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2014 End-of-Year Summary of FDA Promotional Enforcement Activity

August 11, 2015

Food & Drug

This alert reviews trends emerging from the warning and untitled letters issued in 2014 by the Office of Prescription Drug Promotion (OPDP) of the Center for Drug Evaluation and Research (CDER), the Office of Compliance and Biologics Quality (OCBQ) of the Center for Biologics Evaluation and Research (CBER), and the Office of Compliance (OC) of the Center for Devices and Radiological Health (CDRH).

We examined 10 advertising and promotion letters issued by OPDP and two letters issued by OC. OCBQ did not issue any warning or untitled letters during 2014. We tabulated the most frequently cited allegations, leaving out allegations included in only a few letters.

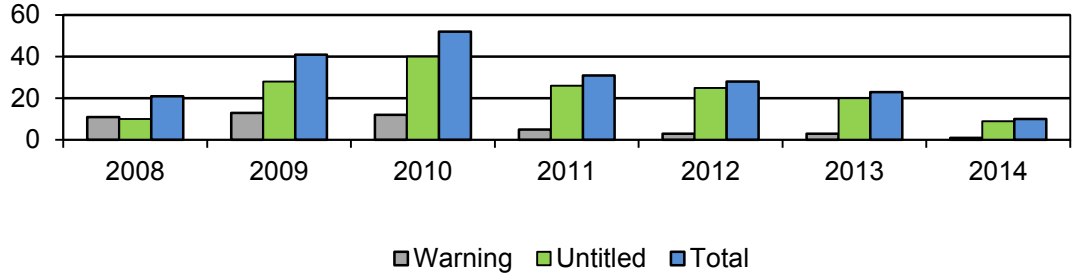
This alert merely summarizes trends in the allegations contained in FDA's letters. It does not contain any analysis, opinions, characterizations, or conclusions by or of Covington & Burling LLP. As a result, the information presented herein does not necessarily reflect the views of Covington & Burling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

Office of Prescription Drug Promotion (OPDP)

I. Enforcement Activity

In 2014, OPDP issued 10 advertising and promotion enforcement letters, significantly fewer than 2013's 23 letters. This represents a four-year decline, reversing a trend of increased enforcement action between the years of 2008 and 2010, which peaked in 2010 with 52 enforcement letters.

OPDP Warning and Untitled Letters (2008-2014)
Source: C&B tabulation, based on letters on FDA website

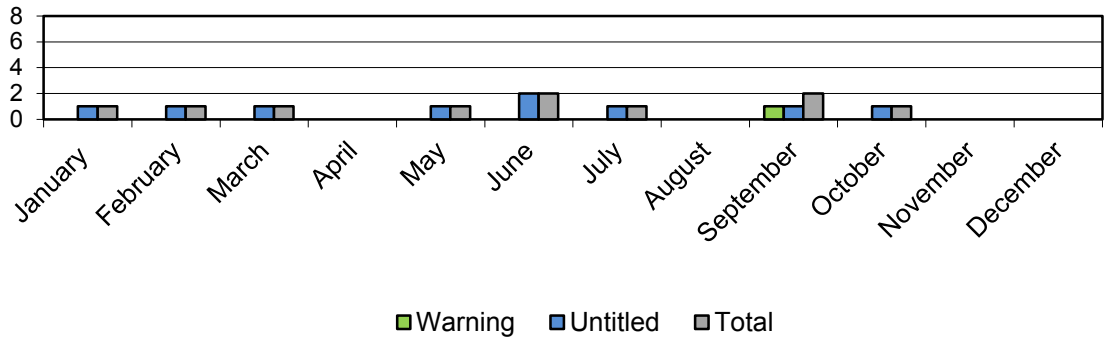


In keeping with its tendency over the last several years, OPDP primarily issued untitled letters (as opposed to warning letters) in 2014. Of the 10 letters OPDP issued in 2014, 90% (nine) were untitled letters and 10% (one) were warning letters.[1] The average number of allegations in each letter was approximately 2.8 (counted by the number of headings in each letter), which constitutes an increase over recent years. In 2011 and 2012, the average number of allegations per letter was 2.3, and in 2013, the average number of allegations per letter was 2.5.

There was no discernible trend in the timing of OPDP's enforcement letters. OPDP issued either one or two letters in the months in which it issued a letter, and OPDP did not issue letters in April, August, November, and December. The number of letters issued by OPDP dipped at the end of the year, with no letters issued in November or December. By contrast, in 2013, the number of letters peaked in November (six letters) and dipped in August and September (zero letters).

OPDP Letters Issued by Month (2014)

Source: C&B tabulation, based on letters on FDA website



II. CONTENT OF ENFORCEMENT LETTERS

A. Promotional Pieces at Issue

Similar to its past practice, OPDP focused largely on materials directed solely at HCPs, rather than materials directed at patients or both patients and HCPs. Materials focused solely on HCPs have historically comprised the most significant portion of materials addressed in enforcement letters. There was a slight departure from this trend in 2013, when OPDP focused on materials directed at both patients and HCPs.

In 2014, materials directed at HCPs comprised 70% of the materials discussed in the letters. Materials that were directed toward both HCPs and patients (e.g., general use websites with no distinguishable audience) made up 20% of promotional materials discussed in the letters, and

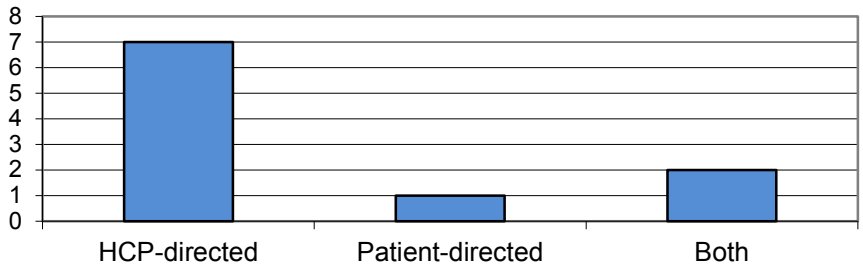
[1] In 2008, 48% of OPDP's enforcement letters were untitled letters; in 2009, 68% were untitled letters; in 2010, 77% were untitled letters; in 2011, 84% were untitled letters; in 2012, 89% were untitled letters; and in 2013, 87%.

materials directed solely at patients comprised 10% of the promotional materials. In contrast, in 2013, letters directed towards both HCPs and patients made up 43% of the materials addressed in the letters.

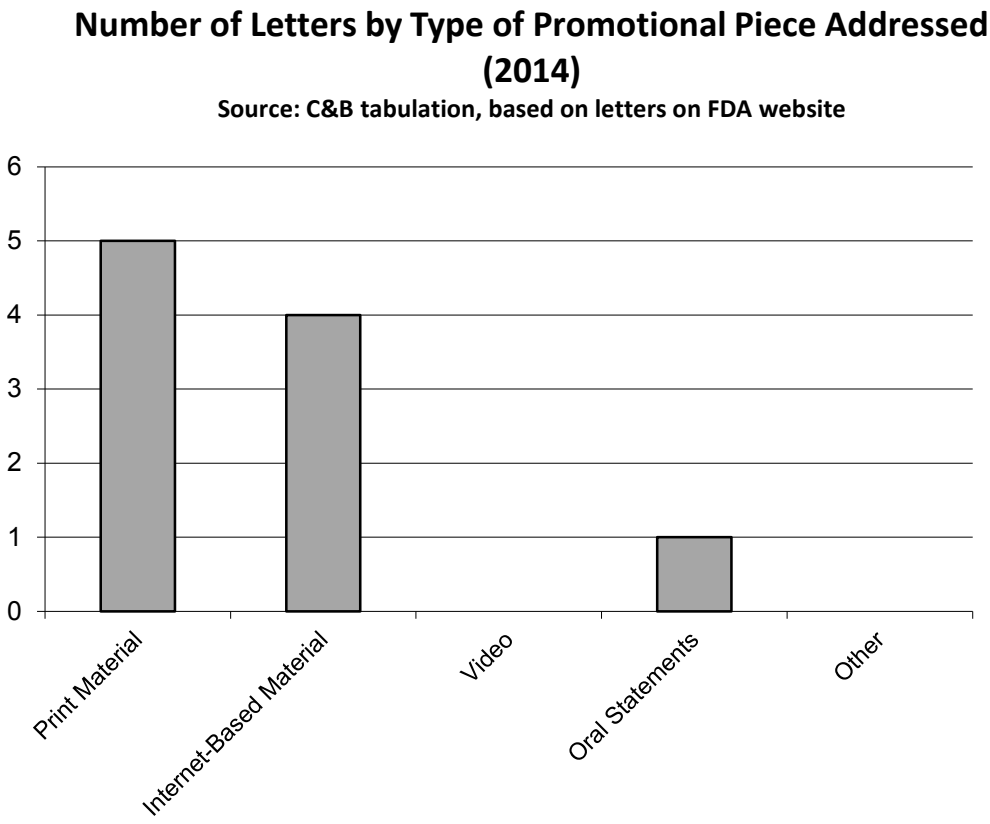
OPDP's focus in 2014 aligns with its historical emphasis on materials directed solely at HCPs. For example, in 2012, materials directed toward both audiences were addressed in only 29% of enforcement letters, which itself was a noticeable increase from 2011, when only 10% of the letters addressed materials directed toward both audiences. The discussion of materials directed solely to patients decreased, with 10% of OPDP's letters in 2014 addressing patient-directed materials, below the ratios in 2012 and 2013 when 25%, and 26% of OPDP's letters addressed these types of materials, respectively.

Number of Letters by Audience (2014)

Source: C&B tabulation, based on letters on FDA website

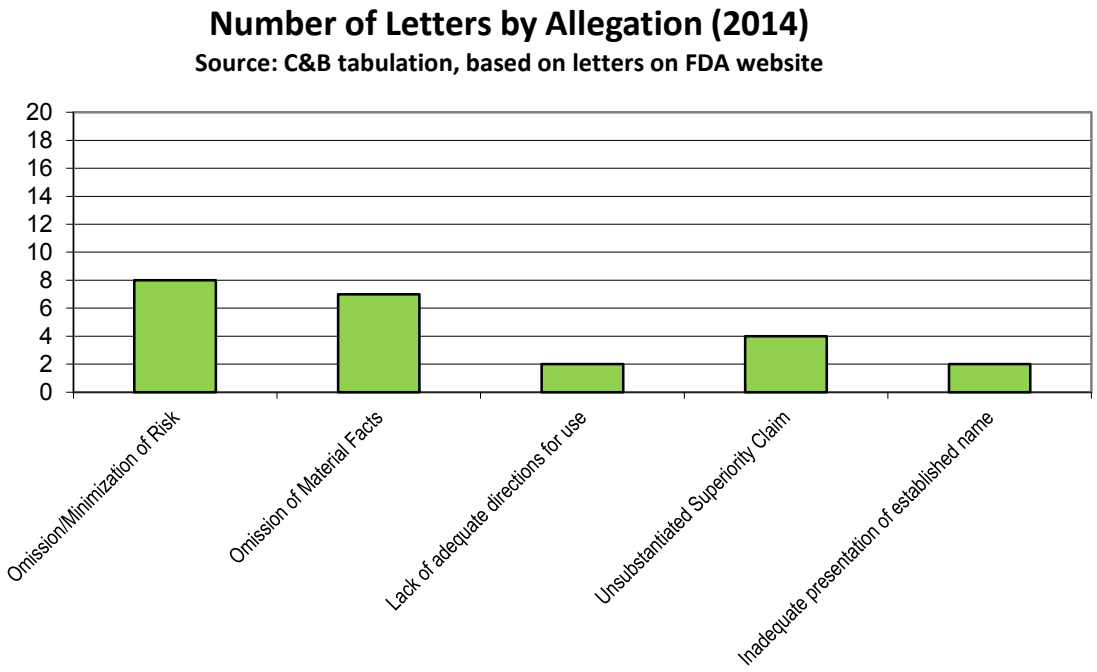


In 2014, OPDP's letters addressed a wide range of promotional pieces, including print materials (e.g., professional sales sheets, sales aids), Internet-based materials (e.g., websites, Facebook webpage, sponsored links), and professional telephone scripts. As in past years, print materials were the most frequently cited medium (50%). By comparison, in 2013, print materials were the subject of 54% of letters, and in 2012, 43% of letters. The ratio of enforcement letters that cited Internet-based materials was higher than it has been in the past. In 2014, 40% of letters addressed Internet-based materials. In contrast, Internet-based materials composed 33% of materials in 2013, 39% in 2012, and 26% in 2011.



B. OPDP's Allegations

OPDP's letters contained allegations similar to those in prior years, focusing primarily on: (1) omission and/or minimization of risk information, (2) omission of materials facts, and (3) unsubstantiated superiority claims (a subcategory within unsubstantiated claims). These areas of focus generally mirror the most frequent allegations in 2013 and 2012, with the exception of omission of material facts. OPDP also issued two letters containing each of the following allegations: (1) lack of adequate directions for use, (2) inadequate presentation of established name, and (3) failure to submit under form FDA-2253.



1. Omission and/or Minimization of Risk Information

Eight of the 10 letters (80%) issued by OPDP in 2014 contained allegations that the promotional piece(s) omitted and/or minimized the risks associated with the drug. Such allegations typically focus on promotional pieces that, according to OPDP, omit all risk information, include risk information but omit a particularly important aspect, or include risk information but present it in a way that minimizes its importance. For example, in a May 2014 untitled letter, OPDP stated that a sales aid was misleading because it included efficacy claims regarding a product, but it omitted any discussion of the risks associated with the product. FDA noted that the omission of any risk information was "particularly concerning" in light of the product's boxed warning.

2. Omission of Material Facts

Seven letters (70%) addressed promotional materials that omitted material facts. These types of allegations focus on promotional materials that fail to include important information, such as the product's approved indication, limitations on such indications, or dosing parameters. In 2014, the letters often focused on the failure to include material information about the product's FDA-approved indication. For example, in one March 2014 letter, FDA alleged that the promotional materials failed to provide material information regarding a product's FDA-approved indication because the materials suggested that the product could be used in patients with hypothyroidism. FDA found that the failure of the promotional material to disclose that the product was not approved "for transient hypothyroidism during the recovery phase of subacute thyroiditis" was misleading.

3. Unsubstantiated Superiority Claims

Four letters (40%) addressed unsubstantiated superiority claims. This percentage is nearly identical to the percentage of letters addressing unsubstantiated superiority claims in 2013 (39%). When FDA alleges that a promotional piece contains unsubstantiated superiority claims, FDA tends to focus on claims that suggest that the subject drug is superior to other treatment options when this has not been demonstrated through substantial evidence. For example, in a

September 2014 untitled letter, OPDP stated that an e-Pharm/alert included unsubstantiated superiority claims because the promotional material indicated that the product provided a clinical advantage over other products in its class. FDA contended that evidence cited by the company in support of the claim did not constitute substantial evidence, and thus the promotional material was misleading.

4. Lack of Adequate Directions for Use

Two letters (20%) alleged that promotional piece(s) lacked adequate directions for use. Generally, these allegations concern the lack of information regarding the safety and efficacy of a product for certain uses. As an example, in a September 2014 letter, OPDP contended that a product lacked adequate directions for use because its prescribing information lacked instructions or information regarding the safety and efficacy of the product for certain uses. OPDP also concluded that disclaimers and disclosures in the promotional material failed to alter the impression that the product was being promoted for certain uses.

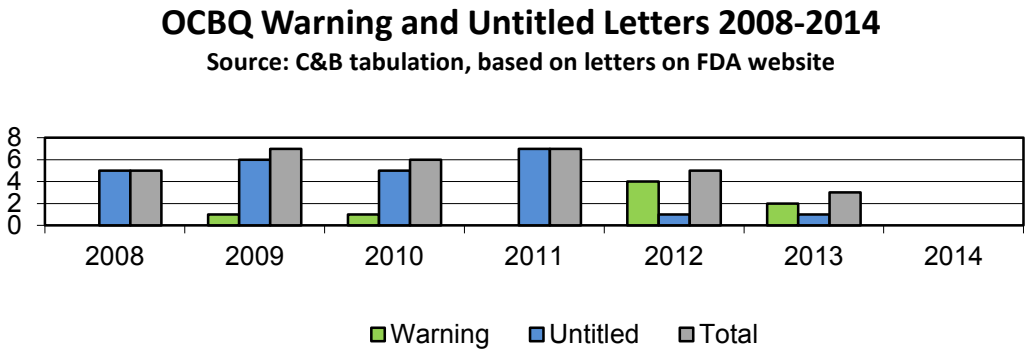
5. Other Allegations

There were also two letters in 2014 alleging the inadequate presentation of an established name and two letters alleging a failure to submit under Form FDA-2253. Less common allegations in OPDP's 2014 letters included broadening of the indication, overstatement of efficacy, unsubstantiated efficacy claim, and unsubstantiated claims.

Office of Compliance and Biologics Quality (OCBQ)

I. Enforcement Activity

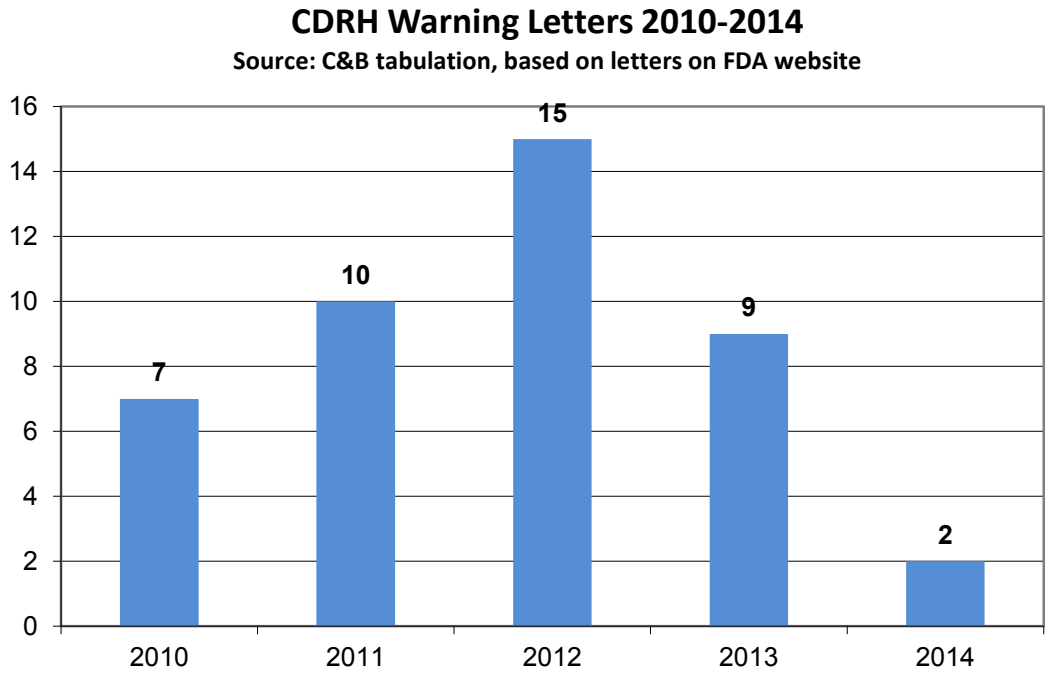
OCBQ did not issue any enforcement letters in 2014 relating to advertising and promotion. This continues a recent downward trend in enforcement letters that began in 2013, when the office issued only three letters total. This was a decrease from previous years. In particular, between 2008 and 2012, OCBQ issued between five and seven letters each year.



Center for Devices and Radiological Health (CDRH) Office of Compliance

I. Enforcement Activity

In 2014, CDRH's Office of Compliance (OC) issued two letters relating to the promotion of approved or cleared medical devices.[2] This number is a steep decrease from previous years. In 2013, the office issued nine letters, and in 2012, the office issued 15 letters. The 2014 number was also inconsistent with the number of letters issued in 2010 and 2011 (seven and 11,[3] respectively). Both of the letters issued by the office in 2014 were warning letters.



II. Content of Enforcement Letters

A. Promotional Pieces at Issue

OC focused on websites in 2014, and both letters issued by the office concerned promotional materials on websites. This is consistent with OC's practice in 2013, when OC also primarily focused on promotional materials that appeared on websites.

B. OC's Allegations

OC's two warning letters focused on allegations that manufacturers' promotional activities established intended uses that were inconsistent with permitted uses for their devices.

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[2] This count does not include letters that were determined to focus on a lack of premarket approval rather than promotional material. For example, the OC issued three letters in May that were primarily concerned that the company was allegedly marketing the device without premarket approval.
[3] One letter is not counted in the final tabulation in the chart.

For example, the warning letter issued in January 2014 involved a therapeutic massager, which is exempt from premarket notification if it is used to relieve minor muscle aches and pains. However, OC contended that the device's website suggested that the device was intended for a different use. OC alleged that the device was intended to be an ultrasonic diathermy device and that the claims concerning the product required that the product be subject to premarket approval.

The March 2014 letter issued by the office alleged that the promotional claims made by the company on its website caused the device to be adulterated and misbranded. The device was cleared "for use with compatible electrosurgical instruments in low power microsurgical applications for the removal, destruction and coagulation of tissue." The office contended that the company's claims about the device represented a "major change or modification" of the device and required a 510(k) clearance or premarket application.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food & Drug practice group:

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