Guidance for Industry Direct-to-Consumer Television Advertisements — FDAAA DTC Television Ad Pre-Dissemination Review Program

DRAFT GUIDANCE

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For questions regarding this draft document contact (CDER) Marci Kiester at 301-796-1200, or (CBER) the Office of Communication, Outreach, and Development at 301-827-1800 or 800-835-4709.

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)

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OPDP

Guidance for Industry Direct-to-Consumer Television Advertisements — FDAAA DTC Television Ad Pre-Dissemination Review Program

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Guidance for Industry[1]
Direct-to-Consumer Television Advertisements — FDAAA DTC Television Ad Pre-Dissemination Review Program

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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 guidance is intended to assist sponsors of human prescription drugs, including biological drug products approved under section 351 of the Public Health Service Act, by describing how FDA plans to implement the requirement for the pre-dissemination review[2] of direct-to-consumer television advertisements (TV ads) according to section 503B of the Federal Food, Drug, and Cosmetic Act (the FD&C Act). The guidance describes the types of TV ads that FDA intends to be subject to this provision, explains how FDA will notify sponsors that an ad is subject to the requirement of review under section 503B, and describes the general and Center-specific procedures sponsors should follow to submit their TV ads to FDA for pre-dissemination review in compliance with section 503B of the FD&C Act.

FDA's guidance documents, including this guidance, do not establish legally enforceable 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

On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85). FDAAA gives FDA the authority to ". . . require the submission of any television advertisement for a drug . . . not later than 45 days before dissemination of the television advertisement" (section 901(d)(2), codified at 21 U.S.C. 353b).

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[1] This guidance has been prepared by the Office of Prescription Drug Promotion (OPDP) in the Center for Drug Evaluation and Research (CDER) in cooperation with the Advertising and Promotional Labeling Branch (APLB) in the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] The term "pre-dissemination review" is used throughout the guidance to refer to review under section 503B of the FD&C Act, which is entitled "Prereview of Television Advertisements."

In conducting a review of a TV ad under this section, FDA may make recommendations with respect to information included in the label of the drug on:

- changes that are necessary to protect the consumer good and well-being, or that are consistent with prescribing information for the product under review; and
- statements for inclusion in the advertisement to address the specific efficacy of the drug as it relates to specific population groups, including elderly populations, children, and racial and ethnic minorities, if appropriate and if such information exists.

21 U.S.C. 353b(b)(1) and (2).

FDA is issuing this guidance to communicate the categories of TV ads it generally intends to require sponsors to submit under this provision, to explain how it will notify sponsors that FDA is requiring review under section 503B for ads for a particular drug or group of drugs, and to provide sponsors with recommendations for the information they need to properly submit these ads to the Agency for pre-dissemination review.

III. CATEGORIES OF TV ADS SUBJECT TO PRE-DISSEMINATION REVIEW

The Agency intends to require sponsors to submit TV ads for pre-dissemination review in the following categories:

Category 1: The initial TV ad for any prescription drug or the initial TV ad for a new or expanded approved indication for any prescription drug
Category 2: All TV ads for prescription drugs subject to a Risk Evaluation and Mitigation Strategy (REMS) with elements to assure safe use (see section 505-1(f) of the FD&C Act)
Category 3: All TV ads for Schedule II controlled substances
Category 4: The first TV ad for a prescription drug following a safety labeling update that affects the Boxed Warning, Contraindications, or Warnings & Precautions section of its labeling
Category 5: The first TV ad for a prescription drug following the receipt by the sponsor of an enforcement letter (i.e. a Warning or untitled 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
Category 6: Any TV ad that is otherwise identified by FDA as subject to the pre-dissemination review provision

These categories reflect a risk-based approach that will enable the Agency to leverage its limited resources to best protect the public health by ensuring that certain high risk and high impact TV ads accurately and effectively communicate key information about advertised products, including their major risks and indications. Specifically, these categories allow the Agency to review and provide comments on TV ads for prescription drugs with particularly serious risks,

and to review and provide comments on TV ads at times when feedback on the risk and indication communication in the ad is particularly critical, including when a product is first advertised on TV and after a product has received a significant safety labeling update or a new or expanded indication.

Category # 1: FDA intends to review and comment on the first TV ad for a prescription drug or the first TV ad for a new or expanded indication for an already-approved product. This will allow us to provide feedback on the *major statement* (i.e., the presentation of risk information in a broadcast ad), which sponsors can apply to both the initial ad and future ads. FDA can also identify any issues with the presentation of the product's indication and, where applicable, the product's specific efficacy in population subgroups, and provide feedback relevant to both current and future ads.

Categories # 2 and # 3: FDA intends to review all TV ads for certain prescription drugs with particularly serious risks relative to benefits — specifically, products with REMS with elements to assure safe use and products that are Schedule II controlled substances. FDA believes it is critically important that the risks associated with such products be appropriately communicated in all promotion, and intends to review all TV ads for such products to help ensure that this occurs.

Category # 4: FDA intends to review and comment on the first TV ad for a prescription drug following a significant safety labeling update to the product's FDA-approved prescribing information (PI). This will allow us to provide feedback on the "major statement" for that product to help ensure that new risk concepts are communicated appropriately in the submitted ad and in future ads for the product. FDA understands that certain safety labeling supplements can be submitted as "Changes Being Effected" supplements (CBE supplements), and that sponsors may begin distribution of the product using the modified labeling contained in the supplement upon receipt of the CBE supplement by FDA.[3] If a sponsor chooses to disseminate a TV ad while such a CBE supplement is pending review and approval by FDA, FDA encourages the sponsor to submit the TV ad under the voluntary advisory review process to the appropriate group (OPDP or APLB). Once FDA has approved the CBE supplement (resulting in a significant safety update to the product's *FDA-approved* labeling), FDA intends to require the sponsor to submit its next TV ad for the product to FDA for pre-dissemination review, even if the same or a substantially similar TV ad was submitted voluntarily prior to the FDA approval of the CBE supplement, to ensure that the ad remains consistent with the labeling as approved.

Category # 5: FDA intends to review and comment on the first TV ad for a prescription drug after a sponsor receives an enforcement letter from FDA for its promotion of that product that either cited a TV ad or caused a TV ad to be discontinued because the TV ad contained violations similar to the ones cited in the enforcement letter. In either of these cases, FDA intends to review the next TV ad for the product before it is publicly aired to ensure that the ad is not false or misleading and that the ad does not contain violations that are the same or similar to those cited in the enforcement letter.

[3] See 21 CFR 314.70(c)(6) and 601.12(f)(2).

Category # 6

In addition, FDA may notify a sponsor that a TV ad for a product is subject to the pre-dissemination review provision in the FD&C Act if such pre-dissemination review is deemed necessary from a public health perspective. This would be done on a case-by-base basis after considering the risks associated with particular products. In such a case, a sponsor will be notified in writing of our decision to apply this provision to its product and of the length of time that the pre-dissemination review requirement will be in effect for its product.

Generally, sponsors have the option of submitting any proposed prescription drug television ad to FDA for advisory review before publicly disseminating the ad (see 21 CFR 202.1(j)(4)). In this way, sponsors can benefit from FDA's input on whether or not ads are accurate, balanced, and nonmisleading before they disseminate the ads. This voluntary submission process also gives sponsors an opportunity to address any problems before the TV ads are shown to the public, improving the quality of the ads. This voluntary submission process is still available to sponsors. However, if a sponsor has been notified that a TV ad for one of its products is subject to the pre-dissemination review provisions in section 503B of the FD&C Act, it will be required to submit this TV ad for pre-dissemination review.

FDA understands that sponsors subject to the 503B pre-dissemination review provision may revise their TV ads after receiving comments from the Agency, but before disseminating the ads. FDA does not expect a sponsor to resubmit its draft TV ad for pre-dissemination review if the revisions made to the ad are in response to the Agency's comments and do not introduce new claims, concepts, or creative themes into the TV ad. If a sponsor does wish to request additional comments on such a TV ad, it should do so under the voluntary advisory submission process.[4] However, if a sponsor revises a draft TV ad following pre-dissemination review under section 503B to add new claims, concepts, or creative themes into the TV ad, the sponsor will be required to resubmit the TV ad to the Agency for pre-dissemination review following the procedures outlined in this guidance.

IV. HOW WILL FDA NOTIFY SPONSORS OF THE REQUIREMENT TO SUBMIT A TV AD FOR PRE-DISSEMINATION REVIEW?

FDA intends to notify drug sponsors of the requirement to submit their TV ads for pre-dissemination review in several different ways. For drugs approved in the future and for approved drugs for which an expanded indication is approved in the future (Category 1), for approved drugs that fall under Categories 4 and 5 as described in this guidance, and for any other drugs for which FDA determines pre-dissemination review of TV ads is required (Category 6), FDA intends to notify sponsors in the letter approving the application or supplement, in the approval of the labeling update, in the enforcement letter, or in other correspondence. For drugs already approved prior to the issuance of this guidance that fall under Categories 1, 2, and 3,

[4] Visit http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090159.htm and www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/AdvertisingLabelingPromotionalMaterials/ucm164120.htm for current information regarding the advisory review submission process.

FDA intends to publish a notice in the *Federal Register* notifying sponsors that their products will be subject to pre-dissemination review in accordance with section 503B of the FD&C Act. However, if a sponsor is developing a TV ad for a product that falls into one of the categories described above and has not yet received written notification, we recommend that the sponsor submit the TV ad for pre-dissemination review as described in this guidance.[5]

V. CONTENTS OF A COMPLETE PRE-DISSEMINATION REVIEW PACKAGE

For FDA to meaningfully review and provide recommendations on TV ads submitted under the section 503B pre-dissemination review provision, the Agency should receive certain information and materials in addition to the ad itself, such as the advertised product's current approved labeling and any references a sponsor is relying on to support claims made in an ad. This section of the guidance outlines what should be included in a sponsor's pre-dissemination review package. Complete pre-dissemination review packages should be sent to either CDER or CBER, depending on which Center regulates the product the TV ad addresses. The following recommendations apply to ***all pre-dissemination review packages*** for TV ads sent to FDA. Specific details regarding submissions to CDER and CBER are provided in the Appendix.

A. What materials should I include in a pre-dissemination review package?

A sponsor should include the following in all pre-dissemination review packages for a TV ad:

1. A cover letter that:
    - Provides the following subject line: Pre-Dissemination Review Package for a Proposed TV Ad for [Proprietary Name/Established Name (dosage form) (for drugs), or Trade name/Proper name (for biologics)] Subject to 503B of the FD&C Act
    - Includes the NDA or STN number
    - Provides the name of the proposed TV ad
    - Lists the contents of the pre-dissemination review package and the number of copies provided of each item contained in the pre-dissemination review package (see Appendix for details on the number of copies to submit to each Center)
    - Provides a sponsor contact's name, title, address, phone, fax, and email
2. Annotated storyboard of the proposed TV ad to show which references support which claims

[5] For current contact information for OPDP, visit http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090142.htm. For current contact information for APLB, visit www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/AdvertisingLabelingPromotionalMaterials/ucm164120.htm.

3. The most current FDA-approved prescribing information (PI) and, if applicable, the FDA-approved patient labeling or Medication Guide with annotations cross-referenced to the storyboard

A sponsor should also include other appropriate documentation, if any of the following apply:

4. Annotated references to support product claims not contained in the PI, cross-referenced to the storyboard

5. Verification that a person identified in a TV ad as an actual patient or health care practitioner is an actual patient or health care practitioner and not a model or actor; and/or

   Verification that a spokesperson who is represented as a real patient is indeed an actual patient; and/or

   Verification that an official translation of a foreign language TV ad is accurate

6. Annotated references to support disease or epidemiology information, cross-referenced to the storyboard

7. A video of the TV ad in an acceptable format,[6] if available. FDA cannot provide final comments on the acceptability of a TV ad without viewing a final recorded version in its entirety. FDA understands that some sponsors may wish to receive comments from the Agency before producing a final recorded version of the ad. In such situations, sponsors can submit a pre-dissemination review package without a final recorded version of the ad, but once the final recorded version is produced, it will need to be submitted to the Agency for pre-dissemination review.

B. What should ***not*** be included in a pre-dissemination review package?

Materials unrelated to a proposed TV ad being submitted for pre-dissemination review should **not** be included in the pre-dissemination review package. For example, do **not** include other draft promotional materials in the pre-dissemination review package. In addition, only one proposed TV ad should be submitted per pre-dissemination review package.

C. How are incomplete pre-dissemination review packages handled?

Pre-dissemination review packages that are missing any of the elements in section V(A) above or that fail to follow the specific details for submissions to CDER or CBER as provided in the Appendix are considered incomplete. If FDA receives an incomplete package, we will:

- Inform the sponsor that the submission is incomplete
- Provide the reason(s) that the package is incomplete
- Request a submission package that contains the missing materials

[6] Visit http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090159.htm and www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/AdvertisingLabelingPromotionalMaterials/ucm164120.htm for current information regarding acceptable formats.

Note that the 45-day review time frame (see below) does not begin until a **complete** pre-dissemination review package is received.

VI. FREQUENTLY ASKED QUESTIONS AND ANSWERS

A. How long does FDA have to review a television ad under section 503B and when does the clock start?

Under section 503B, FDA may require that a TV ad be submitted to FDA for review not later than 45 days before the sponsor intends to disseminate the ad (21 U.S.C. 353b(a); see also 21 U.S.C. 333(g)(3)(C)). The 45-day review clock for proposed DTC TV ads subject to the pre-dissemination review provision begins when CDER or CBER has received a complete pre-dissemination review package from a sponsor.

B. What happens if FDA is not able to complete its review within the 45-day time frame?

FDA will notify the sponsor if the Agency is not able to provide comments within the 45 calendar day time frame. FDA's notification will include an estimate of the date on which FDA expects to provide its comments. In such situations, the sponsor should determine whether it will wait for FDA's comments before disseminating the TV ad or whether it will disseminate the TV ad without waiting for FDA's comments. The sponsor should notify FDA of its decision. Once the 45-day review time has elapsed, there is no specific legal consequence resulting from disseminating the proposed TV ad without waiting for FDA's comments see section VII.A). However, once an ad is disseminated, the sponsor is at risk of enforcement action if the ad violates the FD&C Act and implementing FDA regulations.

C. Will FDA continue its review if I decide to disseminate my TV ad before receiving FDA comments, but after the clock has run?

No. If a sponsor decides to disseminate the proposed TV ad before receiving FDA's comments, but after the 45-day clock has run, FDA will discontinue its 503B review. As noted above, if the ad is disseminated, the sponsor is at risk of enforcement action if the ad violates the FD&C Act and implementing FDA regulations.

VII. ENFORCEMENT

A. What happens if I do not submit a TV ad for review that is required under section 503B or submit a TV ad for review and disseminate the ad before the 45-day comment period ends, without waiting for comments from FDA?

Under section 301(kk) of the FD&C Act (21 U.S.C. 331(kk)), dissemination of a television advertisement without complying with section 503B is a prohibited act. This prohibited activity

can be enjoined (21 U.S.C. 332(a)) and be subject to criminal penalties (21 U.S.C. 333(a)). In addition, if the Agency assesses civil monetary penalties to the sponsor because the TV ad is false or misleading (21 U.S.C. 333(g)), in determining the civil monetary penalty amount, FDA will take into account the fact that the sponsor failed to submit a TV ad for pre-dissemination review that was required to be submitted under section 503B (21 U.S.C. 333(g)(3)(B)), and will take into account the fact that the sponsor, after submitting the ad, disseminated the ad before the end of the 45-day comment period (21 U.S.C. 333 (g)(3)(C)). FDA may also take into account the fact that the sponsor failed to submit the TV ad for pre-dissemination review or disseminated it after submission but before the 45-day comment period without waiting for comments from FDA if it decides to issue an untitled letter or Warning letter to the sponsor for the TV ad.

B. What happens if I disseminate my TV ad without incorporating the Agency's comments?

As previously noted, under section 301(kk) of the FD&C Act (21 U.S.C. 331(kk)), dissemination of a television advertisement without complying with section 503B is a prohibited act. Under section 503B(e), FDA may require specific disclosure of a serious risk listed in the labeling of a drug, and may require the ad to include the date of the product's approval for a period of up to 2 years after that approval, where the absence of either of these pieces of information would render the ad false or misleading. Failure to incorporate these specific required disclosures is a prohibited activity under section 301(kk) that can be enjoined (21 U.S.C. 332(a)) and be subject to criminal penalties (21 U.S.C. 333(a)).

As a result of its review, in addition to requiring disclosures as described above, FDA may also provide comments indicating other elements of the TV ad that it believes would result in the ad being false or misleading, or otherwise violating the FD&C Act or implementing regulations. If the Agency assesses civil monetary penalties to the sponsor because it has disseminated a TV ad that is false or misleading (21 U.S.C. 333(g)), in determining the civil monetary penalty amount, FDA will take into account the fact that the sponsor disseminated the TV ad without incorporating the Agency's comments (21 U.S.C. 333(g)(3)(D)). FDA may also take into account the fact that the sponsor disseminated the TV ad without incorporating the Agency's comments if it decides to issue an untitled or Warning letter.

APPENDIX: CENTER-SPECIFIC SUBMISSION PROCEDURES

CDER

1. **Forms**

No specific form is to be used. Please submit the materials in accordance with the recommendations in this guidance.

2. **Number of Copies**

How many copies should I submit?

For CDER OPDP pre-dissemination reviews, submit the following number of copies in pre-dissemination review packages for a proposed TV ad:

- If a video is being provided, 2 copies in an acceptable format
- 12 copies ***of all other materials*** discussed in V(A)(2)-(6)

As an alternative, all materials discussed above can be submitted on a CD.

3. **Address**

For products regulated in CDER (OPDP), submit proposed DTC TV ads (pre-dissemination review packages and amendment packages) to:

Project Manager
Office of Prescription Drug Promotion
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

It is very important to specify on both the ***outer*** package and the cover letter that the contents concern a pre-dissemination review package subject to section 503B of the FD&C Act. Follow the recommendations discussed in section V(A) of this guidance for the cover letter. Include a large type reference line on the outer package that indicates the package is a 503B pre-dissemination review package, such as the following:

- OPDP Pre-Dissemination Review Package as Required by Section 503B of the FD&C Act

Any questions for OPDP may also be addressed to an OPDP project manager by phone at 301-796-1200.

CBER

1. **Forms**

For pre-dissemination review packages for biologics under the purview of CBER (sent to APLB), include the most current version of Form FDA 2253, with Line 13 checked as "Part 1/Draft." Note that this form is **not** to be included with CDER submissions (see above).

2. **Number of Copies**

For CBER APLB pre-dissemination reviews, submit the following number of copies in each pre-dissemination review package for a proposed TV ad:

- If a video is being provided, 2 copies in an acceptable format
- 2 copies ***of all other materials*** discussed in V(A)(2)-(6)

3. **Address**

For products under the purview of CBER (APLB), submit proposed TV ads (pre-dissemination review packages and amendment packages) to:

Advertising and Promotional Labeling Branch, HFM-602
Center for Biologics Evaluation and Research
Food and Drug Administration,
1401 Rockville Pike, suite 200N
Rockville, MD 20852

It is very important to specify on both the ***outer*** package and the cover letter that the contents concern a pre-dissemination review package subject to section 503B of the FD&C Act. Follow the recommendations discussed in section V(A) of this guidance for the cover letter. Include a large type reference line on the outer package that indicates the package is a 503B pre-dissemination review package, such as the following:

- APLB Pre-Dissemination Review Package as Required by Section 503B of the FD&C Act

Any questions for APLB may also be addressed to APLB by phone at 301-827-3028.