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Client Alert

FDA & Life Sciences Practice Group

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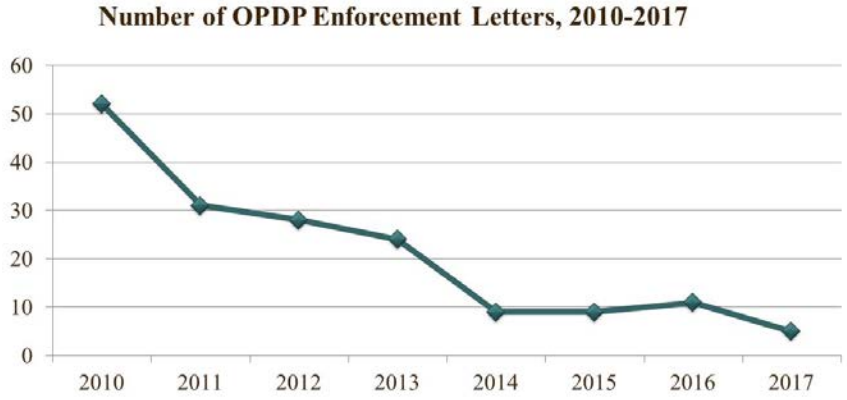
2017 Year in Review: FDA Office of Prescription Drug Promotion Warning and Untitled Letters

In 2017, the U.S. Food and Drug Administration (FDA) Office of Prescription Drug Promotion (OPDP) issued a total of five enforcement letters that cited violations related to the advertising and promotion of prescription pharmaceutical products. Of the five letters, three were Warning Letters and two were Untitled Letters. The number of letters last year represents a record low for the total number of enforcement letters issued by OPDP related to pharmaceutical advertising and promotion.



Risk Presentation Was the Focus of Four of the Five Letters

The focus of OPDP's 2017 enforcement letters was generally similar to recent years, with a majority of the letters focusing on presentation of risk information. FDA cited four of the five companies for false or misleading presentation of risk information.

Cited Violation	Number of Letters Containing Violation
False or Misleading Risk Presentation	4
Omission of Material Fact	2
Misbranding of an Investigational Drug	1
Failure to Submit Under Form FDA-2253	1
False or Misleading Efficacy Claims	1

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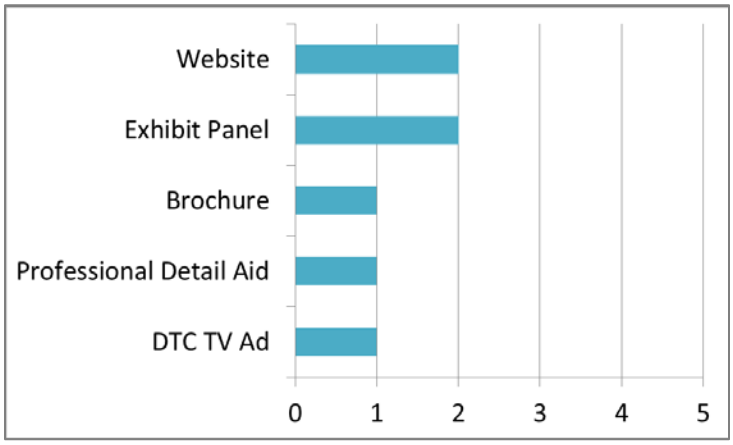
Notable Trends in 2017

The 2017 Warning and Untitled Letters targeted a variety of forms of promotional materials.



Observations and Key Learnings from the 2017 OPDP Letters

- **2017 enforcement letters targeted opioids and weight-loss drugs:** Of the five enforcement letters in 2017, one was issued for promotion of an opioid product. Two letters were issued for drugs indicated for weight loss.

- **Public health concerns and product risk profile appear relevant to the selection of enforcement targets:** OPDP has long stated that one significant factor, among many, in assessing enforcement priorities and selecting targets for issuance of enforcement letters is risk to public health. Notably, in four of the 2017 letters, OPDP specifically highlighted these public health concerns, with several letters noting that the promotional violations were particularly alarming from a public health perspective "given the serious and life threatening risks associated with the drug."

- **Continued enforcement trend on presentation of risk information in direct-to-consumer (DTC) television advertising:** OPDP issued an untitled letter for the DTC television advertisement for Contrave®, a drug indicated for chronic weight management. OPDP objected to the presentation of risk information in the ad, including simultaneous presentation of unrelated risk information in both audio and visual format. The ad displayed superimposed text listing the most common adverse reactions at the same time that a voiceover presented Contrave's contraindication for concomitant opioid use. OPDP stated that the simultaneous presentation of competing messages made it difficult for consumers to adequately process and comprehend the risk information. The Contrave letter continues a trend from 2016, in which two of the 11 letters also focused on DTC television ads. In those letters, OPDP objected to risk information presented simultaneously with fast paced visuals (many of which showed people smiling, dancing and happily engaged in activities) and distracting, upbeat music. FDA noted that the visuals were unrelated to the risk information and the frequent scene changes and fast paced movements competed for consumers' attention.

- **Pre-approval promotion remains an OPDP enforcement target:** OPDP issued an Untitled Letter to UCLA for promotion of an investigational drug, PSMA-PET for use in PET scans to detect prostate-cancer cells. OPDP objected to pre-approval efficacy and safety claims on UCLA's website and in a brochure. The materials included claims regarding accuracy, impact on ability to detect prostate cancer, and lack of side effects and significant risks. This letter continues a trend from 2016, in which four of the 11 letters cited preapproval promotion of investigational drugs. Taken together, these five letters from 2016 and 2017 provide insight into factors that FDA may consider when assessing whether communications regarding investigational drugs cross the line into promotion. Such factors may include:
    - Efficacy claims or safety claims for investigational drugs.
        - In a description of the investigational drug, use of the word "potential" preceding benefits is insufficient to mitigate the misleading presentation.
    - Promotional-sounding statements and descriptions phrased as established facts (e.g., "long-acting," "tamper-resistant").
    - Use of the trade name.
    - Positioning an investigational drug in a manner that suggests the product is approved (e.g., presentation of information about an investigational product alongside information about approved products).
    - Lack of clear and prominent statement (accompanying any investigational drug information) that the drug is investigational and not approved by FDA for any use. Such a statement "one click away" appears to be insufficient.
- **Additional violations cited in the 2017 enforcement letters include the following:**
    - **False or Misleading Presentation of Risk Information or Omission of Risk Information** – Within this category of violations, OPDP's objections can be summarized to include:
        - **Failure to include any risk information in the promotional piece itself** – See, e.g., Conzip and Zolpimist letters.
        - **Cherry-picking important risk information** – See, e.g., Contrave letter, where the DTC TV ad disclosed risks of suicide or suicidal thoughts associated with Contrave and the contraindication for concomitant opioid use, but failed to disclose other contraindications and information about neuropsychiatric reactions also discussed in the product's Boxed Warning.
        - **Presenting risk information in a manner that is distracting or confusing to the audience, resulting in minimization of the overall risk message** – See, e.g., Contrave letter, where OPDP objected to presentation of risk information in competing voiceover and superimposed text.

- **Omission of Material Facts** – Within this category of violations, OPDP's objections can be summarized to include:

  - **Failure to provide full FDA approved indication** – See, e.g., Lomaira letter, where the exhibit panel failed to include material information regarding the product's indication, including that it is indicated as a short term treatment of a few weeks for patients reaching or exceeding a minimum body mass index. The panel also omitted the following statement: "The limited usefulness of agents of this class, including phentermine, should be measured against possible risk factors inherent in their use…"

  - **Failure to provide important limitations of use** – See, e.g., Conzip letter, where the detail aid failed to state that due to the risks of addiction, abuse and misuse, Conzip is indicated only when alternative treatment options are inadequate.

- **False or Misleading Presentation of Efficacy –** The Zolpimist Warning Letter included a citation for False or Misleading Presentation of Efficacy. OPDP's specific objections within this category can be summarized as:

  - **Misleading superiority claims** – Claims misleadingly suggested clinical superiority to other oral zolpidem products based on formulation and mode of delivery, including "mode of delivery offers some very clear advantages as compared to other delivery methods" and "engineered to outperform the oral tablets." OPDP noted that it was unaware of data to support these claims and that no references were provided in the pieces. OPDP also emphasized that Zolpimist was approved under a 505(b)(2) application, demonstrating bioequivalence to Ambien, a zolpidem oral tablet.

  - **Misleading claim regarding onset of action** – Claims that Zolpimist "induces sleep" in ten minutes misleadingly suggested a therapeutic onset of action of ten minutes without supporting data.

  - **Misleading claim regarding food effect** – Claims regarding a lack of food effect with Zolpidem were inconsistent with language in the Zolpidem Prescribing Information indicating a slowed effect of Zolpimist following a meal.

For your reference, we have prepared a chart that lists the five Warning and Untitled Letters issued to pharmaceutical manufacturers for promotional violations in 2017, including summaries of the promotional violations alleged in each letter and hyperlink to each letter and related promotional materials. The chart is available online in a searchable PDF document here.

For summaries of other key actions taken by OPDP in 2017, please see the following King & Spalding Client Alerts: (1) *FDA Defends its First Amendment Position in "Memorandum"* (January 26, 2017), available here; (2) *FDA Issues Draft Guidance Addressing Communications with Payors* (January 20, 2017), available here; and (3) *FDA Takes Action in the Last Days of the Obama Administration to Clarify Some of Its Views on Off-Label Communications* (January 19, 2017), available here.

For a summary of FDA enforcement of medical device advertising and promotion in 2017, please see the King & Spalding Client Alert, *2017 Year in Review: FDA Medical Device Advertising and Promotion Warning and Untitled Letters* (February 23, 2018), available here.

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King & Spalding's FDA & Life Sciences Practice Group was selected by Law360 as a "Life Sciences Practice Group of the Year" for 2017. More than 300 attorneys at the firm practice in life sciences, with a regulatory team of nearly 40 attorneys and consultants who are based in the U.S. and Europe. Our team provides practical legal counseling and technical consulting on a full array of issues involving all FDA-regulated products. In addition, our team calls upon the expertise of lawyers in several related areas within the firm, including the civil and criminal litigation group, the appellate litigation group, and the government advocacy and public policy group, which have effectively represented clients who are the targets of government initiated lawsuits and investigations. Please let us know if you have any questions.