Focus on Life Science Compliance: The Evolution of Medical Affairs Departments

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This article addresses the evolution of medical affairs departments and a variety of key issues that are relevant to pharmaceutical and medical device manufacturers that are establishing or maintaining medical affairs departments. The first section considers the question, "what is medical affairs?" and attempts to define this relatively amorphous function. The second section provides an overview of regulatory and subregulatory guidance applicable to medical affairs departments. The third section discusses several evolving issues that are important for medical device and pharmaceutical companies to consider when evaluating their medical affairs departments. Lastly, this article discusses five medical affairs best practices for medical device and pharmaceutical companies.

"What Is Medical Affairs"?

"Medical affairs" is the broad term that describes the department within a pharmaceutical or medical device company that interacts with physicians and other healthcare professionals who utilize or are involved with research related to the companies' products. Medical affairs departments typically handle a wide variety of medical communications with prescribers, the provision of grants to fund investigators studies, as well as various additional research and other tasks.[1] Communications overseen by a medical affairs department may include responding to requests for information about off-label usage, publications, safety information, and independent medical education.

As discussed in the following section, while the government has encouraged the formation of independent medical affairs departments (sometimes referred to as "clinical affairs" departments), there is not a rigid set of requirements that dictate how a medical affairs department should look or operate. As such, the industry has developed a wide variety of models over the past 20 years, all seeking to address the intensified public and regulatory scrutiny applied to the pharmaceutical and medical device industries.[2]

Generally, medical affairs departments are staffed with personnel that have advanced degrees that enable them to understand and effectively communicate the science behind a device or pharmaceutical product. Medical affairs directors are commonly doctors of medicine (MDs) or doctors of pharmacy (Pharm Ds) and medical affairs departments typically are staffed with medical science liaisons (MSLs) who have advanced masters degrees, Pharm Ds, or MDs to enable them to interact with physicians and healthcare professionals on a professional level.[3]

Are Medical Affairs Departments Required by Law?

As indicated above, medical affairs departments are not the creature of any statutory or regulatory requirement. Instead, they have been developed by industry and encouraged by the Food and Drug Administration (FDA) and the U.S. Department of Health and Human Services Office of Inspector General (OIG) to facilitate effective and legally compliant communications and interactions between life science companies and healthcare professionals. The convention of creating and maintaining a medical affairs department is clearly endorsed by the OIG and the FDA as evidenced in agency guidance and various corporate integrity agreements (CIAs). The establishment and maintenance of a robust medical affairs department is considered a defense against intent-based statutes.

One of the earliest agency guidance releases to address separation between sales and marketing and

various medical affairs functions is found in the OIG's 2003 Compliance Guidance for Pharmaceutical Manufacturers (Compliance Guidance).[4] According to the OIG, separation of sales and medical affairs is critical with respect to research, consulting, and grant funding.[5] For instance, the OIG recognizes that "many grant-funded activities are legitimate and beneficial," but notes that "contracts that originate through the sales or marketing functions—or that are offered to purchasers in connection with sales contacts—are particularly suspect."[6] Furthermore, the OIG advises that compliance with applicable healthcare regulations requires that pharmaceutical manufactures ensure that grant funding is totally independent from physician referrals for manufacturer products.[7]

In addition to the Compliance Guidance, the OIG and Department of Justice (DOJ) have included recommendations for the establishment of medical affairs departments, or the performance of certain functions by medical affairs departments, in a variety of CIAs entered into between the OIG and specific pharmaceutical companies. The September 2008 Cephalon CIA, related to Cephalon's alleged off-label drug promotion, required that the manager of medical affairs, in addition to the managers of other high-risk departments, certify as to the department's compliance with federal healthcare program requirements, FDA requirements under the Food, Drug, and Cosmetics Act (FDCA), and attendant regulations, and the obligations of the CIA.[8]

More recently, the August 2010 Allergen CIA, related to alleged off-label marketing of Botox, required Allergen's sales representatives to refer all requests for information about off-label use of Allergen products to Allergen's medical affairs department, and also required that any materials distributed by the medical affairs department related to off-label drug use are consistent with FDA statutes, regulations, and written directives.[9] While CIAs do not set forth binding regulatory obligations with general applicability to pharmaceutical and medical device companies, they do constitute the OIG's concept of "best practices" for the industry and shed light on what the government believes is necessary to be compliant.

An additional source of government guidance can be found in the FDA's distinction between the "marketing of medical products" and conducting "scientific exchange." In guidance on industry-supported scientific and educational activities, the FDA has stated that while it does regulate marketing of medical products, it does not have the authority to regulate the full scientific exchange of information with healthcare professionals.[10] This means that the FDA cannot prevent physicians from asking about off-label uses of products and unapproved uses of products nor can the FDA prevent pharmaceutical and medical device companies from responding to these questions and engaging in scientific exchange.

This issue was heavily litigated in the Washington Legal Foundation (WLF) series of cases with the FDA, in which the WLF challenged the FDA's restrictions on manufacturers' dissemination of off-label, peer-reviewed scientific articles and support for continuing medical education.[11] The U.S. District Court for the District of Columbia issued an injunction limiting certain aspects of FDA's restrictions on off-label speech and finding certain provisions of the FDCA as amended by the FDA Modernization Act (FDAMA) unconstitutional. However, the District of Columbia Circuit found the case moot after FDA argued that the FDAMA provisions regarding off-label promotion operate only as a "safe harbor" and do not create any new or independent enforcement rights.[12]

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While the FDA cannot regulate scientific exchange, it is important for medical device companies to distinguish scientific exchange from marketing activities. This can best be accomplished through the implementation of formal policies and procedures that create a firewall between the medical and commercial functions—this is discussed in more detail below.

Evolving Issues for Medical Affairs Departments

As discussed above, the lack of clear regulatory requirements for a medical affairs department, combined with the evolving state of the life science industry, has led to a number of issues for medical device and pharmaceutical companies to consider when establishing and maintaining a medical affairs department.

Medical Science Liaisons. The increased use of MSLs or regional medical liaisons to engage in scientific exchange with physicians, including key opinion leaders (KOLs), necessitates robust policies and procedures, and comprehensive training of MSLs and sales and marketing employees. KOLs are physicians who influence their peers' medical practice, including but not limited to prescribing behavior. Over the past ten years, the sales forces employed by pharmaceutical and medical device companies have decreased substantially. According to consulting firm ZS Associates, by the end of 2008, the number of U.S. sales representatives dropped to 90,000 from a peak of about 106,000 in 2006.[13] This trend is expected to continue as the life science companies' marketing efforts shift away

from mass marketing campaigns and move toward targeted marketing for specialty products.[14] At the same time, the *Wall Street Journal* reports that the number of MSLs employed by life science companies has increased steadily, totaling 1,970 in 2008, up 48% from 1,335 in 2003, according to data for 12 major pharmaceutical and biotech companies compiled by PharmaForce International, a market-research firm.[15] Further, recent data suggest that medical affairs departments are spending as much as 19% of their budgets on MSL programs.[16] Thus, companies are reallocating a significant portion of their marketing budget to fund medical compliance through MSL programs.

As the use of MSLs increases, the compliance issues surrounding such practices increase. For example, MSLs must be constantly assessed to ensure they are remaining compliant with the array of regulations affecting scientific communication. Here, it is important that MSLs not revert to the role of sales personnel and engage in off-label promotion of medical products.

FDA Off-Label Publications Guidance. The FDA recently has issued final guidance on the dissemination of off-label communications, off-label journal articles, and enduring materials.[17] Many pharmaceutical and medical device manufacturers engage in the dissemination of these materials to prescribers. The FDA recognizes this practice and the "important public health and policy justification supporting dissemination of truthful and non-misleading medical journal articles and medical or scientific reference publications on unapproved uses of approved drugs and approved or cleared medical devices to healthcare professionals and healthcare entities."[18]

The guidance limits the types of materials that should be disseminated to scientific or medical journal articles that are peer-reviewed, published by an organization with an editorial board that utilizes reviewers with expertise in the subject of the article under review, and are not be written for or at the request of a drug or device manufacturer or otherwise significantly influenced by a drug or device manufacturer.[19] With regard to the manner of dissemination of materials, the scientific or medical information distributed should be in the form of an unabridged reprint or copy of an article or reference publication, accompanied by the approved labeling from the drug or medical device, distributed with any existent publications that reach contrary or different conclusions regarding the unapproved use, and distributed separately from material that is promotional in nature.[20]

One of the primary tasks of most medical affairs departments is to oversee the dissemination of materials that discuss off-label uses. The recent guidance offers a safe process for medical affairs departments to facilitate this form of scientific exchange.

Funding of Independent Clinical Trials. The OIG is increasing scrutiny on the funding of investigator-initiated studies by pharmaceutical grants. As demonstrated by the government's recent settlement with UCB Pharmaceuticals, the use of grants to fund investigator-initiated research can pose risks if the outcomes of the research are utilized improperly to engage in off-label promotion. UCB Pharmaceuticals allegedly promoted Keppra, a drug approved as an anti-epileptic, for use in the treatment of migraines. The UCB CIA builds upon UCB's existing compliance program.

Specifically, the CIA requires that UCB develop policies related to the way it will handle requests for off-label uses of its products and the manner and circumstances under which its medical affairs department participates in interactions with healthcare professionals and healthcare institutions. The OIG also addressed potential concerns that grant funding by pharmaceutical companies could also constitute an inducement for referrals, running afoul of the federal Anti-Kickback Statute (AKS). In response to this concern, the CIA requires UCB to implement written policies and procedures relating to the appropriate ways to conduct promotional and product services-related functions, such as grant funding, in compliance with the AKS. Further, the CIA requires UCB to establish a grant monitoring program to conduct audits of medical education grants to ensure compliance with applicable UCB policies, such as UCB's policy that the sales and marketing departments have no involvement in, or influence over, the review and approval of medical education grants.[21]

Globalization of Medical Affairs. As life science companies are increasingly becoming global entities, the medical affairs department also must develop capabilities to support the company's operations in the countries in which it is operating. It is common for global drug companies to have medical affairs staff on the ground in most countries where their products are marketed. However, a 2008 study that surveyed pharmaceutical companies about the structure of their medical affairs departments revealed that only about 26% of participating companies had global medical affairs functions in place.[22] The same study determined that most drug manufacturers are expanding medical affairs responsibilities worldwide to enhance communication with medical professionals and develop better treatments.[23] Companies must successfully coordinate medical affairs functions between all of the countries in which the company operates. Furthermore, as the European Union develops more standardized regulations for clinical trials and marketing communications, medical affairs teams are preparing to develop more integrated policies, guidelines, and strategies to incorporate European markets.[24]

Best Practices for Establishing and Maintaining a Medical Affairs Department

With these issues related to medical affairs departments in mind, there are several key best practices that can be implemented by pharmaceutical and medical device manufacturers.

- *Independence of Medical Affairs.* The OIG has made it clear that a medical affairs department must have meaningful separation from commercial departments within a pharmaceutical or medical device company.[25] This does not mean that medical affairs personnel are not allowed to interact with the other employees. However, a company should work to establish meaningful separation from commercial departments. For example, interactions between

commercial personnel and MSLs should be appropriately managed and safeguards should be implemented to ensure that interactions do not run afoul of the company's culture of compliance. Moreover, sales personnel should not have the ability to use grant programs to incentivize purchases of product.

- *Reporting Structure.* Medical affairs departments should report up to an organization's C-suite, compliance officer, or research and development, rather than to a commercial department. Further, the OIG believes it is generally not advisable for the compliance function to be subordinate to a manufacturer's general counsel, or comptroller or similar financial officer.[26]
- *Funding.* A medical device or pharmaceutical company cannot establish meaningful separation between its commercial organization and medical affairs if the medical affairs department is reliant on sales to provide all or a portion of its funding on a periodic basis. Therefore, separate line items in budgets should be established for medical affairs and this funding should not be dependent on the achievement of sales or marketing targets. Although some flexibility based on growth is acceptable, the funding decisions should not be sales driven. Further, funding should be adequate to appropriately staff the compliance aspects of the department.
- *Off-Label Literature.* Although not all life science companies have elected to fully comply with the FDA's final guidance for dissemination of off-label literature, it is important that companies establish a policy that governs the dissemination of off-label materials. The policy should elect and implement the risk option that best suits the individual. For example, some medical device and pharmaceutical companies permit unsolicited dissemination of publications that discuss off-label uses. Others limit dissemination of these materials only to situations where a healthcare professional affirmatively requests the information. Regardless of the risk determination made by the company, a policy should memorialize the acceptable practice to ensure guidance is available for all personnel.
- *Grant Review Boards.* If the medical affairs department is charged with providing medical education funding or investigator-initiated trial funding, education grant and trial grant boards should be established. The board should be comprised of primarily medical affairs and research and development staff and should be provided with clear guidance related to its decision-making protocol when evaluating study funding applications and grant requests. While grants and studies may support medical education or trials on off-label or unapproved uses, the grant board itself should have the guidance on how it should be making its decisions.
- *Medical Science Liaisons.* Medical affairs departments should establish clear guidance for the role of MSLs within the company. Specifically, MSLs should know how the organization expects them to respond to off-label use inquires and how to respond to grant, medical education, and investigator-initiated trial grant requests, as well as a variety of other issues. Establishing clear guidance for MSLs can help to ensure that MSLs do not become extensions of the sales organization. Medical affairs programs should keep documented evidence of MSL training. Such documentation should include retention of materials discussed, training logs that reflect the attendees, training session times, and the results of any tests or quizzes conducted during training. In the event of an investigation, an organization's ability to produce such documentation will demonstrate a commitment to compliance, and may provide evidence of individual rather than organizational non-compliance.

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- *Compliance with Federal and State Marketing Laws.* Following the passage of the Patient Protection and Affordable Care Act of 2010, pharmaceutical and medical device manufacturers must report any payment or transfer of value made to healthcare professionals and academic medical centers. In addition, several states have adopted marketing transparency laws applicable to pharmaceutical and medical device companies. These reports include research grants and honoraria for participating in medical education programs. Such laws generally require some combination of the following elements (1) adoption of a compliance plan, (2) registration with a state agency, (3) disclosure of certain payments or transfers of value, and (4) prohibitions on certain transfers, including samples. Medical affairs departments often are responsible for compliance with these various laws and should maintain state-specific policies and procedures, and implement tracking mechanisms to track and report all transfers of value.
- *Establishing and Maintaining an Active Compliance Program.* A medical affairs department should have current policies and procedures to support a culture of compliance, and should ensure employees and organizational leadership undergo training on the same. The department should have policies that address the dissemination of off-label literature, responding to solicited and unsolicited requests for information regarding off-label usage grant funding, medical letters, screening consultants, MSL relationships with physicians and KOLs, disclosure of payments to healthcare professionals, and any other activity that falls under the purview of the medical affairs department. As the law

changes, policies and procedures also should be updated, and employees affected by such changes should be trained accordingly. Policies and procedures that are nothing more than dust collectors on a book shelf will be inadequate to defend the organization in the event of an OIG or FDA investigation.

It is vital for pharmaceutical and medical device companies to stay abreast of ever-changing regulations and "best practices" in the area of medical affairs. Doing so can help avoid violations of law and ensure a culture of compliance. C

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