REGULATORY FOCUS

FDA Enforcement Trends for Broadcast Advertisements

By Justin Mann and Julie Tibbets

This article presents recent FDA enforcement trends related to broadcast advertisements and explains how regulatory professionals can approach the review and approval of promotional materials. The article also provides a review of relevant FDA authorities and guidance, as well as practical takeaways for industry with a focus on product ads appearing on TV or YouTube that may distract viewers from important risk information.

Introduction

From January 2016 through August 2017, the Food and Drug Administration's (FDA's) Office of Prescription Drug Promotion (OPDP) issued 13 enforcement letters, four Warning Letters and nine Untitled Letters. Most of the letters (nine of 13, including all four Warning Letters) were related to the promotion of approved products. All of those nine approved product letters included at least one reference to concerns with risk presentation – **Figure 1**. Nearly half of all letters were for promotional videos through broadcast TV or YouTube.com – **Figure 2**. This article provides a detailed analysis of these letters and some key observations and takeaways for industry.

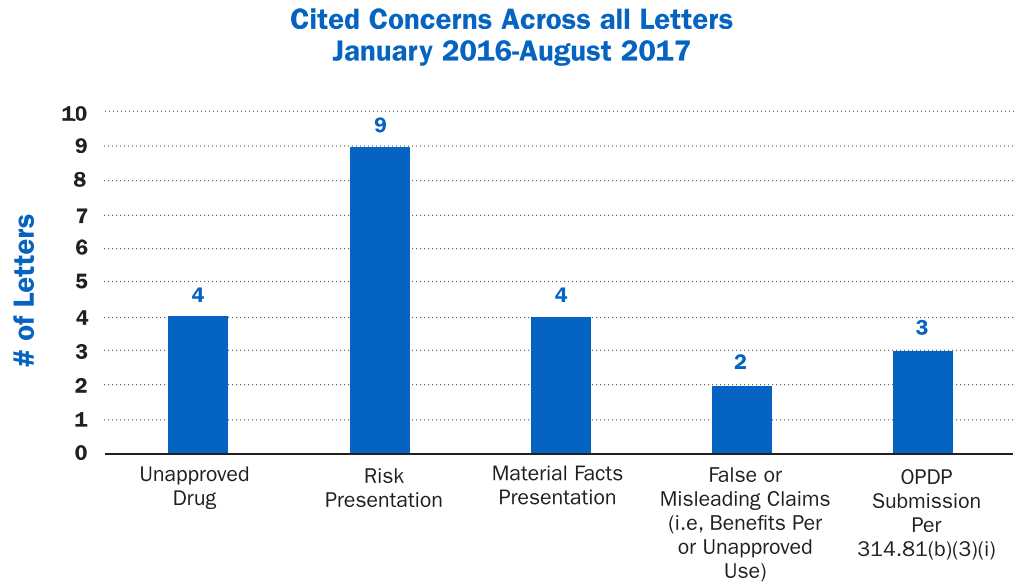
Recent Letters Related to Direct-to-Consumer Broadcast Television Advertisements

As noted in **Figure 2**, FDA issued three letters related to direct-to-consumer broadcast television advertisements (TV Ads) in the past 18 months, to Orexigen Therapeutics Inc., (Orexigen Letter), Celgene Corporation (Celgene Letter) and Sanofi-Aventis US (Sanofi Letter).

Orexigen Letter

The Orexigen Letter was issued in May 2017 for Contrave® (naltrexone HCl and bupropion HCl).{1} One of the areas of focus for this letter was the omission of certain risk information from the contraindications and the black box warning. The letter stated that their TV ad addressed Contrave®'s contraindication for opioid use, but not other

Figure 1. Cited Concerns Across all Letters



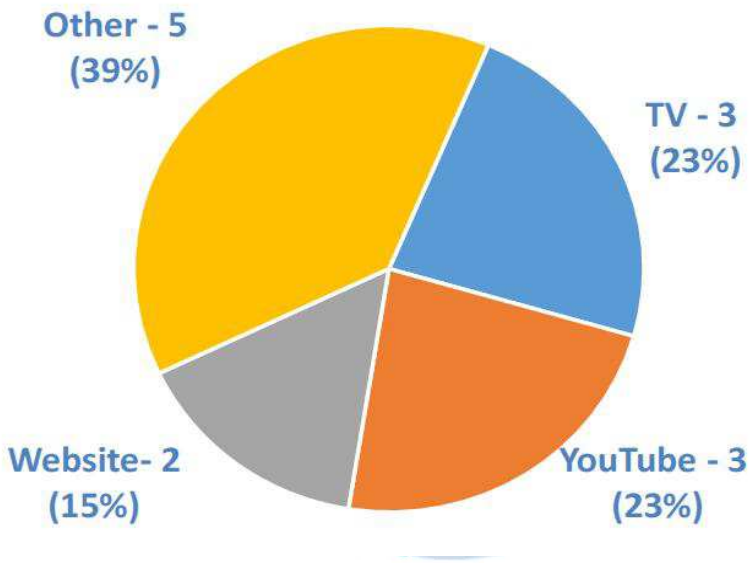
contraindicated conditions (e.g., seizure disorders). Similarly, the ad included a statement about the risk of suicidal ideation and behavior from the black box, but not for additional psychiatric warnings. FDA also stated that the ad failed to present psychiatric side effects from the boxed warning.

In addition to the omitted information cited above, OPDP found issue with the manner in which risk information was presented. First, OPDP claimed a specific violation of 21 C.F.R. § 202.1(e)(1), which requires important risk information to at least be presented in the audio portion of the ad. The violation occurred when certain important risk information was only presented visually (i.e., through superimposed onscreen text (SUPERs)). In a separate part of the ad, two different types of important risk information were presented simultaneously, one visually and one through audio. OPDP found this simultaneous presentation as having "misleadingly minimize[d] the risks associated with the use of Contrave[®]."

Celgene Letter

The Celgene Letter was issued in December 2016 for Otezla® (apremilast).{2} Here, OPDP's main concern was that the non-risk-related components of the ad (e.g.,

Figure 2. Promotional Medium Cited in Letters



"compelling and attention-grabbing visuals…[and] frequent scene changes") were so distracting that the consumer may not be able to pay full attention to the risk information. Similarly, the letter also cites a scene where "a loud brass interjection is played over several audio risk disclosures." In addition to being distracting, the letter also emphasized a concern with audio risk information being conveyed while this unrelated material is presented (e.g., a woman enjoying the process of trying on a dress while the audio discusses the risk of depression and suicidality).

Sanofi Letter

The Sanofi Letter also was issued in December 2016, for Toujeo® (insulin glargine injection).{3} Using language almost identical to the Celgene Letter, OPDP's concern in this letter was that "[t]he presentation of these compelling and attention-grabbing visuals, all unrelated to the risk message presented in the audio and on-screen SUPERS, in addition to the frequent scene changes and the other competing modalities such as the background music, compete for the consumers' attention." Here, the ad showed a man dancing through multiple scenes while music plays and the important risk information is presented through audio and SUPERs.

All three letters were untitled and related to approved products. The only concerns FDA cited in these letters related exclusively to the presentation of risk information or "False or Misleading Risk Presentation." Common across all three letters was the concern that the consumer be able to focus on the presentation of important risk information, without the "attention-grabbing" aspects of the ad preventing them from being able to fully "process and comprehend" the risks associated with taking a drug. In the Orexigen Letter, OPDP discusses this concern in the form of two different sets of risk information being simultaneously presented, one through visual and one through audio means. From the Celgene and Sanofi Letters, OPDP explains this concern in terms of the commercial effects generally common to TV advertisements (e.g., "attention-grabbing visuals…[,] frequent scene changes and the other competing modalities"). Across all three letters, OPDP's description of this concern for diverting the consumer's attention includes references to the presented risk information being unrelated to, and possibly thematically conflicting with, what else is presented in the ads, which FDA felt ultimately minimized the risk information associated with these products.

Overview of FDA Authorities and Guidance

The US Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the Federal Food, Drug, and Cosmetic Act (FDCA) to provide that for prescription drug advertisements "presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear, conspicuous, and neutral manner."{4} However, FDAAA also created a requirement that FDA promulgate regulations to establish standards for meeting this "clear, conspicuous, and neutral manner" requirement. While FDA did issue a proposed rule in 2010, the docket for that proposed rule (Docket # FDA-2009-N-0582) is listed as "Long-term Action," and there have been recent reports that FDA has put this rule on hold.{5} Without a clear regulatory interpretation and no enforcement actions citing this provision, the rest of this article will focus on the current regulatory requirements in force along with FDA's guidances.

Two regulatory requirements specific to broadcast advertisements (e.g., television and radio) are 1. the audio, or audio and video, must include "major side effects and contraindications" and 2. the communication of "a brief summary of all necessary information related to side effects and contraindications, ['unless adequate provision is made for dissemination of the approved or permitted package labeling']".{6} FDA refers to these as: 1. the major statement requirement and 2. the adequate provision requirement. In addition, the FDCA provides that FDA take into account "the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates."{7} The focus of the following discussion will be on the major statement requirement, as this is where FDA's focus has been in the TV Ads enforcement letters issued by OPDP in the last 18 months.

In August 1999, FDA issued two final guidance documents specific to broadcast advertisements: *Guidance for Industry: Consumer-Directed Broadcast Advertisements*{8} and

Guidance for Industry: Consumer-Directed Broadcast Advertisements Questions and Answers.{9} Unfortunately, these two guidance documents were focused almost exclusively on the adequate provision requirement. However, the *Guidance for Industry: Consumer-Directed Broadcast Advertisements Questions and Answers* did provide some indirect insight on the major statement requirement. For example, FDA speculated that sponsors may be "reluctant to promote products with serious risks to consumers in a broadcast format," which raises the question of whether FDA believes there are drugs that are so high risk that attempting to properly present a major statement for them may not be feasible. Later in the guidance, while discussing the display of information for the adequate provision requirement, FDA expresses its concern about visual components of an ad distracting from the major statement. The guidance states that there were two cases that "were violative because information about different risks was simultaneously presented in the audio and visual parts of the presentation, making both topics unlikely to be adequately comprehended or processed." It is significant to note that this guidance was written nearly 20 years prior to the enforcement letters summarized above.

FDA's general draft guidance on the presentation of risk information, *Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion,*{10} more directly expresses FDA's views on the major statement requirement for broadcast advertisements. Toward the beginning of the guidance, after describing a scene with a positive visual of a patient accompanied by loud music and audio describing serious risk information, FDA indicates that the risk presentation in the example may be inadequate due to the "accompanying discordant visuals and distracting music." As part of a later section dedicated to formatting, FDA provides the general rule that "risk and benefit information should be comparably noticeable or conspicuous," and then provides some factors specific to broadcast advertisements that it takes into consideration: "location, proximity, type size, type style, []contrast …[,] other visual components [(e.g., graphics)],…audio components, motion within the visual component, the juxtaposition of visual and audio components, and duration of exposure." These are particularly important for SUPERs, as presenting risk information through SUPERs raises concerns of "readability, comprehensibility, and proximity to benefit information." Additionally, manufacturers should be careful when using SUPERs to qualify an otherwise misleading statement, as well as when presenting competing SUPERs. As long-established by the US Federal Trade Commission, "disclaimers may not cure otherwise deceptive messages."{11} For audio components, manufacturers should take into account vocal qualities (e.g., prominence, volume, pace) and the use of music, particularly when comparing the audio effects between presentations of risk information versus benefit information.

In addition to discussing situations to avoid, the guidance also offers pointers for meeting the major statement requirement. For example, using commercial effects as signals can make the risk presentation more effective (e.g., changing the announcer to hint that the audio to follow is important). Also, the most important risk information should be presented at the beginning and the end of the ad. As part of organizing an ad, consider whether the order of lines in the script could give the false impression that certain risks are limited to discrete situations (e.g., warning against the use of alcohol and then discussing drowsiness as a potential side effect could make the viewer think that drowsiness is only a risk while using alcohol).

Outside of the regulations and guidances noted above specific to broadcast advertising, it is also worth remembering general rules that are applicable to broadcast advertisements. For example, nearly the entire risk presentation guidance applies to broadcast advertisements, including its guiding principles that promotional material:

- cannot be false or misleading in any particular
- must reveal material facts about the product being promoted, including facts about the consequences that can result from use of the product as suggested in the promotional piece
- should present information about effectiveness and information about risk in a balanced manner

The broadcast advertisement also will be subject to FDA's "net impression" rule, which requires that "the piece *as a whole* conveys an accurate and non-misleading impression of the benefits and risks of the promoted product."

YouTube: the New Frontier for DTC Advertising and FDA Enforcement

Advertisements on YouTube pose many similarities to advertisements on broadcast TV, especially in terms of viewership, programming and advertising medium. As such, manufacturers should consider applying the same standards they use for broadcast TV advertisements to their advertisements on YouTube. For the purpose of this section, when we are discussing "advertisements" on YouTube, we are referencing the short videos that may appear before, during, or after the primary video the viewer selected for viewing on YouTube (e.g., a 60 second broadcast TV-like advertisement on Drug A that comes before watching a how-to video on a completely unrelated subject).

According to Google, YouTube's parent company, "more people watch YouTube than watch cable networks."{12} In addition to supplying cat videos, YouTube also has a service called "YouTube TV" that offers many of the same programs offered through traditional TV providers.{13} YouTube also offers a similar platform for advertisements, with short video advertisements conveyed directly to the consumer interspersed among the primary videos. Advertisements through YouTube also pose the similar risk that the limited amount of time allowed for the entire advertisement means a small window to educate the consumer in a balanced manner on both benefits and risks.

In addition to the similarities between YouTube and TV as advertising platforms, FDA also appears to be focusing additional attention on YouTube. Of the 13 enforcement letters identified at the beginning of this article, three of those letters (23 percent) were related to YouTube; although it is worth noting that those letters were related to longer primary videos on YouTube, not broadcast TV-like "advertisements." Conversely, prior to 2016, we have seen FDA use this audio/video presentation language in enforcement letters for longer videos that traditionally would not be considered "broadcast advertisements."{14}

Finally, the regulations and guidances highlighted above are not specific to TV advertisements. They refer to broadcast advertising more broadly, using terms like "[a]dvertisements broadcast through media" and "Consumer-Directed Broadcast Advertisements."

While regulations and FDA guidance to date have not directly addressed advertisements on YouTube, manufacturers should consider treating their YouTube advertisements like their TV advertisements. This would apply for both the rules specific to broadcast advertisements (e.g., major statement and adequate provision), as well as the general rules regarding risk presentation.

Closing Observations and Takeaways for Industry

Of the 13 letters that OPDP recently issued, 23 percent were for TV advertisements and another 23 percent were for promotional videos on YouTube. Based on the trend in enforcement letters as well as the authorities and guidances discussed above, industry would be prudent to give careful attention to the preparation and scripting of any video advertisements, on TV or YouTube. Notably, FDA's letters object to many of the types of details that cannot be conveyed or commented on – both internally by promotional review committee members as well as externally by FDA – when new ads or videos are in a conceptual storyboard state. Onscreen movement in each storyboard window, the timing of scene changes, and background music levels are among those features that a storyboard cannot fully capture, but which can have a significant impact on how effectively the ad or video communicates the major statement of product risks. As a result, the translation from storyboard to finished video is an entry point for regulatory risk and requires careful legal, regulatory and medical review in both the video footage capturing and editing stages to ensure the finished video satisfies FDA's requirements.

In assembling a finished broadcast ad, the regulations explicitly require that, at minimum, the important risk information (i.e., "information relating to the major side effects and contraindications") must be presented through the audio. As such, in light of the increased enforcement focus of FDA on these ads, companies would be wise to ensure the following:

- Employ a minimal amount of other distractions (e.g., quick scene changes, flashy SUPERs and sounds/music).
- Challenge yourself on whether the components you choose to use (both audio and video) distract (and detract) too much from the risk information.

- Examine whether other components are making it harder to understand the risk information (e.g., music level competing with the audio voice-over risk information).
- Consider whether the visual information is so incongruous with the risk information that it could be perceived as minimizing the risk information.

Additionally, as part of your general approach to broadcast advertisements:

- Consider a policy of waiting for OPDP review and advisory comments on broadcast advertisements before airing the advertisement, which is a policy adopted by some companies.{15} If you do not choose to follow this practice for all broadcast advertisements, consider a risk-based approach, using the categories of advertisements and general principles from FDA's proposed, but not yet formally implemented, *DTC Television Ad Pre-Dissemination Review Program* to guide your company's policies.{16}
- Consider how your company's policy with DTC ads comports with the *PhRMA Guiding Principles: Direct to Consumer Advertisements About Prescription Medicines* (e.g., designing these ads to "responsibly educate the consumer.")){17}
- Because the ad will be subject to FDA's "net impression" standard on misleading impressions, consider testing the advertisement with consumers drawn from the target audience, whether informally or through market research.

We do not know whether the companies cited in recent FDA enforcement letters sought advisory comments from FDA on their storyboard drafts. However, if any of these companies received feedback from FDA before launching their ads, these enforcement letters would underscore that decisions around how to implement FDA's feedback are as important as decisions around whether to seek FDA's feedback. Insufficiently addressing FDA's feedback can lead to an enforcement risk. In addition, companies often employ two different teams – one that interfaces with FDA and another that conducts the day-to-day review of promotional materials. These separate teams also can create an opportunity for enforcement risk in the finished ad by increasing the potential for comments from FDA to be downplayed or even overlooked in the finished ad. As a result, promotional review committee members for product brands should be intimately involved in both the comments sought and received from FDA as well as the implementation of those comments in the final product, including video, audio and onscreen presentations (e.g., SUPERs).

With the proliferation of online media platforms that are TV-like, and companies' increased utilization of these platforms in the future, it is unlikely that FDA will lessen its enforcement focus in this area. On the contrary, on 21 August 2017, FDA published a request for information and comments related to the content of the major statement (e.g., "What are the potential effects of only including risks from the FDA-approved product labeling that are severe, serious, or actionable…?") indicating that this is a focus of the current FDA administration.{18} While continuing to monitor future enforcement letters from FDA, companies should consider formalizing a process regarding their handling of the preparation and finalization of both TV and online ad content.

References

1. US Food and Drug Administration. Letter #4100080 to Orexigen Therapeutics, Inc. https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm560127.htm. FDA website. Accessed 21 September 2017.
2. US Food and Drug Administration. Letter #4026192 to Celgene Corporation. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM533292.pdf. FDA website. Accessed 21 September 2017.
3. US Food and Drug Administration. Letter #4026224 to Sanofi-Aventis US. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM533300.pdf. FDA website. Accessed 21 September 2017.
4. *US Food and Drug Administration Amendments Act of 2007*, Pub. L. No. 110-85, § 901, 121 STAT. 940.
5. "FDA to Cease Work on Certain Tobacco, Advertising, Food Safety Rules." *InsideHealthPolicy*. July 2017. https://insidehealthpolicy.com/daily-news/fda-cease-work-certain-tobacco-advertising-food-safety-rules. Accessed 21 September 2017.
6. 21 C.F.R. § 202.1(e)(1).Prescription-Drug Advertisements. https://www.accessdata.fda.gov/scripts/

cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=202.1. Accessed 28 September 2017.
7. 21 U.S.C. § 321(n). Definitions, Generally. Legal Information Institute. https://www.law.cornell.edu/uscode/text/21/321. Accessed 28 September 2017.
8. US Food and Drug Administration. *Guidance for Industry: Consumer-Directed Broadcast Advertisements.*https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm070065.pdf. FDA website. Accessed 21 September 2017.
9. US Food and Drug Administration. *Guidance for Industry: Consumer-Directed Broadcast Advertisements Questions and Answers*. https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm122825.pdf. FDA website. Accessed 21 September 2017.
10. US Food and Drug Administration. *Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion.* https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm155480.pdf. FDA website. Accessed 21 September 2017.
11. Federal Trade Commission. FTC Policy Statement on Deception. October 1983. https://www.ftc.gov/system/files/documents/public_statements/410531/831014deceptionstmt.pdf. Accessed 21 September 2017.
12. ThinkwithGoogle. YouTube Insights. https://www.thinkwithgoogle.com/_qs/documents/922/youtube-insights-jan-2014_research-studies.pdf. Issue 3 January 2014.
13. YouTube TV. https://tv.youtube.com/welcome. Accessed 28 September 2017.
14. US Food and Drug Administration. Letter #3694177 to Luitpold Pharmaceuticals, Inc. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM432965.pdf. FDA website. Accessed 21 September 2017. “While the audio portion of the interview discusses IDA and the benefits of Injectafer treatment, it fails to discuss any risks associated with Injectafer. Instead, the risk information appears in a super which is displayed on-screen for approximately 30 seconds out of the nearly seven-minute video segment…. Furthermore, the risk information appears at the bottom of the video segment and is displayed at the same time as the audio portion of the interview, which distracts the audience from the risk information.”
15. Merck Sharp and Dohme Corp. Public Policy Statement: Direct-to-Consumer Broadcast Advertising in the United States. https://www.merck.com/about/views-and-positions/direct_to_consumer_advertising2009.pdf. Accessed 21 September 2017.
16. US Food and Drug Administration. *Guidance for Industry: Consumer-Directed Broadcast Advertisements.* https://www.fda.gov/ucm/groups/fdagov-public/documents/document/ucm295554.pdf. FDA website. Accessed 21 September 2017.
17. The Pharmaceutical Research and Manufacturers of America (PhRMA), PhRMA Guiding Principles: Direct to Consumer Advertisements About Prescription Medicines. http://phrma-docs.phrma.org/sites/default/files/pdf/phrmaguidingprinciplesdec08final.pdf. December 2008. Accessed 21 September 2017.
18. Register Document Number 2017-17563: Content of Risk Information in Major Statement in Prescription Drug Direct-to-Consumer Broadcast Advertisements. Published 21 August 2017.

About the Authors

Justin Mann is an associate at Alston & Bird LLP in the food, drug and device/FDA practice group whose areas of focus span across the product lifecycle, from product promotion to responding to inspection observations and warning letters. He can be reached at Justin.Mann@alston.com.

Julie Tibbets is a partner at Alston & Bird LLP in the food, drug and device/FDA practice group whose core experience includes advising manufacturers and marketers on corporate communications, product promotion, and interactions with healthcare professionals. She can be reached at Julie.Tibbets@alston.com.

Cite as: Mann, J. and Tibbets, J. “FDA’s Enforcement Trends for Broadcast Advertisements.” *Regulatory Focus*. September 2017. Regulatory Affairs Professionals Society.