Guidance for Industry

Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

January 2014
Advertising

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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's or Agency's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This draft guidance is intended to describe FDA's current thinking about how manufacturers, packers, and distributors (firms), that may either be the applicant or acting on behalf of the applicant, of prescription human and animal drug and biological products (drugs) can fulfill regulatory requirements for postmarketing submissions[1] of interactive promotional media for their FDA-approved products.[2,3] For the purposes of this guidance, the phrase *interactive promotional media* includes modern tools and technologies that often allow for real-time communications and interactions (e.g., blogs, microblogs, social networking sites, online communities, and live podcasts) that firms use to promote their drugs. Although some interactive promotional media are substantially similar in presentation and content to certain traditional promotional media, such as print media, FDA recognizes that in other cases they possess certain unique technological features and offer novel presentation and content features. This draft guidance describes FDA's current thinking on what the Agency considers to be interactive promotional media and outlines the considerations taken into account in determining if product communications using interactive technologies are subject to FDA's postmarketing submission requirements. Furthermore, this draft guidance provides FDA's recommendations for how firms can fulfill the regulatory requirement to submit postmarketing promotional materials to the FDA in a practical manner to address the potential

[1] 21 CFR 314.81(b)(3)(i); 21 CFR 601.12(f)(4); and 21 CFR 514.80(b)(5)(ii). See Section III for a detailed description of these postmarketing submission requirements.

[2] This draft guidance has been prepared by the Office of Prescription Drug Promotion (OPDP) in the Center for Drug Evaluation and Research (CDER) in consultation with the Center for Biologics Evaluation and Research (CBER) and the Center for Veterinary Medicine (CVM).

[3] The recommendations in this draft guidance also apply to biological products that are approved for marketing under section 351 of the Public Health Service Act (PHS Act). Because each biological product also meets the definition of "drug" or "device" under the Federal Food, Drug, and Cosmetic Act (FD&C Act), it is also subject to provisions of the FD&C Act applicable to drugs or devices, as well as the regulations implementing these provisions, except that a biological product licensed under section 351 of the PHS Act is not required to have an approved new drug application under section 505 of the FD&C Act (21 U.S.C. 355). See PHS Act section 351(j), (42 U.S.C. 262(j)). The recommendations in this draft guidance do not apply to veterinary biological products regulated under the Virus-Serum-Toxin Act (21 U.S.C. 151, et seq.) by the U.S. Department of Agriculture.

volume of real-time information that is continuously posted and shared through various interactive promotional media platforms.

The organization of the draft guidance is as follows: after some background information regarding postmarketing submission requirements (Section II), a brief legal overview of statutory and regulatory requirements for labeling and advertising is presented, including postmarketing submission requirements (III). Then, considerations related to submission of interactive promotional media are discussed with some illustrative examples (IV), and, finally, FDA's recommendations for submitting such promotional materials are provided (V).

FDA's guidance documents, including this draft guidance, do not establish legally enforceable rights or responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

FDA's regulation of prescription drug product promotion extends both to promotional activities that are carried out by the firm itself, and to promotion conducted on the firm's behalf. In determining whether the firm is accountable for a communication about its product(s), the Agency considers whether the firm or anyone acting on its behalf is influencing or controlling the product promotional activity or communication in whole or part. Firms may have a variety of options for how much control they exert over activities that utilize interactive promotional media, regardless of whether the promotional activity occurs on firm-sponsored or third-party venues. For example, a firm may promote its products through product websites, discussion boards, chat rooms, or other public electronic forums that it maintains and over which it has full control. In addition, third-party sites (i.e., websites and other venues that are either entirely independent of a firm's control and influence, or not fully controlled by a firm) may promote a firm's products.

As part of the postmarketing reporting requirements under the Federal Food, Drug, and Cosmetic Act (FD&C Act), application holders are required to submit all promotional labeling and advertising pieces at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a drug. However, for some interactive promotional media, submission "at the time of initial dissemination" may pose a challenge for firms, particularly when these media communicate information that is displayed in real time. While "at the time of initial dissemination" does not refer to submissions on a weekly, monthly, or other routine schedule, FDA intends to exercise its enforcement discretion under certain circumstances due to the high volume of information that may be posted within short periods of time using interactive promotional media that allow for real-time communications. If a firm submits interactive promotional media in the manner described in this draft guidance, FDA intends to exercise enforcement discretion regarding the regulatory requirements for postmarketing submissions related to promotional labeling and advertising.

III. LEGAL OVERVIEW OF STATUTORY AND REGULATORY REQUIREMENTS FOR LABELING AND ADVERTISING

Under the FD&C Act, the Agency has responsibility for regulating the manufacture, sale, and distribution of drugs in the United States. This authority includes oversight of the labeling and advertising of prescription drugs and biologics (21 U.S.C. 352 (a) & (n)).

Section 201(m) of the FD&C Act defines *labeling* as "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article" (21 U.S.C. 321(m)).[4] The U.S. Supreme Court has explained that the language "accompanying such article" in the "labeling" definition is interpreted broadly, to include materials that supplement or explain an article. No physical attachment between the materials and the article is necessary; rather, it is the textual relationship between the items that is significant. *Kordel v. United States*, 335 U.S. 345, 350 (1948). FDA generally recognizes two types of labeling for drugs: FDA-required labeling and promotional labeling. Promotional labeling is generally any labeling, other than the FDA-required labeling, that is devised for promotion of the product. Examples of promotional labeling pieces are described at 21 CFR 202.1(l)(2).

Also, under the FD&C Act and FDA's implementing regulations, the applicant shall submit specimens of mailing pieces and any other labeling or advertising devised for promotion of the drug product at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product. Each submission is required to be accompanied by a completed Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) (21 CFR 314.81(b)(3)(i) and 21 CFR 601.12(f)(4)).

For prescription and over-the-counter new animal drugs, the applicant must submit at the time of initial dissemination one set of specimens of mailing pieces and other labeling. For prescription new animal drugs, the applicant must also submit one set of specimens of any advertisement at the time of initial publication or broadcast. Each submission of promotional labeling or advertisements must be accompanied by a completed Form FDA 2301 (21 CFR 514.80(b)(5)(ii)).

IV. FACTORS CONSIDERED IN DETERMINING POSTMARKETING SUBMISSION REQUIREMENTS FOR INTERACTIVE PROMOTIONAL MEDIA

FDA considers the following in determining a firm's responsibility for submitting interactive promotional media to FDA as required by postmarketing submission requirements:

1. A firm is responsible for product promotional communications on sites that are owned, controlled, created, influenced, or operated by, or on behalf of, the firm.

Such product promotional communications may include firm-sponsored microblogs (e.g., Twitter), social networking sites (e.g., Facebook), firm blogs, and other sites that are under the control or influence of the firm. In determining whether a firm must submit promotional material about its product(s) to FDA, the Agency considers whether the firm, or anyone acting on its behalf, is influencing or controlling the promotional activity or communication in whole or part. Thus, a firm is responsible if it exerts influence over a site in any particular, even if the influence is limited in scope. For example, if the firm collaborates on or has editorial, preview, or review privilege over the content provided, then it is responsible for that content.

Example 1: A firm provides on its product website an online forum that gives users the opportunity to post comments about the use of its product. In this case, the firm is responsible for submitting to FDA the product website to meet the postmarketing submission requirements because the firm created, owns, or

[4] See also 21 CFR 1.3(a).

operates the website. (See the discussion regarding user generated content (UGC) on firm-owned or firm-controlled venues at the end of this section.)

2. Under certain circumstances, a firm is responsible for promotion on third-party sites.

A firm is responsible for promotion on a third-party site if the firm has any control or influence on the third-party site, even if that influence is limited in scope. For example, if a firm collaborates, or has editorial, preview, or review privilege, then it is responsible for its promotion on the site and, as such, that site is subject to submission to FDA to meet postmarketing submission requirements. However, if a firm provides only financial support (e.g., through an unrestricted educational grant) and has no other control or influence on that site, then the firm is *not* responsible for information on a third-party site, and has no obligation to submit the content to FDA. Furthermore, if a firm is merely providing promotional materials to a third-party site but does not direct the placement of the promotion within the site and has no other control or influence on that site, the firm is responsible only for the content it places there and, thus, is responsible only for submitting to FDA promotional content that was disseminated on that site.

Example 2: A firm does not have any control of, or influence on, information on an independent third-party site but chooses to promote its product on this site (e.g., by providing specific promotional content such as firm-initiated UGC). In this situation, to meet postmarketing submission requirements, the firm is responsible for submitting to FDA the promotional content it provided to the site. (See Section V for FDA's recommendations for how to submit.)

Example 3: A firm makes suggestions on the placement of its promotional messages on an independent third-party site. Because the firm influenced the placement of its promotion within the third-party site, the firm is responsible for submitting to FDA the promotion, along with the surrounding pages, to adequately provide context to facilitate the review of the third-party site, in order to fulfill the postmarketing submission requirements.

In summary, regardless of financial support, if a firm has any control of, or influence on, the third-party site, even if limited in scope, it is responsible for submission to FDA to meet the postmarketing submission requirements.

3. A firm is responsible for the content generated by an employee or agent who is acting on behalf of the firm to promote the firm's product.

FDA's regulation of prescription drug product promotion extends both to promotional activities that are carried out by the firm itself, and to promotion conducted on the firm's behalf. Therefore, a firm is responsible for the content generated by its employees or any agents acting on behalf of the firm who promote the firm's product. For example, if an employee or agent of a firm, such as a medical science liaison or paid speaker (e.g., a key opinion leader) acting on the firm's behalf, comments on a third-party site about the firm's product, the firm is responsible for the content its employee or agent provides. A firm is also responsible for the content on a blogger's site if the blogger is acting on behalf of the firm. Therefore, a firm is responsible for UGC and communications of its employees or anyone acting on behalf of the firm and, as such, those materials are subject to submission to FDA to meet the postmarketing submission requirements.

All UGC meeting these parameters for interactive promotional media should be submitted to the FDA as recommended below in Section V.

Example 4: A sales representative acting on behalf of a firm posts comments about the innovative release mechanism of the firm's product on an independent third-party site. Because the sales representative is acting on behalf of the firm, the firm is responsible for submitting the comments to FDA to meet the postmarketing submission requirements.

Example 5: A representative of a firm, such as a blogger paid by the firm, maintains a blog about the firm's product. The firm is responsible for submitting the blog to FDA to meet the postmarketing submission requirements.

FDA recommends that a firm be transparent in disclosing its involvement on a site by clearly identifying the UGC and communications of its employees or third parties acting on behalf of the firm. This could be achieved by inclusion of the firm's identifier (e.g., name or logo) as part of the communication. However, a firm generally is not responsible for UGC that is truly independent of the firm (i.e., is not produced by, or on behalf of, or prompted by the firm in any particular).[5] FDA will not ordinarily view UGC on firm-owned or firm-controlled venues such as blogs, message boards, and chat rooms as promotional content on behalf of the firm as long as the user has no affiliation with the firm and the firm had no influence on the UGC.

FDA recommends that a firm submit to the Agency on Form FDA 2253 or Form FDA 2301 specimens of the interactive promotional media being used on the firm-owned or firm-controlled venue (e.g., blog, message board, or chat room), as described below in Section V. FDA recognizes that firms may be submitting both firm-generated and independent UGC on Form FDA 2253 or Form FDA 2301 as both firm-generated and independent UGC may be dispersed throughout the interactive promotional venue.

V. RECOMMENDATIONS FOR SUBMITTING INTERACTIVE PROMOTIONAL MEDIA

FDA recognizes the challenges of submitting promotional materials that display real-time information and, in this section, recommendations for submitting interactive promotional media are provided. If a firm submits interactive promotional media in the manner described in this draft guidance, FDA intends to exercise enforcement discretion regarding the regulatory requirements for postmarketing submissions related to promotional labeling and advertising. However, the Agency's expectations for submitting static promotional materials (e.g., sites that do not allow real-time communications and emails with predetermined content) that are substantially similar to traditional promotional materials in presentation and content remain unchanged.[6]

Unless otherwise specified in this guidance, the principles set forth below apply to the submission of interactive promotional media that display real-time communications, regardless of the target audience.

[5] Cf. 47 U.S.C. 230(c)(1) ("no provider or user of an interactive computer service shall be treated as the publisher or speaker of any information provided by another information content provider"). The Communications Decency Act further defines "information content provider" as someone "responsible, in whole or in part, for the creation or development of information provided through the Internet or any other interactive computer service." 47 U.S.C. 230(f)(3).

[6] Please note that the Agency expects that submissions of static promotional materials should remain unchanged. For example, a firm should submit its entire static product website at the time of first use. If the firm then updates one page or section of this static product website, the firm can submit only the updated page or section with a cross-reference to the original submission of the website noted on Form FDA 2253 or Form FDA 2301, including the date of the original submission. If the website is substantially revised, the firm should submit the revised website in its entirety.

The examples and recommendations provided are intended to provide guidance and illustrate possible approaches. Firms are free to use alternative approaches if these approaches satisfy the requirements of the statute and regulations.

1. At the time of initial display, a firm should submit in its entirety all sites for which it is responsible on Form FDA 2253 or Form FDA 2301. For example, the firm should submit the comprehensive static product website with the addition of the interactive or real-time components.[7]

The firm should include annotations to describe the parts that are interactive and allow for real-time communications. Any subsequent changes should be annotated and resubmitted to the Agency on Form FDA 2253 or Form FDA 2301 at the time of initial display (i.e., resubmission). The firm should also provide a cross-reference by noting the submission date of the most recent version of the site in the comments section of the form. However, after the initial submission or resubmission, if the site is publically accessible without restrictions such as a password or subscription ("non-restricted") and remains unchanged other than displaying real-time information, FDA does not intend to object if the firm submits to the Agency on Form FDA 2253 or Form FDA 2301 an updated listing of the site that does not include screenshots or other visual representations of the actual interactive or real-time communication, as described in number 3 below. If access to the site is restricted (e.g., is password protected or a subscription is required), see number 4 below.

2. For third-party sites on which a firm's participation is limited to interactive or real-time communications, a firm should submit the home page of the third-party site, along with the interactive page within the third-party site and the firm's first communication, on Form FDA 2253 or Form FDA 2301 at the time of initial display.

The firm may include any annotations that describe its communications within the third-party site. After the initial submission, if the firm remains an active participant on the third-party site, and that site is non-restricted, FDA does not intend to object if the firm submits to the Agency on Form FDA 2253 or Form FDA 2301 an updated listing of the site that does not include screenshots or other visual representations of the actual interactive or real-time communication, as described in number 3 below. If access to the site is restricted, see number 4 below.

3. Once every month, a firm should submit an updated listing of all non-restricted sites for which it is responsible or in which it remains an active participant and that include interactive or real-time communications. Firms need not submit screenshots or other visual representations of the actual interactive or real-time communications with the monthly updates.

Once every month, the firm should submit a Form FDA 2253 or Form FDA 2301 for the non-restricted sites for which the firm is responsible or in which it remains an active participant and that include interactive or real-time communications. Multiple sites and the corresponding documents can be submitted with a single Form FDA 2253 or Form FDA 2301. Firms should include a separate document for each site which includes the site name, URL, and date range, as well as a cross-reference to the date of the most recent submission of the site. Screenshots or other visual representations of the actual interactive or real-time communications need not be submitted with the monthly updates if the site is non-

[7] It is preferable for the firm to submit the interactive or real-time communications in an archivable format that allows FDA to view and interact with the submission in the same way as the end user (e.g., working links). Alternatively, firms should submit screen shots or other visual representations.

restricted. The appropriate FDA center (CDER, CBER, or CVM) should be informed via general correspondence on the first day the firm ceases to be active on a site.

4. However, if a site has restricted access and, as such, FDA may not have access to the site, a firm should submit all content related to the discussion (e.g., all UGC about the topic), which may or may not include independent UGC, to adequately provide context to facilitate the review. Screenshots or other visual representations of the actual site, including the interactive or real-time communications, should be submitted monthly on Form FDA 2253 or Form FDA 2301.

5. When submitting the site, FDA recommends that a firm take formatting factors (e.g., appearance, layout, visual impression) into consideration to enable the Agency to view the communications as a whole.