Preparing *your* Sales Force

Keeping Legal Issues in Mind, From Training to Trial

Part I of II

Preparing Your Sales Force on the Front End — Initial Training[1]

To the learned intermediary, the face of your company is not the board of directors, not your Chief Executive Officer; not your scientists, physicians, and epidemiologists; and not the multitude of people with whom you may interact on a day-to-day basis, who address the regulatory, manufacturing, and distribution issues related to your products. Rather, to a physician using or prescribing your device or drug, the face he or she most often associates with your company is that of the sales representative. This face could be someone who has been with your company for twenty years or a young twenty-two year old, fresh out of college and working in a full-time job for the first time. Perhaps most importantly, this face may also be the one that a jury associates with your company at trial and whose testimony may be instrumental in securing a favorable defense result. The importance of training and preparing your sales representatives — from a sales perspective and testimony perspective — cannot, therefore, be understated. This article, while not exhaustive, provides a list of possible actions to take during initial training that will give your sales representatives the foundation to be successful in the field and ultimately may limit your company's exposure.

Initial Training: Compliance

It goes without saying that sales representatives should be trained on anatomy and physiology, medical terminology, and pharmacology, and must undergo training tailored to the specific drugs or devices that the individuals may be detailing. Likewise, sales skills lessons are important to ensure that a consistent, focused message gets to the end user in the manner intended. From a legal perspective, compliance training — teaching the sales representatives what they can and cannot say, do, or use when calling on physicians or other healthcare providers — merits special attention. Educating representatives on the underlying rules and regulations which govern their sales activities and potential ramifications for failing to adhere to the federal, industry, and company mandates, provides context for their application of your company's policies.

I. Federal Regulations

A. The Approval Process

Although the approval history of a particular drug or device may not seem important on its face in training sales representatives, its purpose is twofold. First, it gives the trainees an appreciation and understanding of what has gone into developing the drug or device

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and getting it to market; second, it offers a history of the development of the labeling — which will essentially provide the four corners within which the sales message must be contained. If applicable, a review of the development process should also include a backgrounder on the relevant clinical trials used by the company to prove the product's safety and effectiveness to the FDA, knowledge which the sales personnel may find helpful in fielding questions from physicians. For a pharmaceutical product, the approval history would include a review of the investigational new drug (IND) application and the new drug application (NDA). For a medical device, this would include a review of the investigational device exemption (IDE), the Premarket Approval (PMA) application, or the Premarket Notification (510k) submission, depending on the device.

Furthermore, a review of the approval process exposes sales representatives to those regulations which form the background of their compliance mandates. Sales representatives are able to see, first-hand, that the FDA heavily regulates labeling and marketing materials. As a result, they may develop a better understanding of why certain things such as off-label promotion and undocumented sampling are off limits.

B. Key Regulations Regarding Sales and Promotion of Drugs and Devices

1. Regulations Regarding Off-Label Promotion

To secure FDA approval for a drug or medical device, the manufacturer must demonstrate that the product is safe and effective for its intended use as labeled.[2] The Food, Drug, and Cosmetics Act defines labeling as "all labels and other written, printed, or graphic matters […] upon any article or any of its containers or wrappers, or […] accompanying such article."[3] The regulations define labeling as:

> Brochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints and similar pieces of printed, audio, or visual matter descriptive of a drug, and references published (for example, the *Physician's Desk Reference*) for use by medical practitioners, pharmacists, or nurses, containing drug information supplied by the manufacturer, packer, or distributor of the drug and which are disseminated by or on behalf of its manufacturer, packer, or distributor are hereby determined to be labeling as defined in section 201(m) of the FD&C Act.[4]

Regardless of what promotional *item individuals use when detailing,* sales representatives should always *provide and/or present a package insert* with every promotional material *given to or reviewed by a physician.*

The FDA considers the approved product labeling to be adequate directions for use and adequate warning.[5]

The product's uses that are approved by the FDA are sometimes referred to as "labeled" uses because they appear in the product's approved labeling.[6] Uses that do not appear in the labeling and that are not approved by the FDA are often referred to as "off-label" uses.[7] Off-label uses can include a physician's using an FDA-approved drug to treat a condition not indicated in the drug's FDA approved labeling, using the drug to treat an indication but changing the dosing, or using the drug for a different patient population from that in the drug's approved labeling.[8] While it is clear that a physician may prescribe a drug for any means he or she deems appropriate, regardless of whether that drug has been approved for use for that purpose by the FDA, the same standard does not apply for off-label marketing of a drug or device.[9] In fact, a manufacturer may promote a product only for its intended uses; to do otherwise would be considered "misleading," and the product itself would be deemed "misbranded." Some examples of marketing activities that would qualify as misleading under the regulations are:

- promoting a product by suggesting that a product is better, more effective, safer, or has fewer or less serious side effects than have been demonstrated by substantial evidence or substantial clinical experience;
- representing that a product is safer or more effective than another product when no such proof exists;
- using literature, quotations, or references for the purpose of recommending or suggesting conditions of use that are not permitted or approved in the package labeling; and
- using a pictorial or other graphic matter in a way that is misleading.[10]

a. Penalties for Off-Label Promotion

Avoidance of civil and criminal liability, both for the company and individually, is a powerful incentive for employees to adhere to company policy and FDA regulations. As illustrated by a slew of recent enforcement actions, the government is committed to detecting and prosecuting off-label promotion. For example, in 2004, the federal government began investigating Eli Lilly for the off-label promotion of Zyprexa. By January 2009, Lilly was facing criminal prosecution by the U.S Attorney, a civil investigation by the federal government, and civil investigations brought by the State Medicaid Fraud Control Units of the states, all relating to the off-label promotion of Zyprexa. On January 15, 2009, Eli Lilly agreed to enter a global resolution of the criminal and civil action.

Altogether, Lilly agreed to pay over $1.4 billion and enter into a Corporate Integrity Agreement with the Office of the Inspector General of the U.S. Department of Health and Human Services to settle the civil and criminal claims.[11]

According to Gregory G. Katsas, Assistant Attorney General for the Department of Justice Civil Division, the settlement with Lilly "demonstrates the Department's ongoing diligence in prosecuting cases involving violations of the Food, Drug, and Cosmetic Act and recovering taxpayer dollars used to pay for drugs sold as a result of off-label marketing campaigns."[12] That "diligence" was on display just days later when Pfizer announced as part of its 2008 fourth quarter earnings a $2.3 billion charge resulting from an agreement in principal with the United States Attorney from the District of Massachusetts "to resolve previously disclosed investigations regarding allegations of past off-label promotional practices concerning Bextra, as well as other open investigations."[13]

Sales representatives may also have personal exposure for their actions. In February of this year, a former medical device company sales manager pled guilty in federal court to one count of felony misbranding for illegally promoting the combined use of devices approved only for individual applications.[14] At sentencing in May, he faces up to three years in prison, followed by one year of supervised release and a $250,000 fine.

b. What You Can Do to Minimize the Possibility of Off-Label Promotion

Developing a program to minimize the possibility of off-label promotion will help develop a sales force with the tools and the training to promote in accordance with the regulations and policies. Moreover, a thoroughly developed and properly applied training program can help you demonstrate at trial that your company has a commitment to full compliance with the federal mandates. Elements to consider which will minimize the potential for off-label promotion include the following:

Draft Written Standard Operating Procedures/Codes of Conduct

Enact written standard operating procedures (SOP) for promotion and marketing, and have your sales force trained and tested on the procedures. Enact and enforce a code of conduct based on the SOPs, and have your sales personnel sign a certificate stating that they have been trained on the SOPs and that they will pledge to follow them in the course and scope of their jobs.

Audit Your Sales Team

Periodically audit your sales team, from the detail representatives all the way up to senior management. The audit should include a review of promotional materials, call notes, speakers, and sales team meeting agendas and minutes.

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Assess Each Brand for Risk

Some products will be more susceptible to off-label use by physicians than others. Identify which products may fall into this category and proactively train and retrain the sales personnel responsible for promoting these products.

Train, Train, and Retrain

Sales personnel in the field should be constantly reminded of their detailing obligations and restrictions. Representatives should be promptly trained and retrained upon the issuance of new regulations or guidance.

Establish a Written Protocol to Handle Off-label Questions

Sales representatives expect off-label questions from their healthcare provider clients. Sales personnel should be trained to automatically default to the written company protocols for referring off-label questions to the company's medical relations/professional relations departments. Off-label discussions should *never* originate from the sales representative.

Establish a Written Protocol for Use of Call Notes

If your sales force uses call notes, the call notes should accurately reflect any detailing sessions where an off-label question comes up. The note should explain the nature of the question, actions taken by the representative, and the manner in which follow-up took place. Call notes should never merely reference an off-label question, inquiry, or discussion without making it clear that: 1) the discussion was initiated by the physician, not the sales representative; and 2) that the question was referred to the medical representatives per company protocol.

Train Sales Representatives on Proper Distribution of Medical Journal Articles on Unapproved Uses

In its recent January 2009 industry guidance document,[15] the FDA addressed its position on the distribution of medical journal articles or publications regarding unapproved uses. While the guidance document should be referenced for the complete details, in sum, scientific or medical journal articles that are distributed should be: a) reputable; b) peer-reviewed; c) neither published nor influenced by drug or device manufacturers; d) supported by sound clinical investigations or trials; e) distributed in unabridged form without marks, notes, or highlights; f) accompanied by the label; g) distributed separately from promotional materials; h) accompanied by a statement describing the information therein as an unapproved use; i) accompanied by conflict of interest

statements; and j) accompanied by a listing of significant risks associated with unapproved uses not referenced in the journal.

No Homemade Sales Pieces

All sales and detail pieces should be approved and distributed by the company. Any homemade sales pieces — to include modification of existing approved sales pieces — should be viewed as a violation of company protocol resulting in counseling or termination.

Make It Clear Violations Will Not Be Tolerated

Sales personnel should be informed in writing that violations involving off-label promotion are serious and could result in not only a negative review and/or termination, but could also result in civil and/or criminal liability.

Reiterate and Review Exactly What Comprises Off-Label Usage

The current indications and labeling should be well understood by the sales team. If it is not in the label, it cannot be promoted.

2. Regulations Regarding Sampling

Product sampling is an effective way to provide physicians with a means to distribute samples of your product to patients. A drug sample is defined as a unit of the drug "that is not intended to be sold […] and is intended to promote the sale of the drug."[16] Furthermore, "No person may sell, purchase, or trade or offer to sell, purchase, or trade any drug sample."[17] Pharmaceutical companies may provide samples to practitioners upon request so long as the samples provided to physicians are documented by the physician's name, date, quantity of drug, and type of drug.[18] The sample form should be signed by the healthcare provider receiving the samples.[19] Liability associated with improper sampling methods can be limited by the following:

- ensuring that all sampled products are accompanied by the appropriate package inserts and, if required, the appropriate patient information sheet;
- training the sales representatives to inform the sample recipients that the samples provided may not be sold or billed (this can be incorporated in the sample receipt form signed by the healthcare provider);
- labeling individual samples as sample units that cannot be sold;
- ensuring that all sample recipients verify samples and sign for samples;
- training sales representatives to keep accurate sampling records; and
- conducting periodic, random sampling audits to ensure that sample inventories maintained by sales representatives match the sample distribution paper trail.

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3. Regulations Regarding Fair Balance

Promotional and advertising materials must present a fair balance between effectiveness and risk information.[20] The fair balance requirement is set forth in greatest detail with regard to advertising; essentially the same requirements apply with respect to promotional labeling through the FDCA provisions that prohibit false or misleading statements.[21] Related to the fair balance requirement is the mandate that prescribing information accompany most pieces of advertising and promotional materials.[22] Prescribing information in and of itself though is not adequate to meet the fair balance requirements; the promotional materials must still present the information in a manner not only consistent with the labeling, but also in a balanced, equitable fashion.[23]

The only promotional materials sales representatives should use are the ones distributed to the sales force by the company. Accordingly, issues regarding fair balance in promotional materials should be addressed at the outset by representatives from marketing, legal and regulatory prior to distribution to the sales force. Regardless of what promotional item individuals use when detailing, sales representatives should always provide and/or present a package insert with every promotional material given to or reviewed by a physician. Sales representatives should also be timely notified to stop using any and all distributed promotional materials which the FDA may later deem misleading or lacking fair balance.[24]

II. Industry Guidance

In addition to the guidance provided by the federal regulations and statutes, companies may also look to industry standards for ethical behavior between healthcare professionals and pharmaceutical and medical device companies. These standards provide a supplement to the regulatory guidelines and provide further proof in the courtroom that your company is taking steps — over and above the federally mandated requirements — to ensure that the sales and marketing message is delivered consistently and equitably in an ethical, responsible manner.

For pharmaceuticals, the Pharmaceutical Research and Manufacturers of America (PhRMA) has promulgated guidelines via its *Code on Interactions with Healthcare Professionals*.[25] For devices, the Advanced Medical Technology Association (AdvaMed) likewise recently revised its *Code of Ethics on Interactions with Health Care Professionals*.[26] For training purposes, the principles

in both Codes provide an ethical compass that sales representatives may use as a reference point — alongside the federal regulations — when detailing their products. Topics covered in the respective Codes include the following:

- cash payments, gratuities, and gifts to healthcare providers;
- educational and practice-related items to healthcare providers;
- entertainment and recreational activities for healthcare providers;
- product sampling;
- conference and meeting guidelines;
- continuing medical education (CME) guidelines and subsidies;
- third-party conferences;
- grants and donations;
- financial assistance, scholarships, or educational funding for medical students;
- sales and promotional meetings;
- consultants;
- reimbursement, billing, coding, and other technical information to healthcare professionals;
- research funding;
- formulary issues; and
- sales force training guidance.

In addition, the PhRMA Code provides a good summary of what companies should consider when training their sales force which touches on many of the subjects raised here:

Companies should ensure that all representatives who are employed by or acting on behalf of the companies and who visit healthcare professionals receive training about the applicable laws, regulations, and industry codes of practice, including this Code, that govern the representatives' interactions with healthcare professionals. In addition, companies should train their representatives to ensure that they have sufficient knowledge of general science and product-specific information to provide accurate, up-to-date information, consistent with FDA requirements.

Companies should provide updated or additional training in all of these areas as needed for their representatives who visit healthcare professionals.

Companies should also assess their representatives periodically to ensure they comply with relevant company policies and standards of conduct. Companies should take appropriate action when representatives fail to comply.[27]

III. Conclusion

As plaintiffs' trial strategies continue to evolve more and more towards alleged marketing and promotional violations, it is imperative that sales representatives have a thorough understanding and appreciation of the compliance obligations inherent in their job. A comprehensive training program provides a foundation for these individuals to effectively challenge any such allegations while also providing the company with an effective way to demonstrate that, at all times, regulatory and industry compliance was at the forefront of its marketing plan.

[1] Part II of this series, which will appear in the next *Pro Te: Solutio*, will focus on preparing your sales representatives if and when they are called to testify at deposition or trial.

[2] 21 U.S.C. §355.

[3] 21 U.S.C. §321(m).

[4] 21 C.F.R. §202.1(l)(2).

[5] *See* Food and Drug Administration, Center for Drug Evaluation and Research, Advertising/Labeling Definitions at <http://www.fda.gov/cder/handbook/adverdef.htm>.

[6] 59 Fed. Reg. 59820 (Nov. 18, 1994).

[7] *Id.*

[8] Fritch, David M., *Speak No Evil, Hear No Evil, Harm the Patient? Why the FDA Needs to Seek More, Rather Than Less, Speech from Drug Manufacturers on Off-label Drug Treatments,* 9 Mich. St. J. Med. & Law 315, 332 (2005).

[9] *Washington Legal Foundation v. Henney*, 202 F.3d 331, 333 (C.A.D.C. 2000).

[10] 21 C.F.R. 202.1(e)(6). This list is illustrative and not exhaustive.

[11] "Lilly Resolves Investigations of Past Zyprexa Marketing and Promotional Practices," *available at* <http://newsroom.lilly.com/releasedetail.cfm?ReleaseID=359242>.

[12] USDOJ Press Release "Eli Lilly and Company Agrees to Pay $1.415 Billion to Resolve Allegations of Off-Label Promotion of Zyprexa."

[13] "Pfizer Reports Fourth-Quarter and Full-Year 2008 Results and 2009 Financial Guidance" *available at* <http://www.pfizer.com/news/press_releases/pfizer_press_releases.jsp>.

[14] *United States v. Demming*, No. 1:08-CR-10379-NG. *agreed statement of facts filed* (D. Mass. Feb. 10, 2009); "Salesman Admits to 'Off-label' Medical Device Promotion, 16 No. 1 Andrews Med. Devices Litig. Rep. 3.

[15] *Available at* <http://www.fda.gov/oc/op/goodreprint.html>.

[16] 21 U.S.C. §353(c)(1).

[17] *Id.*

[18] 21 U.S.C. §353(d)(3)(A).

[19] *Id.*

[20] *See* DDMAC Frequently Asked Questions at <http://www.fda.gov/cder/ddmac/faqs.htm#presentation>.

[21] Bruce N. Kuhlik, "The FDA's Regulation of Pharmaceutical Communications in the Context of Managed Care: A Suggested Approach," *50 Food & Drug L.J.* 23, n. 83 (citing 21 C.F.R. §201.1(l)(e)(6),(7); 21 U.S.C. §§502(a), 201(n).

[22] *Id.* at 38; *see also*, 21 C.F.R. §§201.100(d), 202.1(e).

[23] *See* DDMAC Frequently Asked Questions at <http://www.fda.gov/cder/ddmac/faqs.htm#presentation>.

[24] Companies are required to submit promotional materials "at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product." 21 C.F.R. §314.81(b)(3)(i). FDA may subsequently require withdrawal or revision of sales pieces if deemed misleading or lacking fair balance.

[25] *Available at* <www.phrma.com>. For an in-depth analysis of the PhRMA Code, *see* Baltz, Melissa, "The New PhRMA Code and the Potential Benefits of Compliance," *Pro Te: Solutio*, 2.1, 10.

[26] *Available at* <www.advamed.com>.

[27] PhRMA *Code on Interactions with Healthcare Professionals* at 7.

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