FDLI UPDATE
Food and Drug Law, Regulation and Education

Available Online
Free to Members
www.fdli.org

Register for FDLI's Food Week: February 5–8, 2013 | www.fdli.org

U.S. & Brazil Conference Photos and Recap

More inside on page 34

Enforcement Issue

contents

Issue 6 ▪ November/December 2012

*EDITOR'S NOTE: There was an error in the Sept/Oct issue of Update magazine. Martha Healey, Partner, Norton Rose LLP, was listed as the author for "The Safe Food for Canadians Act." The correct author of the article is Sara Zborovski, Partner, Gilbert's LLP. The error has been corrected in the Sept/Oct digital issue.

FDLI News

Columns

UPDATE
Food and Drug Law, Regulation and Education

ISSN: 1075-7635 - Issue 6 (2012)

General Information:

Update is published six times per year by The Food and Drug Law Institute (FDLI).

FDLI is a non-profit organization that provides a marketplace for discussing food and drug law issues through conferences, publications and member interaction. The scope of FDLI includes food, drugs, animal drugs, biologics, cosmetics, diagnostics, dietary supplements, medical devices and tobacco. As a not-for-profit 501(c)(3) organization, FDLI does not engage in advocacy activities.

Articles and any other material published in *Update* represent the opinions of the author(s) and should not be construed to reflect the opinions of FDLI, its staff or its members. The factual accuracy of all statements in the articles and other materials is the sole responsibility of the authors.

Diversity Policy Statement:

In principle, and in practice, FDLI values and seeks a diverse and inclusive membership and welcomes full participation by all people, regardless of race, gender, creed, age, sexual orientation, national origin or disability.

Membership:

FDLI members receive *Update* as a part of their membership. For information about membership, contact FDLI's Membership Department at 202-371-1420 or membership@fdli.org.

Subscription:

Subscription to *Update* is available for $100.00 per year (6 issues). Additional copies or back issues are available at $50.00 each. Individual articles are available at $25.00 each. To order, contact Customer Service at 202-371-1420 or comments@fdli.org.

Article Contributions:

We invite you to share your expertise and perspective and to comment on articles or ideas covered in recent issues of *Update*. All manuscripts are subject to editing for style, clarity, sexist language, and length. Manuscripts and inquiries should be directed to Michael Levin-Epstein, Editor-in-Chief, FDLI, 1155 15th St., NW, Ste. 800, Washington, DC 20005, via e-mail to mdl@fdli.org, or via telephone at 202-222-0897.

Send notices of change of address to FDLI six to eight weeks in advance. Please include both old and new addresses. Notices also may be sent to comments@fdli.org.

Advertising in *Update*:

If you would like to see your organization or product in *Update*, and reach nearly 7,000 of the industry's key decision makers, contact Stephanie Barnes for advertising rates and a media kit at 202-222-0894 or skb@fdli.org

Application to mail at periodicals postage rates is pending at Washington, DC and at additional mailing offices.

ECO BOX

Update text and cover pages are printed on SFI-certified Anthem Matte paper using soy ink.

- The Sustainable Forestry Initiative® program promotes sustainable forest management.
- The Sustainable Forestry Initiative® program integrates the perpetual growing and harvesting of trees with the protection of wildlife, plants, soils, and water.
- The Sustainable Forestry Initiative® program promotes responsible forest management.

ISSN: 1075-7635 Issue 6 (2012)

PRINTED WITH SOY INK

SUSTAINABLE FORESTRY INITIATIVE Certified Sourcing www.sfiprogram.org SFI 00284

Postmaster:
Send changes of address to:

FDLI *Update*
1155 15th St., NW, Ste. 800
Washington, DC 20005

Unsolicited Requests From Companies Conducting Product Evaluation/Formulary Placement:

Processes and regulatory/legal considerations for manufacturers

By Elizabeth Sampsel, Bridget Olson and David Restaino

Recent fines by the federal government for off-label marketing highlight the critical regulatory and legal environment that pharmaceutical and medical device manufacturers continue to face. Off-label use is the practice of prescribing pharmaceuticals or using medical devices for an indication or intended use in an age group, dose or dosing schedule, duration of use, or route of administration not contained in the approved product labeling (i.e., package insert [PI]). While it is considered lawful for a physician to independently decide to prescribe a drug or use a medical

Elizabeth Sampsel is the Assistant Director at Pharmacy Affairs at the Academy of Managed Care Pharmacy and is the AMCP staff liaison for the AMCP Format Executive Committee.

Bridget Olson is a member of the Dymaxium Healthcare Innovations executive board and the original architect of the AMCP eDossier System.

David Restaino is a Partner at Fox Rothschild LLP, and is based out of the firm's Princeton, NJ Office.

device for off-label indications when in the best interest of a patient, it is illegal for manufacturers to promote off-label uses of their products or devices.

FDA Guidance

For years, the pharmaceutical industry has been looking for ways to effectively communicate the value and/or superiority of their companies' products, while adhering to often vague compliance guidelines surrounding how requests are classified, as well as what constitutes an appropriate, legally acceptable response. More recently, the medical device manufacturers have come under the same scrutiny by government officials and are now facing similar challenges. As presented in a May/June 2012 Update magazine article, the Food and Drug Administration (FDA) recently released draft guidance to the industry, entitled "Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices."[1, 2] The article provided an overview of the Guidance, including distinctions between solicited and unsolicited requests, handling of non-public and public unsolicited requests, implications for the industry, and several unanswered questions related to online and social media promotion topics.

FDA Overview

Elaine Hu Cunningham, Senior Regulatory Review Officer with the FDA's Office of Prescription Drug Promotion (OPDP), also recently presented an overview of the [Draft] Guidance at the 24th Annual Meeting & Expo of the Academy of Managed Care (AMCP).[3] In her presentation, Cunningham highlighted examples through which the distinction between solicited and unsolicited requests is made clear. Specific guidelines to which firms should adhere to regarding responses to requests, accompanying documentation that should be provided to the requestor along with the requested information, and the maintenance of detailed records - including the nature of the request, details related to the requestor and the provided response – as well as any follow up inquiries from the requestor were also highlighted.

Industry Examines Impact

Also presenting at the April 2012 AMCP Meeting, Iris Tam, Pharm.D., Director of Managed Care Medical Communications at Genentech, and a member of the AMCP Format Executive Committee focused on the impact of the Guidance on the industry and P&T and pharmacy and therapeutics and formulary processes.[4] According to Dr. Tam, the Guidance has been highly anticipated by the industry. In general, however, she stated that the principles and practices of medical communication departments across the industry already align with the new Guidance, as their practices have been informed by previous FDA opinions.

Opportunities for Mitigating Risk

In addition to discussing the Guidance in general terms, Dr. Tam also provided an overview of mechanisms by which the industry complies with previously communicated FDA opinions and the current [Draft] Guidance, including the AMCP *Format for Formulary Submissions (*AMCP *Format)* – a template and guideline for standardizing product related information provided by drug companies to health care decisions makers (HCDMs) upon an authentic unsolicited request.[5] Comprehensive product dossiers, created according to the AMCP *Format,* contain product information, clinical studies (on-label and off-label), disease background, comparative effectiveness research, treatment guidelines, technology assessments, economic studies, and economic models. The purpose of the *Format* is to improve timeliness, scope, quality, and relevance of information provided in response to an unsolicited request, as well as streamline the evidence acquisition and review processes performed by decision makers across the health care sector.

Upon review, criteria outlined within the AMCP *Format* were found to generally align with the FDAs' [Draft] Guidance, including those related to the requirement of an unsolicited request, confidential provision of a dossier containing off-label evidence, documentation of the request, inclusion of truthful, non-misleading, accurate, and balanced scientific information, and inclusion of a product's full FDA-required labeling and primary resources and citations (upon request).

Documentation of unsolicited requests for off-label information is a critical risk management process for many companies. Developed as a companion distribution mechanism for dossiers prepared in accordance with the AMCP Format, the AMCP eDossier System has also been designed to, not only improve the effective and timely communication of critical evidence during the decision making process, but also to further mitigate risks associated with the provision of product dossiers, which may contain off-label information.[6] The System both streamlines and strengthens the request and documentation processes associated with unsolicited requests for such information. It also provides an additional layer of security for manufacturers by requiring that HCDMs not only initiate the request electronically, but that they also verify that the request is truly unsolic-

ited before being granted access to the product dossier.

Most importantly, the provision of off-label information to a HCDM must be documented in detail, according to the new Guidance. Many manufacturers have invested significant resources (human and financial) to ensure that appropriate documentation is entered, validated, and stored. Medical and Outcomes Liaison teams across the industry are trained to carefully listen to the requests of HCDMs, supply the most accurate and relevant information, and then document, not only the response, but the details leading up to the submission of the unsolicited request. These activities are in line with the FDA Guidance, however, they pose significant challenges to manufacturers in day-to-day practice as they cannot risk omissions in their documentation processes given the regulatory environment.

The eRequest Tool within the AMCP eDossier System provides several critical features that can assist these teams, as well as their legal and regulatory departments, with monitoring compliance to unsolicited request guidelines. A few key capabilities of the eRequest Tool include: (a) registration process that ensures individuals accessing the System, via a password-protected login, are true health care decision makers (HCDM); (b) opportunity for HCDMs to clearly, concisely, and electronically communicate specific requests for information to manufacturers via a centralized, online tool (i.e., eRequest); and (c) ability for a manufacturer to track the history of all requests initiated by HCDMs and fulfilled in a single location. With the eDossier System, compliance officers have a potential single source of independently validated information to review statistics on the number of requests, individuals requesting information, and the type of information requested. Because the System is self-contained, there are no additional steps required to collate this information from multiple sources, or manually enter requests from various team members into a separate database. In addition, this data may be exported for use by legal/regulatory teams for reporting purposes – making audit trails seamless. The eRequest Tool is available at no cost to all qualified health care decision makers and all manufacturers.

Furthermore, the way in which the systems were designed [facilitate adherence to the draft guidelines by including] accompanying product information such as a PI, a prominent statement that the use is not FDA approved, a prominent statement of the FDA-approved indications, a prominent statement providing all important safety information, and references for all information disseminated in the response. These core pieces of information can be easily included as electronic Appendices to a product's eDossier, accessible 24/7 by the requesting party.

And So We Wait

While the industry awaits FDA's release of the final-Guidance (comment period ended in March 2012), it appears that those manufacturers utilizing some of the currently available resources and tools are complying with these regulatory guidelines. Even so, all current policies, procedures, and systems of operation should be examined going forward and updated in an effort to retain integrity of information supplied to HCDMs in response to unsolicited requests for off-label information. It is also critical that manufacturers have effective systems in place to ensure the collection and tracking of critical compliance data related to, strike and, insert for information after requests.

Case Study: Potential Implementation of the eRequest Tool for Unsolicited Requests

A hypothetical, yet realistic, example based on discussions with legal representatives, health care decision makers, and pharmaceutical manufacturers is outlined below.

Pharmaceutical company A has had several drugs receive new indications in the past 2 years, and also is anticipating the launch of at least two new products pending FDA approval within the next 18 months. As expected, the company has received a large number of unsolicited requests for information both on the existing products with new indications, but also for data related to the products in development.

Tracking the status of these requests as well as documenting that the requests are within current guidelines and addressed in a timely manner has been challenging. Recently, a company audit found that request came in from over 200 managed care and hospital/IDS formulary decision-makers and that these were sent to over 35 different company employees. Each of these requests had to be manually logged into a database as well as manually verified for adherence to company policy. There were numerous areas where errors could have been made using the current process, and the number of individuals involved often resulted in delays in getting information to key stakeholders.

Company A decided to leverage the eRequest Tool on the AMCP eDossier System to help streamline the process and also speed up the approval and delivery of information. The majority of unsolicited requests were being submitted through the eRequest system.

Individuals who submit a request outside the system receive a standard message directing them to use the eRequest system.

All requestors are already pre-screened by the System to be qualified decision makers that meet FDA guidelines on the type of individuals who are eligible to receive this type of information. If the requestor is a registered user, the request for information is forwarded automatically. If the company has dossier information on the system, the request can be fulfilled immediately by the manufacturer. If the company needs to manually fulfill the request, it is forwarded to the company contact for fulfillment.

- The System tracks the following information for review and audit:
- Requestor name, title, company, telephone, email
- Requested information
- Date Requested
- Direct verification of the unsolicited request by the originating requestor
- Date fulfilled (if automatic)
- Close date (documentation manual request was fulfilled)
- Individual fulfilling manual request

The above information is available for immediate download and review by manufacturers (and their legal counsel) so that audits may be done in real time or retrospectively.

- After implementation, Company A was able to:
- Ensure all requestors met the definition of a qualified health care decision maker
- Evaluate the types of requests received
- Store all information regarding requests/requestors in single database
- Conduct quality Improvement analysis on fulfillment times
- Prevent documentation errors by using a single request system vs. manual entries and multiple email requests

References

1. Restaino D. FDA'S New Off-Label Guidance: What it Says and What it Leaves Unanswered. Update. Food and Drug Law Institute (FDLI). May/June 2012: pp 44-46.
2. 76 Fed. Reg. 82303 (Dec. 30, 2011), Guidance available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM285145.pdf (PDF) Accessed 7/9/2012.
3. Cunningham EH. FDA Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices. Presented at AMCP's 24th Annual Meeting & Expo, San Francisco, CA (April 20, 2012).
4. Tam I. FDA Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices and the AMCP Format for Formulary Submissions. Presented at AMCP's 24th Annual Meeting & Expo, San Francisco, CA (April 20, 2012).
5. AMCP Format Executive Committee. The AMCP *Format for Formulary Submissions, Version 3.0*. October 2009. Available at: http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=9917. Accessed 7/9/12.
6. Dymaxium Healthcare Innovations, Ltd. (DHI). AMCP eDossier System by DHI. Available at: https://amcp.edossiers.com/global/default.aspx. Accessed 7/9/12.