Published on *The National Law Review* https://natlawreview.com

FDA Issues Draft Guidance Implementing Direct-to-Consumer Television Ad Pre-Dissemination Review Program

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The Food and Drug Administration Amendments Act of 2007 authorizes the U.S. Food and Drug Administration (**FDA) to "require the submission of any television advertisement for a drug … not later than 45 days before dissemination of the television advertisement."** The FDA recently issued draft guidance that describes how the agency intends to exercise this authority. This newsletter provides a summary of the draft guidance and identifies some of its potential implications.

On March 12, 2012, the U.S. Food and Drug Administration (FDA) issued a long-awaited draft guidance that describes how the agency intends to exercise its authority to **require pre-dissemination review of direct-to-consumer (DTC) television advertisements for drugs, as authorized under the Food and Drug Administration Amendments Act of 2007 (FDAAA).** The draft guidance, which is entitled Guidance for Industry Direct-to-Consumer Television Advertisements – FDAAA DTC Television Ad Pre-Dissemination Review Program, addresses the categories of TV advertisements that will be subject to the pre-dissemination submission requirement, describes how the agency will notify sponsors that submission of a particular ad is required, details the required components of a pre-dissemination submission package and provides answers to several frequently asked questions.

Categories of TV Ads Subject to Pre-Dissemination Review

FDA proposes to require pre-dissemination FDA review of all television advertisements for drugs, which fall within six types of "high risk and high impact" television ads:

- The initial TV ad for any prescription drug, or the initial TV ad for a new or expanded approved indication for any prescription drug. The agency intends to provide feedback on the presentation of risk information, the presentation of the product's indication and, where applicable, the presentation of information pertaining to the efficacy of the product in population subgroups. FDA intends for such feedback to be relevant to both current and future ads.
- All TV ads for prescription drugs subject to a Risk Evaluation and Mitigation Strategy (REMS) with elements to ensure safe use. The agency intends to ensure that information regarding the risks associated with drugs subject to an REMS is appropriately communicated to the public.

- All TV ads for Schedule II controlled substances. As with the previous group, the agency intends to ensure that the public is provided with appropriate risk information.
- The first TV ad for a prescription drug following a safety labeling update that affects the Boxed Warning, Contraindications, Warnings & Precautions section of its labeling. The agency intends to review these ads to ensure that information regarding new risk concepts is communicated appropriately.

  Insofar as a labeling change is submitted as a "Changes Being Effected" (CBE) supplement to an approved marketing application—and thus may be distributed with the labeling change by the sponsor prior to receiving FDA approval of the change—the agency encourages sponsors to submit the ad under the voluntary review process while the labeling change is under review by FDA. Even if the same or a substantially similar ad was submitted prior to the FDA's approval of the CBE supplement, however, the agency intends to require the sponsor to submit its first advertisement after approval of the CBE supplement to ensure that the ad remains consistent with the labeling as approved.

- The first TV ad for a prescription drug following the receipt by the sponsor of an enforcement letter for that product that either cites a TV ad or causes a TV ad to be discontinued because the TV ad contained violations similar to the ones cited in the enforcement letter. The agency intends to ensure that such ads are not false or misleading and do not contain violations that are the same or similar to those violations alleged in the enforcement letter.
- Any TV ad that is otherwise identified by FDA as subject to the pre-dissemination review provision. FDA intends to subject additional ads to the pre-dissemination review requirements as it deems necessary "from a public health perspective." The agency will make this determination on a case-by-case basis after considering the risks associated with particular products. Sponsors will be notified in writing of the agency's decision to require pre-dissemination review under this provision, and of the length of time that the pre-dissemination review requirement will be in effect for their product.

All sponsors have the option of voluntarily submitting a proposed advertisement for pre-dissemination review. Insofar as a sponsor has been notified that its advertisement falls within one of the above categories, however, the sponsor will be required to submit this ad for pre-dissemination review.

To the extent that a sponsor revises its ad after receiving comments from FDA, but does not introduce new claims, concepts or creative themes, the agency will not require such sponsor to resubmit its ad. (Sponsors interested in receiving additional comments on such ads should nonetheless utilize the voluntary submission process.) Insofar as the revised ad adds new claims, concepts or creative themes after initial submission, however, the sponsor will be required to re-submit the ad in accordance with the procedures laid out in the guidance.

Notification of the Requirement to Submit a TV Ad for Pre-Dissemination Review

FDA proposes to notify sponsors of the requirement to submit an ad for pre-dissemination review using one of two methods (depending on the reason for which pre-dissemination review is required and/or the date on which the drug received FDA marketing approval).

Sponsors will be notified via correspondence from the agency (e.g., inclusion in a letter approving an application, supplement or labeling update, or an enforcement letter) insofar as pre-dissemination review is required for advertisements regarding the following:

- Drugs approved in the future
- Approved drugs for which an expanded indication is approved in the future
- Approved drugs that receive a safety labeling update that affects the Boxed Warning, Contraindications, or Warnings & Precautions section of its labeling
- Approved drugs that are the subject of an enforcement letter that cites a TV ad or causes a TV ad to be discontinued because of violations
- Any other drugs for which FDA determines pre-dissemination review of TV ads is required

Alternatively, sponsors will be notified via advance notice in the Federal Register insofar as pre-dissemination review is required for advertisements regarding the following:

- Initial TV ads for drugs approved prior to issuance of the guidance
- Initial TV ads for a new or expanded approved indication for drugs approved prior to issuance of the guidance
- Drugs approved prior to issuance of the guidance that are subject to an REMS
- Drugs approved prior to issuance of the guidance that are Schedule II controlled substances

If a sponsor is developing a TV ad that falls into one of the six above-referenced categories, yet the agency has not notified the sponsor through the Federal Register that pre-dissemination review is required, the agency recommends that the sponsor nonetheless submit the ad for pre-dissemination review.

Contents of a Complete Dissemination Review Package

The draft guidance also outlines what should be included in a sponsor's pre-dissemination review package. All dissemination review packages should include the following:

- Cover letter. A cover letter should include the New Drug Application (NDA) or Submission Tracking Number (STN), the name of the proposed ad and the sponsor's contact information (among other items).
- Annotated storyboard of the ad. The annotated storyboard should show which references support which claims made in the ad.
- Most current FDA-approved prescribing information. If applicable, the package insert (PI) should be annotated to include cross-references to the storyboard.

The review package should contain the following additional documentation (if any of the following apply):

- Annotated references to support product claims not contained in the PI. Such references should be cross-referenced to the storyboard.
- Spokesperson verification. The package should include verification that the person identified in a TV ad as an actual patient or health care practitioner is actually a patient or health care practitioner.
- Verification that the translation of a non-U.S. TV ad is accurate.
- Annotated references to support disease or epidemiology information. Such references should be cross-referenced to the storyboard.
- A video of the TV ad (if available). FDA cannot provide final comments on the acceptability of a TV ad until it has reviewed the final recorded version of the ad in its entirety.

In the event that FDA receives an incomplete review package, the agency will inform the sponsor that

its submission package is incomplete, describe the reason(s) that the package is incomplete and request that the sponsor submit a complete package.

Frequently Asked Questions and Answers

The guidance provides several additional details regarding the new program. Highlights include the following:

- The agency's goal is to review each DTC advertisement within 45 days. The review clock starts when the Center for Biologics Evaluation and Research (CBER) or the Center for Drug Evaluation and Research (CDER) has received a complete dissemination review package.
- If the agency does not respond within 45 days, a sponsor will not be subject to legal consequences if it decides to run the ad without waiting for the agency's comments. Once an ad is disseminated, however, FDA may take enforcement action against the sponsor insofar as such ad violates the Federal Food, Drug and Cosmetic Act (FDCA) and/or its implementing regulations.
- The failure to submit an ad as required, the dissemination of an ad before FDA has provided comments and/or the dissemination of an ad prior to the end of the 45-day review period may result in enjoinment, criminal penalties and, if the ad is false or misleading, civil monetary penalties (CMPs). FDA has indicated that it will consider the sponsor's refusal to comply with the submission requirement if it issues an enforcement letter and/or imposes CMPs.
- FDA may require sponsors to revise an advertisement to disclose a serious risk listed in the labeling of a drug and/or to include the date of the product's approval for up to two years post-approval. Otherwise, sponsors are not required to comply with the agency's suggestions, but failure to do so may result in more severe enforcement action if the ad is later deemed to be violative. A sponsor's refusal to incorporate the above-referenced required disclosures is prohibited and may result in enjoinment or criminal penalties. Moreover, notwithstanding FDA's inability to require sponsors to comply with other types of recommendations, the agency has indicated that it will consider the sponsor's refusal to incorporate its suggestions if it issues an enforcement letter and/or imposes CMPs because it considers a disseminated ad to be false or misleading.

FDA has requested that interested parties submit comments regarding the draft guidance by May 14, 2012.

Implications

The draft guidance, if implemented, would require pre-dissemination review by FDA for virtually every type of DTC TV advertisement for drugs. Indeed, the only advertisements that would not appear to be subject to the pre-dissemination review requirement are advertisements that meet all of the following requirements:

- The advertisement is for one or more established indications of a product that is already FDA-approved.
- The product that is the subject of the advertisement is not subject to an REMS.
- The product that is the subject of the advertisement is not a Schedule II controlled substance.
- The advertisement is not the first ad for a prescription drug following a safety labeling update.
- The advertisement is not the first ad for a prescription drug following the receipt of an enforcement letter that cites a TV ad or causes a TV ad to be discontinued.
- The advertisement is not otherwise identified by FDA as subject to the pre-dissemination

review provision.

A critical unanswered question raised by the guidance is how quickly FDA will be able to provide sponsors with meaningful feedback to a pre-dissemination submission. Although the agency's goal is to respond within 45 days of receiving a complete submission, the draft guidance acknowledges that, in some cases, it may take the agency longer to respond. In these cases, a sponsor may be put in the unenviable position of choosing to wait to begin marketing until FDA responds, or moving ahead with commercializing its product and subjecting itself to potential civil monetary penalties under FDAAA as well as traditional enforcement actions for disseminating a false or misleading ad.

Given the FDA's intent to require robust FDA pre-review and its stated intent to consider the purported refusal to follow FDA recommendations in determining the type and extent of enforcement action it will take for ads it later deems to be violative, FDA should be required to complete its review within the 45-day period. Absent such review, the enforcement mechanism would appear to unfairly prohibit commercial marketing of product with an otherwise lawful advertisement.

Sponsors of drugs that fall within any of the six above-referenced categories should carefully review the required elements of a pre-dissemination package. Although the package generally consists of the same information as is currently required for submissions to the agency's advisory review process for television advertisements, there are certain differences, particularly with respect to the number of copies required of a particular item.

National Law Review, Volume II, Number 100