FDA Guidance for Industry: Industry-Supported Scientific and Educational Activities (Nov. 1997)**
  http://www.fda.gov/cder/guidance/isse.htm
- **Guidance for Industry on General/Specific Intended Use**
  http://www.fda.gov/cdrh/modact/genspec.html

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  http://www.fda.gov/cdrh/dsma/470.pdf
- Write it Right
  http://www.fda.gov/cdrh/dsma/897.pdf
- Device Labeling Guidance #G91-1 (blue book memo)
  http://www.fda.gov/cdrh/g91-1.html
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  http://www.fda.gov/cdrh/ohip/guidance/1128.html
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- Human Factors Principles for Medical Device Labeling
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References

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  http://www.fda.gov/cdrh/mdufma/bluebook/g03-1.html
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- **RX Labeling:** Alternative to Certain Prescription Device Labeling Requirements
  http://www.fda.gov/cdrh/comp/rxlabeling.html
  http://www.fda.gov/cdrh/comp/rxlabeling.pdf

THANK YOU !

QUESTIONS ?