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Summary of FDA Advertising and Promotion Enforcement Activity in 2015

Food, Drugs, and Devices

This e-alert is part of a series of alerts summarizing publicly-available FDA enforcement letters relating to the advertising and promotion of prescription drugs, medical devices, and biologics. This alert reviews warning and untitled letters issued in 2015.

In 2015, FDA's Office of Prescription Drug Promotion (OPDP) posted the following letters on FDA's website:

- Untitled letter to Luitpold Pharmaceuticals, Inc. re: Injectafer (ferric carboxymaltose injection) (January 29, 2015)
- Untitled letter to Semel Institute for Neuroscience and Human Behavior re: [F-18] FDDNP (February 20, 2015)
- Untitled letter to Discovery Laboratories, Inc. re: NDA 021746 SURFAXIN (lucinactant) Intratracheal Suspension (March 3, 2015)
- Untitled letter to Otsuka Pharmaceutical Development & Commercialization, Inc. re: ABILIFY (aripiprazole) Tablets (April 17, 2015)
- Untitled letter to Oak Pharmaceuticals, Inc. re: Nembutal Sodium Solution (pentobarbital sodium injection, USP) CII (May 15, 2015)
- Untitled letter to Actavis Laboratories UT, Inc. re: Rapaflo (silodosin) Capsule for oral use (May 19, 2015)
- Untitled letter to ASCEND Therapeutics US, LLC re: EstroGel 0.06% (estradiol gel) for topical use (June 23, 2015)
- Warning letter to ECR Pharmaceuticals re: TussiCaps (hydrocodone polistirex and chlorpheniramine polistirex) Extended-release Capsules CII (July 27, 2015)
- Warning letter to Duchesnay, Inc. re: DICLEGIS (doxylamine succinate and pyridoxine hydrochloride) delayed-release tablets, for oral use (August 7, 2015)

The Office of Compliance and Biologics Quality (OCBQ) in FDA's Center for Biologics Evaluation and Research (CBER) posted one letter in 2015, which Covington discussed in a previous alert.

The Office of Compliance (OC) in FDA's Center for Devices and Radiological Health (CDRH) did not post any enforcement letters relating to advertising and promotion on FDA's website in 2015.

This alert merely summarizes the allegations contained in FDA's letters. It does not contain any analysis, opinions, characterizations, or conclusions by or of Covington & Burling LLP. As a result, the information presented herein does not necessarily reflect the views of Covington & Burling LLP or any of its clients.

Office of Prescription Drug Promotion (OPDP) Letter Summaries

Luitpold Pharmaceuticals, Inc. (January 29)

OPDP alleged that a video segment about Injectafer provided evidence that the product was intended for an unapproved new use and that its labeling lacked adequate directions for use.

Lack of Adequate Directions for Use

OPDP contended that the video segment was misleading because its claims implied that Injectafer can be used to treat all patients with iron deficiency anemia (IDA) "regardless of concomitant disease or prior treatment, in addition to the two limited subsets of patients specified later in the claim." In contrast, FDA only approved Injectafer for use as a "second line treatment in adult IDA patients who have an intolerance or unsatisfactory response to oral iron, or to patients who have non-dialysis dependent chronic kidney disease." OPDP stated that Injectafer's approved labeling omits instructions for use in all patients who have IDA.

Minimization of Risk

OPDP also contended that the video segment was misleading because it failed to "convey significant risk information associated with Injectafer." In particular, the video segment included interviews discussing Injectafer's benefits, but it omitted discussions of any risks associated with the product. The only statement regarding risk in the video segment was a display of the risk information on screen for 30 seconds without any audio. OPDP found that this presentation was "misleading" because the video failed "to provide sufficient emphasis for Injectafer's important risk information in the main part of the video."

OPDP also contended that the video segment minimized risk information because it included a dialogue discussing risks associated with other IDA treatments, but it omitted statements that Injectafer is associated with many similar risks. OPDP found that this unbalanced discussion of risk further worsened the misleading nature of the video segment.

Omission of Material Fact

OPDP found that the video segment was misleading because it did not provide information about the approved dosing regimen for Injectafer. Specifically, the video segment included a statement that Injectafer is "the first FDA-approved iron approved as a high single dose IV iron and a total dose of IV iron." OPDP determined that this claim was misleading because it suggests that Injectafer can be administered as a "single, high dose of iron," which is not the dosing regimen for which FDA approved the product.

Misleading Claims

OPDP determined that the video segment included claims suggesting that Injectafer could "drastically improve" the quality of life of an IDA patient. In particular, OPDP found that statements such as Injectafer "really changed her life" and the patient "blossomed like a rose" were misleading because they indicated that the product had a broad positive impact on a patient's life. OPDP also found that statements that implied that Injectafer possesses advantages over existing approved treatments were misleading.

Semel Institute/Gary W. Small, MD (February 20)

OPDP contended that a website for the investigational new drug [F-18] FDDNP constituted pre-approval drug promotion.

Promotion of an Investigational New Drug

OPDP contended that the website detailed the use of FDDNP in brain PET scans for the diagnosis of traumatic brain injuries, Alzheimer's disease, and certain neurological conditions. OPDP noted that those particular uses of the drug would require a prescription from a physician. OPDP listed various claims on the website that OPDP contended promoted the drug for the purpose for which it was investigated. These included statements such as "Protecting our athletes who want to know about the consequences of concussive brain injuries;" "Get started, get safe;" and "The FDDNP PET scan… is the only currently available method to measure brain tau proteins in living people." OPDP also stated that the website implied the safety and efficacy of the product, but FDA has not approved the product for any use.

Discovery Laboratories (March 5)

OPDP alleged that a webpage for SURFAXIN Intratracheal Suspension was false and misleading because the webpage included unsubstantiated superiority claims and lacked adequate directions for use.

Unsubstantiated Superiority Claims

OPDP alleged that the website's claims were misleading because they included comparisons to other drugs that were not supported by substantial evidence. The claims on the website included "Surfaxin, the only available synthetic alternative to animal-derived surfactants approved by the FDA" and "Direct clinical comparisons to Exosurf, Survanta, and Curosuf." OPDP contended that the comparisons were misleading because they implied that Surfaxin was superior "because it has 'evolved' from more primitive, animal-derived surfactants." OPDP also contended that there is no substantial evidence to support claims that Surfaxin is superior to other approved drugs. Finally, OPDP contended that the claims were misleading because they implied that there had been a "therapeutic evolution" in the class of drugs.

OPDP also contended that the webpage was misleading because it included claims that "Sinapultide (KL4 peptide) mimics critical surfactant protein B function." OPDP stated that FDA was unaware of substantial evidence to support claims that KL4 "mimics endogenous human SP-B." Finally, OPDP contended that the claim "Neonatologists and parents share concerns regarding animal-derived medications" was misleading because it implies that Surfaxin is superior to other surfactants because of its synthetic formulation.

Lack of Adequate Directions for Use

OPDP contended that the website's claims were misleading because they provided evidence that Surfaxin was intended for a use for which it had not received approval. In particular, OPDP identified statements such as "Surfaxin, the only available synthetic alternative to animal-derived surfactants approved by the FDA" and "First U.S. FDA approved alternative to surfactants made with animal extract in more than 20 years." OPDP alleged that these claims implied that Surfaxin was an alternative to other surfactants for all uses. OPDP contended that Surfaxin's label lacks adequate directions for use for those purposes.

Otsuka Pharmaceutical Development & Commercialization, Inc. (April 17)

OPDP alleged that a pharmacology aid for ABILIFY tablets was false and misleading because it included "misleading claims and presentations about the drug."

Misleading Claims and Presentations

OPDP contended that the pharmacology aid's claims about the mechanism of action of Abilify were false and misleading. OPDP first alleged that the totality of the claims "misleadingly implies a greater degree of certainty about the mechanism of action of Abilify in humans" than currently exists. OPDP noted that the references cited in the pharmacology aid failed to support the claims in the aid. OPDP also found that in their entirety, the claims were misleading because the claims implied that Abilify possessed advantages over other approved treatments for bipolar disorder and major depressive disorder.

Oak Pharmaceuticals, Inc. (May 14)

Omission of Risk Information

OPDP found that a Booth Graphic 48x60 Vinyl banner (exhibit banner) for Nembutal Sodium Solution CII was misleading because it omitted important risk information about the product. OPDP identified statements in the exhibit banner, such as "Control the Uncontrollable" and "the control you need when seizures are their worst," but noted that the exhibit banner omitted all contraindications, warnings and precautions, and common adverse reactions associated with the product's use.

Omission of Material Facts

OPDP also contended that the exhibit banner was misleading because it omitted material facts regarding Nembutal's FDA-approved indication. OPDP noted that the exhibit banner made claims regarding Nembutal's use for the treatment of seizures. However, OPDP found that the exhibit banner omitted the following from the Indications and Usage section: "Anticonvulsant, in anesthetic doses, in the emergency control of certain acute, convulsive episodes, e.g., those associated with status epilepticus, cholera, eclampsia, meningitis, tetanus, and toxic reactions to strychnine or local anesthetics." Because the exhibit banner omitted such information about the approved indication, OPDP found that the banner was misleading.

Actavis Laboratories UT, Inc. (May 19)

Unsubstantiated Claims

OPDP determined that the homepage of the website for RAPAFLO Capsule for oral use was misleading because it included unsubstantiated claims. OPDP found that a claim and a presentation on the website were not supported by adequate and well-controlled clinical studies. Specifically, OPDP identified the following statement, "BPH symptom relief that works nights so

he can work days" and a picture of a man who was walking to the bathroom from bed at night. OPDP found that those representations were misleading because they implied that Rapaflo had been demonstrated to improve sleep disturbance and work productivity. However, OPDP noted that the website cites to no references for support of such claims. OPDP also noted that the pivotal studies of the drug did not measure individual symptoms, and they did not study the effect of Rapaflo on sleep quality or work productivity. Thus, OPDP found that such claims were not supported by substantial evidence.

ASCEND Therapeutics US, LLC (June 23)

OPDP contended that a professional EstroGel Zazzle Card A-IS for EstroGel 0.06% for topical use was false or misleading because it omitted important risk information regarding the product.

Omission of Risk Information

OPDP alleged that the Zazzle card was misleading because it included efficacy claims regarding EstroGel, but it omitted important risk information. In particular, FDA stated that the Zazzle card failed to include information from the boxed warning. FDA also noted that the Zazzle card included the following statement: "Estrogen therapies increase the risk of certain cancers, cardiovascular disorders, and probable dementia." However, OPDP noted that the card failed to discuss specific risks related to cancer and cardiovascular disorders in the Boxed Warning. Finally, OPDP noted that the card failed to discuss the drug's contraindications. For these reasons, OPDP concluded that the Zazzle card omitted important risk information, and thus was misleading.

ECR Pharmaceuticals (July 27)

OPDP contended that a professional sales aid for TussiCaps Extended-release Capsules CII was false or misleading because it omitted risk information, inadequately communicated the full indication for the drug, and included unsubstantiated claims.

Omission of Risk Information

OPDP alleged that the sales aid was misleading because it included "numerous efficacy claims" regarding TussiCaps but omitted any risk information about the product. OPDP noted that the omission of any risk information included the omission of potentially serious and fatal risks. OPDP alleged that this omission implied that the drug is safer "than has been demonstrated," which was especially concerning in light of the drug's potential public health impact. The fact that the brochure contained a disclaimer that it was to remain in the sales representative's possession and that appropriate product labeling should accompany discussions with health care professionals did not mitigate the omission of risk information from the sales aid.

Inadequate Communication of Indication

OPDP also contended that the sales aid failed to convey the full approved indication for TussiCaps. OPDP noted that the sales aid included the claim that TussiCaps is used "for the relief of cough and upper respiratory symptoms associated with colds or allergies."

However, OPDP noted that TussiCaps is indicated "for relief of cough and upper respiratory symptoms associated with allergy or a cold in adults and children 6 years of age and older." OPDP also noted that TussiCaps is contraindicated for children less than 6 years old. OPDP acknowledged that the sales aid provided usual dosages for "patients six years of age and older," but it explained that this presentation did not mitigate the misleading impression created

by the sales aid. OPDP also noted that the omission of age information was particularly misleading in light of an image in the sales aid of a "coughing young child."

Unsubstantiated Claims

OPDP contended that the sales aid was misleading because it included statements suggesting that patients prefer TussiCaps over oral liquid formulations because TussiCaps is a capsule. OPDP identified claims in the sales aid, such as "Patient Preferred Capsule" and "73% of adult prescription cough syrup users said they prefer capsules over liquid medications." OPDP also identified an image with a zip bag with liquid medication spilled at the bottom.

OPDP alleged that these claims in total suggested that patients prefer TussiCaps capsules over liquid formulations. OPDP noted that the study cited to support these claims did not "specifically evaluate" whether patients preferred TussiCaps to liquid formulations. Accordingly, OPDP concluded that the cited study was "insufficient" to support the claims in the sales aid.

Duchesnay, Inc. (August 7)

OPDP alleged that a social media post about DICLEGIS delayed-release tablets was false and misleading because it presented efficacy claims but failed to communicate any risk information and because it omitted material facts. OPDP noted that Duchesnay's alleged violations were particularly troubling because Duchesnay had received an untitled letter regarding promotional activities for DICLEGIS in 2013.

Omission of Risk Information

The promotional material at issue was a social media post by public figure Kim Kardashian. Kardashian posted a picture of herself holding a bottle of DICLEGIS tablets and stated that DICLEGIS reduced her morning sickness at "no increased risk to the baby." The post referred the reader to www.DiclegisImportantSafetyInfo.com for risk information about DICLEGIS.

OPDP concluded that the link to the DICLEGIS Safety Information site did not mitigate the misleading omission of risk information and concluded that the post "entirely omit[ted] **all** risk information."

Omission of Material Fact

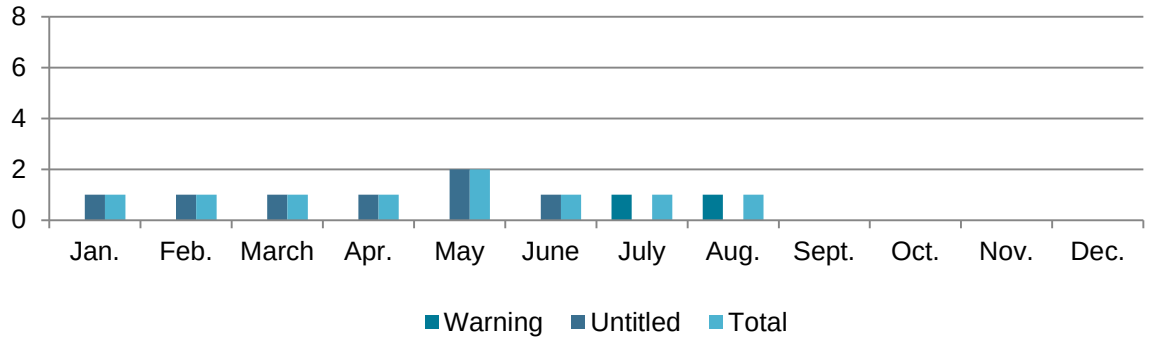
OPDP also found the post misleading because it failed to provide material information regarding DICLEGIS's full approved indication, including limitations of use. The post did not mention that DICLEGIS had not been studied in women with hyperemesis gravidarum (severe nausea during pregnancy).

Office of Prescription Drug Promotion (OPDP) Year-in-Review

I. Timing of Enforcement Letters

OPDP's 2015 enforcement letters were generally evenly distributed throughout the year. There was at least one letter per month for the first eight months of the year. No letters were issued in the final four months of 2015.

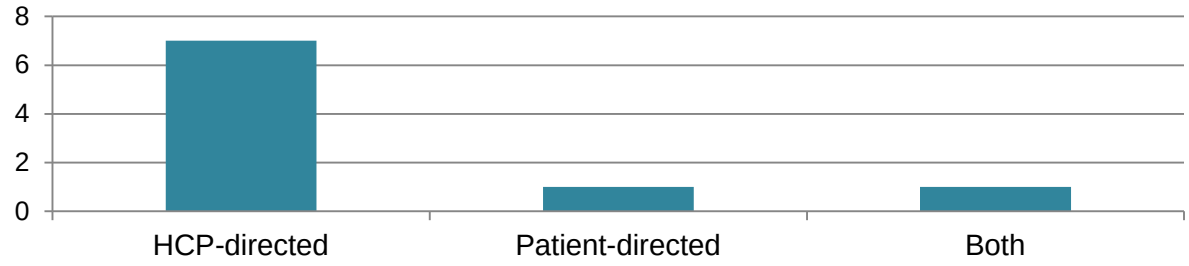
OPDP Letters Issued by Month (2015)
Source: C&B tabulation,
based on letters on FDA website



II. Content of Enforcement Letters

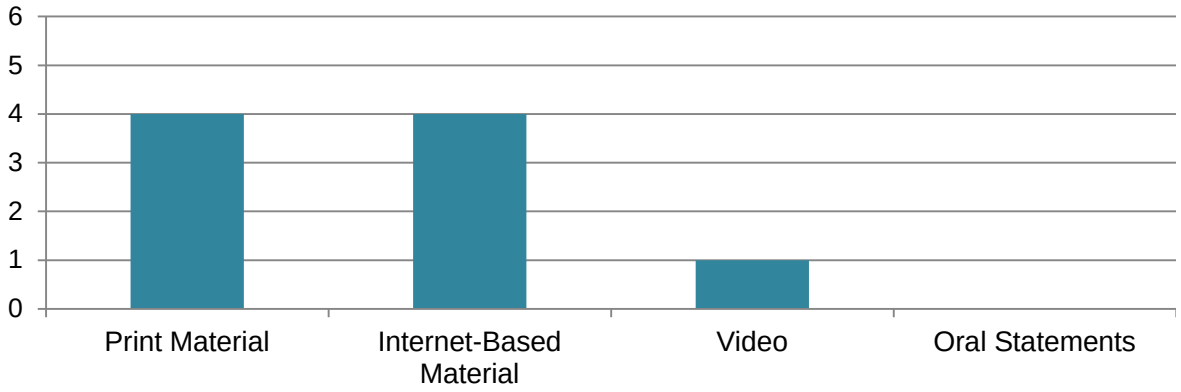
Of the nine letters issued by OPDP, seven concerned promotional materials directed at healthcare professionals. One letter addressed materials directed at patients, and one letter addressed materials directed at both patients and healthcare professionals.

OPDP Letters Issed by Audience (2015)
Source: C&B tabulation, based on letters on FDA website

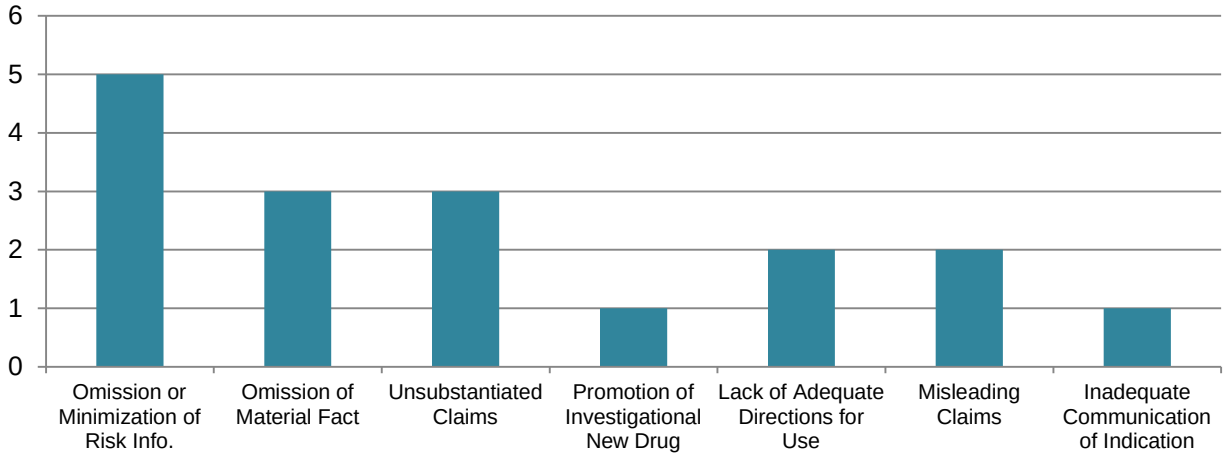


In 2015, OPDP's letters focused on print materials (such as exhibit banners and sales aids) and internet materials (such as websites and a social media post). Only one letter addressed a video. The enforcement letters included a wide range of allegations. The most common allegation was Omission or Minimization of Risk Information (5) followed by Omission of Material Fact (3) and Unsubstantiated Claims (3).

OPDP Letters by Type of Promotional Piece Addressed (2015)
Source: C&B tabulation, based on letters on FDA website



Number of Letters by Allegation*(2015)
Source: C&B tabulation, based on letters on FDA website



*Allegations exceed the total number of enforcement letters issued, as several letters contained more than one allegation.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food, Drugs, and Devices practice:

Stefanie Doebler	+1 202 662 5271	sdoebler@cov.com
Michael Labson	+1 202 662 5220	mlabson@cov.com
Scott Cunningham	+1 415 591 7089	scunningham@cov.com
Claire O'Brien	+1 202 662 5776	cobrien@cov.com