Device Off-Label Promotion: Difficult "Intended Use" Questions

Pharmaceutical Regulatory & Compliance Congress
November 3, 2011

Greg Levine

FDA Device Center's Expansive View of "Intended Use"

- Draft Guidance, Commercially Distributed IVD Products Labeled for Research Use Only or Investigational Use Only (June 2011)
  - In determining manufacturer's intended use, FDA will consider sales to labs the manufacturer knows, or has reason to know, use the product in clinical use, and support (including technical support) for such use
  - If a manufacturer learns that a clinical lab to which it sells its IUO/RUO-labeled IVD product is using these IVDs non IUO/RUO use, it should halt sales or comply with FDA premarket review requirements

Device On-Label Promotion– Difficult Questions

- Promoting specific indication within broader approved/cleared use
- Promoting to pediatricians and pediatric hospitals
- Providing training to physicians or assistance during medical or surgical procedures

General/Specific – Lack of FDA Guidance

- FDA regulations require a new 510(k) when a previously cleared device is about to undergo a "major change or modification in the intended use of the device."
  - **21 C.F.R. 807.81(a)(3)(ii)**

General/Specific – Lack of FDA Guidance

- Guidance for Industry, “General/Specific Intended Use” (1998)
  - A second related issue is, when would a specific intended use that falls within a general use not require a submission of any kind, i.e. be considered a use already cleared under a current 510(k)? This question will not be directly addressed in this document. Guidance in making that determination is available in the ODE guidance document entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device."

General/Specific – Lack of FDA Guidance

- Guidance for Industry, "Deciding When to Submit a 510(k) for a Change to an Existing Device" (1997)
  - A ... difficult case is where the change [in indications for use] expands use to closely related populations. In determining whether [such] a change … raises issues of safety or effectiveness, the manufacturer should ask whether the change poses any additional risks, expands the use to a new and distinguishable patient population, etc. If the expansion is to a population with similar demographics, diagnosis, prognosis, comorbidity and potential for complications … then a new 510(k) is not ordinarily expected.

General/Specific – Questions

- May manufacturers promote to specialists if a device has a general clearance but is known to be used in particular procedures?
- Must manufacturers deduct “off label” uses that fall within general use from sales rep quotas?
- Will the ongoing 1st Amendment litigation have an impact?
- When do manufacturers have a duty to ask FDA what it thinks? What process should be followed?

Pediatric Promotion – Lack of FDA Guidance

- FDA, "Premarket Assessment of Pediatric Devices" (2004)
  - Age Ranges of Pediatric Subgroups

Newborn (neonate)	Birth to 1 month
Infant	1 month to 2 years
Child	2 to 12 years
Adolescent	12 to 21 years

  - FDA will consider a pediatric use to be any use of a medical device in a pediatric population, as defined above, in which there is a primary pediatric indication. General indications, where considerable pediatric application is anticipated, are also included.

Pediatric - Questions

- If a device does not specify adult or pediatric use, may a manufacturer:
  - Promote to pediatricians?
  - Promote in pediatric institutions?
  - Promote to non-pediatricians known to do a substantial number of pediatric procedures?
  - Buy exhibit space or sponsor CME at pediatric conferences?
  - Donate product or cash to pediatric charities?

Providing Assistance During Procedures – Lack of FDA Guidance

- If you find some, please let me know!

Training & Assistance During Procedures - Questions

- May a device company train a doctor on an off-label use? In response to a request to do so?
- May a device rep be present during an off-label procedure?
- Is there a duty to notify the physician/surgeon that a use is off label? If so, when?
- What can the device rep do or not do during the procedure?
- What can the rep say or not say during the procedure?

Off-Label Promotion – Conduct Alleged in Other Cases

- Use of studies to “create a market”
- Patent filings claiming off-label use
- Targeting physicians with off-label specialties
- Unsolicited literature dissemination
- Sales quotas tied to off-label sales
- Unrestricted grants for research or teaching on off-label uses
- Trade show booths at symposia featuring off-label discussions
- Comparative claims against “on label” devices

Off-Label Promotion: Lessons Learned

- Consider breadth of indication carefully in establishing regulatory strategy
- Do not assume that an indication is not required just because nobody else has it
- Do not assume a 1st Amendment right to disseminate all truthful information
- Consider “execution risk” by sales personnel and third party speakers
- Be familiar with the government’s compliance expectations as shown through Corporate Integrity Agreements

Off-Label Promotion: Lessons Learned

- Mandate regulatory/legal review of all
  - "Labeling" and advertising of any kind, including press releases and web site
  - Internal training materials
  - HCP training programs, advisory boards, etc.
  - Speaker program materials
  - Continuing medical education support
  - Reimbursement support programs
  - Compensation plans? Marketing plans?