

**Gleaning Some Practical Compliance Advice Concerning “Off Label” Promotion from Recent Corporate Integrity Agreements and FDA Guidance**

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Life Sciences companies that make and sell products that may be used by providers for non-FDA approved (i.e., “off label”) purposes continue to grapple with the competing pressures of promoting their products while operating within the confines of laws and regulations restricting “off label” promotion. Recent industry developments, including corporate integrity agreements and FDA guidance, have added greater detail to some of the practical issues that Life Sciences should consider when implementing their compliance policies and procedures. In this paper, we suggest that Life Sciences companies use these developments as a point of comparison when assessing the adequacy of their processes and procedures for managing, tracking, and monitoring dissemination of medical information to health care providers, particularly where such medical information concerns “off label” uses of drugs or devices.

***Background***

In recent years, spurred on in many instances by *qui tam* relators, the Department of Justice and other government agencies have actively pursued investigations and enforcement actions against Life Sciences companies targeting allegedly improper promotion of “off label” or unapproved uses of FDA-regulated drugs and devices. Some of these actions involve allegations concerning the allegedly inappropriate dissemination of medical information about “off label” uses. In this regard, several recent corporate integrity agreements between HHS-OIG and several Life Sciences companies following on the heels of “off label” investigations (“Off-Label

CIA’s”),<sup>1</sup> presumably embodying HHS-OIG’s and other interested federal agencies’ views on “best” or “good” compliance practices, set forth specific requirements for the tracking and monitoring of medical information.<sup>2</sup> In this regard, therefore, these recent CIAs can be viewed as setting forth practical guidance for other Life Science companies to consider when reviewing the efficacy of their own compliance policies and procedures governing the distribution of materials and information pertaining to “off-label” device or drug uses.

*Channeling Information Requests and Responses Through a “Gatekeeper”*

With regard to distribution of information about “off-label” product use, the Off-Label CIAs anticipate in the first instance that instead of distributing information directly to providers, Life Sciences sales representatives will refer all information requests and inquiries to a separate functional business area. The separate business area is, in turn, charged with abiding by policies that address: (1) the types of information that may be distributed; (2) the manner in which the company responds to requests; (3) the form and content of the information disseminated; and (4) the internal review process for the information disseminated. In essence, the CIAs require “off-label” information requests and responses to be handled by a “gatekeeper” distinct from the sales function and responsible for ensuring compliant handling of those requests and responses. The “gatekeeper” thus serves as a compliance “check and balance.”

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<sup>1</sup> E.g., *Corporate Integrity Agreement Between the Office of Inspector General of the Dept. of Health and Human Svcs. and Pfizer, Inc.*, (Aug. 31, 2009) available at <http://oig.hhs.gov/fraud/cia/agreements/pfizerinc.pdf>; *Corporate Integrity Agreement Between the Office of Inspector General of the Dept. of Health and Human Svcs., and Eli Lilly and Co.*, (Jan. 14, 2009) available at [http://oig.hhs.gov/fraud/cia/agreements/elililly\\_and\\_company\\_01142009.pdf](http://oig.hhs.gov/fraud/cia/agreements/elililly_and_company_01142009.pdf); *Corporate Integrity Agreement Between the Office of Inspector General of the Dept. of Health and Human Svcs. and Cephalon, Inc.*, (Sept. 29, 2008) available at <http://oig.hhs.gov/fraud/cia/agreements/cephalon.pdf>.

<sup>2</sup> By referencing these CIAs, we in no way suggest, or endorse any view to the contrary, that the subject companies’ historic compliance policies and procedures were deficient. Nor do we endorse the government’s theory of liability in cases involving truthful “off-label” promotion that “bootstraps” a technical violation of the Food, Drug, and Cosmetics Act into a False Claims Act case.

Looking at this “gatekeeper” function in a practical manner, not all Life Sciences companies will necessarily have the resources to support an entire business function dedicated exclusively to information dissemination. Nonetheless, the underlying concept — namely, that a separate “gatekeeper” should vet and monitor “off-label” information requests — is seemingly scalable. For instance, if unable to create and support an entire business unit dedicated to the task, a smaller company could form a compliance and review committee comprising senior executives to serve as the “gatekeeper” which would, presumably, meet the oversight aspirations embodied in the Off-Label CIAs.

### ***Tracking and Monitoring Information Distribution to Providers***

The Off-Label CIAs also set forth, with particularity, how the “gatekeeper” should document its “off-label” compliance procedures. The CIAs anticipate databases designed to track all requests for information about products and responses thereto, and dictate the minimum level of data that must be captured in the database, including: (1) dates and form of inquiry; (2) identity of the requesting health care provider; (3) nature and topic of requests (including verbatim recording of written requests); (4) nature/form of the response (including a record of the materials provided); and (5) the name of the associated sales representative(s) who requests the information or who called on the requesting provider. Thus, the Off-Label CIAs require a log of all communications, including their contents where possible, between the company and providers concerning information bearing on “off-label” product use.

HHS-OIG also expects close monitoring of the “gatekeeper’s” tracking database. Specifically, the CIAs require policies and procedures that include a process whereby an alert is triggered when certain systematic threshold of sales representative facilitated medical information requests are exceeded. These thresholds can include, for example, an inordinate

number of requests for “off-label” information from a particular sales representative. They might also include other indicia of potentially improper conduct.

*Practical Takeaways from the Off-Label CIAs*

We can glean from the Off-Label CIAs several practical elements for compliance “best practices,” at least as HHS-OIG sees them. First, control over the dissemination of “off-label” information might ideally be ceded to a “gatekeeper,” a business unit or function separate and distinct from the sales function. Again, for smaller companies unable to establish a business unit exclusively dedicated to this function, a distinct committee or other group might be considered. This “gatekeeper,” in turn, would assume responsibility for ensuring compliant information dissemination practices. Second, to the extent possible, a company should track, with as much detail as possible, all requests for “off-label” information (e.g., reprints of articles from scientific journals). Indeed, in the current regulatory environment, a Life Sciences company should consider tracking all information flow between sales representatives and health care providers to the extent possible. Such additional information could include product specifications, marketing materials, or other clinical information. Third, if implementing a formal tracking system, Life Sciences companies should take the affirmative step of monitoring or auditing information-related data for purposes of discerning potentially problematic trends or aberrations. For instance, a sales representative who initiates dozens of putative provider requests for a reprint concerning an “off-label” study should trigger further compliance review in order to determine whether the surrounding circumstances raise any compliance concerns.

*The FDA's Recent Reprint Guidance*

In a related development, the FDA recently published substantive guidance concerning the dissemination of reprints addressing “off-label” or unapproved uses of drugs and devices.<sup>3</sup> (Such reprints are the type of information for which the Off-Label CIAs require tracking and monitoring.) The FDA categorizes the types of scientific and medical information that should or should not be distributed, and recommends, for the types of information that may be distributed, a number of “good reprint practices.” Reproduced in their entirety, these recommendations state as follows:

*Scientific or medical information that is distributed should:*

- *be in the form of an unabridged reprint, copy of an article, or reference publication;*
- *not be marked, highlighted, summarized, or characterized by the manufacturer in any way (except to provide the accompanying disclosures discussed in this section);*
- *be accompanied by the approved labeling for the drug or medical device;*
- *be accompanied, when such information exists, by a comprehensive bibliography of publications discussing adequate and well-controlled clinical studies published in medical journals or medical or scientific texts about the use of the drug or medical device covered by the information disseminated (unless the information already includes such a bibliography);*
- *be disseminated with a representative publication, when such information exists, that reaches contrary or different conclusions regarding the unapproved use; especially those in cases where the conclusions of articles or texts to be disseminated have been specifically called into question by another published article (s) or text(s); and*

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<sup>3</sup> *Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices* (January 2009), available at <http://www.fda.gov/oc/op/goodreprint.html>

- *be distributed separately from information that is promotional in nature. For example, if a sales representative delivers a reprint to a physician in his office, the reprint should not be physically attached to any promotional material the sales representative uses or delivers during the office visit and should not be the subject of discussion between the sales representative and the physician during the sales visit. Similarly, while reprints may be distributed at medical or scientific conferences in settings appropriate for scientific exchange, reprints should not be distributed in promotional exhibit halls or during promotional speakers' programs.*

*The journal reprint or reference publication should be accompanied by a prominently displayed and permanently affixed statement disclosing;*

- *that the uses described in the information have not been approved or cleared by FDA, as applicable to the described drug or medical device;*
- *the manufacturer's interest in the drug or medical device that is the subject of the journal reprint or reference text;*
- *any author known to the manufacturer as having a financial interest in the product or manufacturer or who is receiving compensation from the manufacturer, along with the affiliation of the author, to the extent known by the manufacturer, and the nature and amount of any such financial interest of the author or compensation received by the author from the manufacturer; [footnote omitted]*
- *any person known to the manufacturer who has provided funding for the study; and*
- *all significant risks or safety concerns known to the manufacturer concerning the unapproved use that are not discussed in the journal article or reference text.*

Though these “good reprint practices” are not technically backed by the force of law, given their source, prudence dictates that Life Sciences companies strongly consider implementation of policies and procedures to meet these recommendations. While a substantive analysis of these requirements is beyond the scope of this paper, we suggest that the very specific FDA reprint guidance, coupled with HHS-OIG’s emphasis on tracking information dissemination in the recent CIAs, underscores the need for Life Sciences companies to know, in detail, the who/what/why/how/when of their sales representatives’ communications with providers to the extent possible.

*Conclusion*

The government's interest in how Life Sciences companies provide information to providers concerning "off label" or unapproved uses of drugs and devices will not wane in the foreseeable future, and compliance policies and procedures in this area remain important. In light of the HHS-OIG's emphasis, as embodied in recent CIAs, on the tracking and monitoring of "off label" information as part of an overall compliance program, and the specificity of the FDA's "good reprint practices," Life Sciences companies may want to consider if and how they might be able to improve their capabilities with respect to managing, tracking, and monitoring their dissemination of product-related information to health care providers.

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