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E-ALERT | Food & Drug

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2011 END-OF-YEAR SUMMARY OF FDA PROMOTIONAL ENFORCEMENT ACTIVITY

This client alert reviews the warning and untitled letters issued in 2011 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 the 31 warning and untitled letters issued by OPDP, the 7 untitled letters issued by OCBQ, and the 11 letters regarding promotional activities for approved or cleared devices issued by OC. We tabulated the most frequently cited allegations, leaving out allegations included in only a few letters.

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.

OPDP

I. ENFORCEMENT ACTIVITY

In September 2011, FDA announced that the Division of Drug Marketing, Advertising, and Communications (DDMAC) would be reorganized into the Office of Prescription Drug Promotion (OPDP), which includes the Division of Direct-to-Consumer Promotion and the Division of Professional Promotion. For ease of reference, this alert refers only to OPDP. The elevation to an office-level entity is expected to give OPDP a small increase in staff and budget.[1]

In 2011, OPDP issued 21 fewer letters than it did in 2010 (31 letters versus 52 letters). This significant decrease in agency enforcement action reversed a steady increase that was seen from 2008 to 2010. The average number of allegations in each letter also dropped. In 2010, each letter averaged approximately 3.2 allegations (counted by the number of headings in each letter). By 2011, this average had decreased to approximately 2.3. Of the 31 letters issued by OPDP in 2011, 84% were untitled letters and only 16% were warning letters. This continues a steady trend towards increased use of untitled letters by OPDP from 2010 (77% untitled letters), 2009 (68% untitled letters), and 2008 (48% untitled letters).

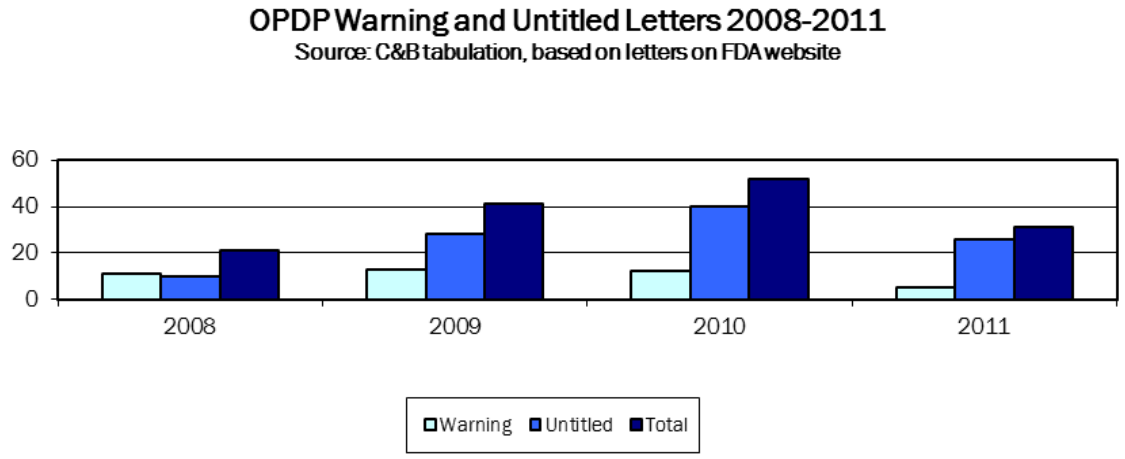
The cause of the decreased enforcement by OPDP is unclear. According to trade press, the decline in OPDP enforcement letters is likely due to a combination of (1) FDA's risk-based approach to drug promotion oversight and (2) improved industry understanding of FDA's expectations for drug promotion. One recent publication quoted OPDP Director Thomas Abrams as saying that "things

[1] *DTC Pre-Review Guidance In The Works For Rx TV Ads, FDA's Abrams Says*, The Pink Sheet (Nov. 14, 2011).

seem to be improving, especially presentation of risk information."[2] It is also possible that the decrease was a result of OPDP's reorganization and focus on issuing guidance related to promotional activities.

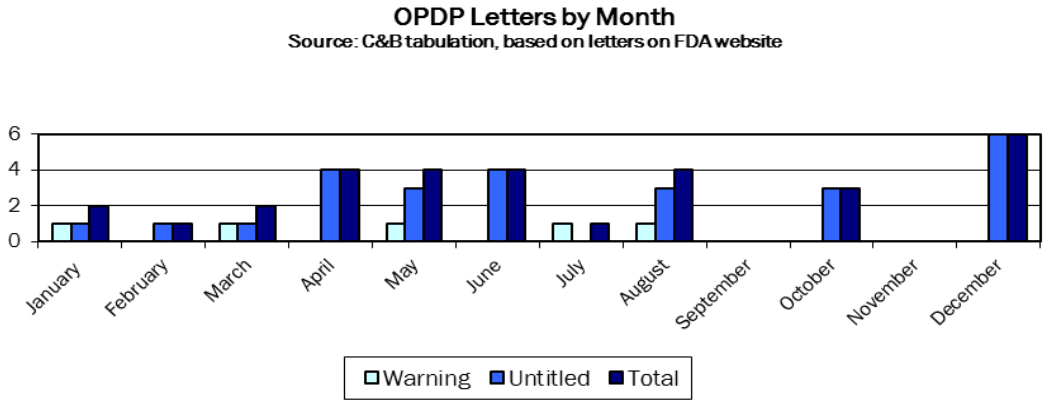
In May 2010, OPDP announced the launch of its "Bad Ad" program.[3] The program is designed to encourage healthcare providers to report false or misleading drug advertising and promotional materials to FDA. The agency has provided materials to healthcare providers to educate them on the requirements of drug advertising and promotion. The agency also has provided an email address and phone number through which healthcare providers can report violations. OPDP issued one letter in 2010 as a result of promotional materials reported through the Bad Ad program. In 2011, OPDP issued at least five enforcement letters as a result of such reports.

In the first year of the Bad Ad program (May 2010 to May 2011), FDA received 328 reports of potentially untruthful or misleading promotion.[4] 188 were submitted by healthcare professionals, 116 were submitted by consumers, and 24 were submitted by industry representatives. A 2011 report on the program stated that before the launch of the Bad Ad program, FDA historically received an average of about 104 similar reports per year. Of the 188 reports submitted by healthcare professionals, 87 were identified for a "comprehensive review" by OPDP. Of the 116 reports submitted by consumers, 24 were identified for such a review. Finally, of the 24 reports submitted by industry, 14 were identified for such a review. The agency explained that those reports that did not result in comprehensive reviews nonetheless helped to focus "FDA's surveillance efforts in other ways or were referred to other FDA Centers (i.e., potentially misleading ads for dietary supplements sent to the Center for Food, potentially misleading ads for devices sent to the Center for Devices and Radiological health, etc.)."



[2] *FDA's Rx Enforcement Letter Output Drops In 2011; OPDP Sees Improvement In Promotions*, The Pink Sheet (Jan. 16, 2012).
[3] *See* Press Release, FDA, 'Bad Ad Program' to Help Health Care Providers Detect, Report Misleading Drug Ads (May 11, 2010), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm211611.htm.
[4] FDA, Bad Ad Program: 2010-2011 Year End Report, *available at* http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/surveillance/drugmarketingadvertisingandcommunications/ucm258719.htm.

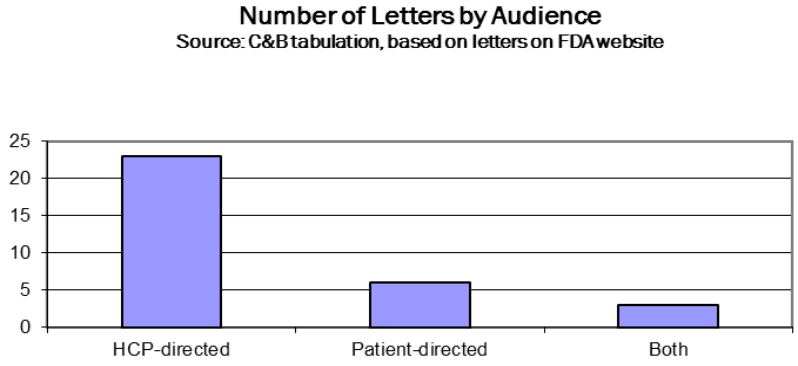
In 2011, the number of letters issued per month varied over the year. No letters were issued in September and November, and the highest amount of letters were issued in December (6). The lack of letters in September and November may be a result of OPDP's reorganization.



II. CONTENT OF WARNING AND UNTITLED LETTERS

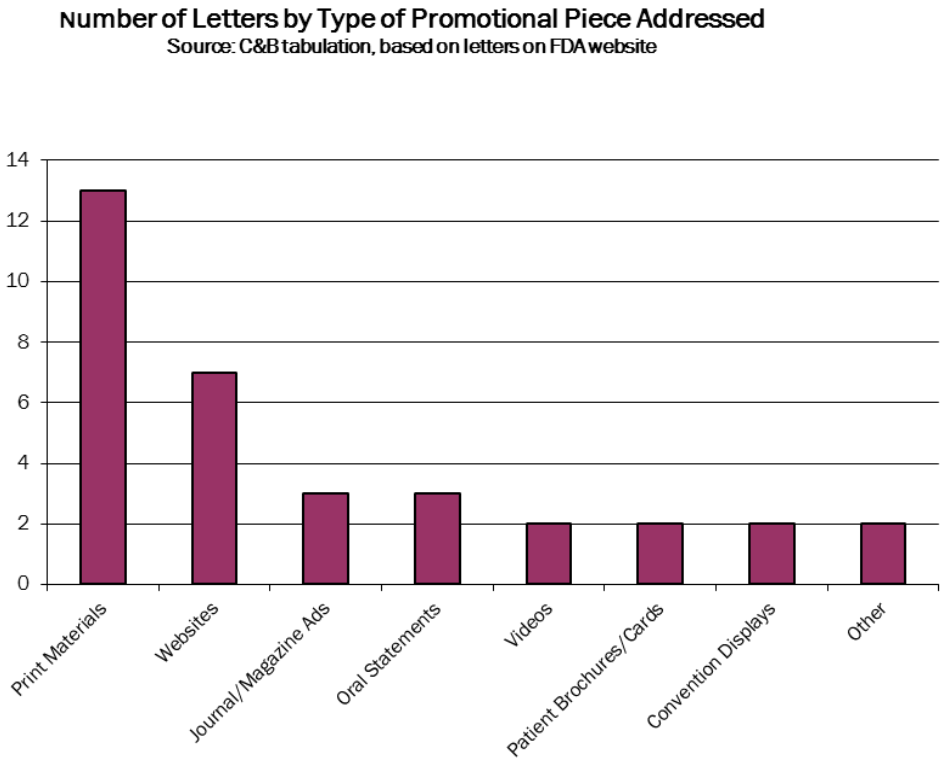
A. Promotional Pieces at Issue

As in previous years, materials intended for healthcare professionals were a significant focus of OPDP activity. In 2011, 74% of OPDP's letters addressed materials specifically directed at healthcare professionals, such as healthcare professional websites and sales aids. This is an increase from 2010, when 54% of OPDP letters addressed healthcare professional materials. In 2011, only 20% of OPDP's letters addressed patient-directed materials, a decrease from 40% in 2010. 10% of the 2011 letters addressed materials that were targeted to both healthcare professionals and patients (e.g., a website that did not readily distinguish between audiences).[5]



[5] These percentages do not add up to 100% because one letter discussed multiple types of promotional pieces (i.e., a professional sales aid and a patient brochure).

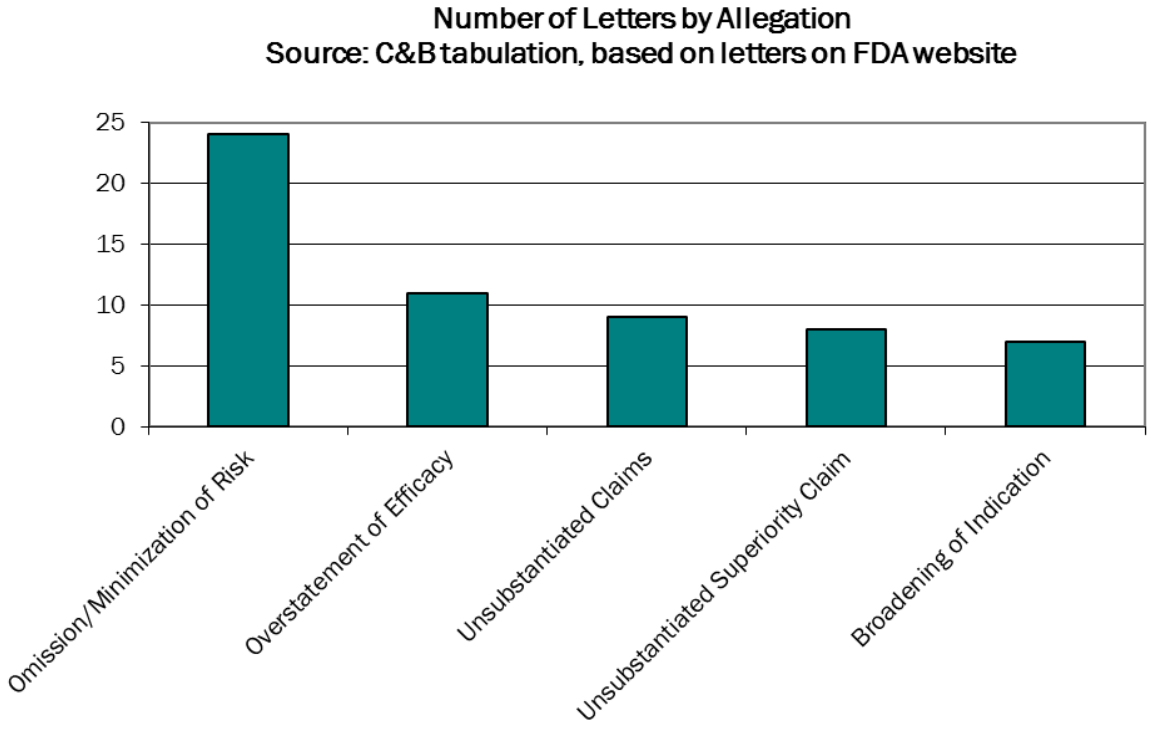
OPDP letters from 2011 addressed a wide variety of promotional media, including print materials (e.g., direct mailers, a white paper, and flashcards, but not including patient brochures); websites; journal and magazine advertisements; oral statements by sales representatives; videos; patient brochures and rebate cards; and convention displays. By a significant margin, the highest number of letters addressed print materials, which was consistent with OPDP's focus in 2010.



In 2011, 26% of OPDP's letters addressed Internet-based materials (e.g., a YouTube video), which is nearly identical to the percentage in 2010.

B. OPDP's Allegations

In 2011, OPDP's letters focused primarily on the following allegations: (1) omission and/or minimization of risk information, (2) overstatement of efficacy, (3) unsubstantiated claims, (4) unsubstantiated superiority claims (a more narrow category than unsubstantiated claims), and (5) broadening of indication. These areas of focus were also the top-five most cited allegations in 2010 (in descending order of prevalence: (1) omission and/or minimization of risk information, (2) overstatement of efficacy, (3) unsubstantiated superiority claims, (4) broadening of indication, and (5) unsubstantiated claims).



1. Omission and/or Minimization of Risk Information

Of the 31 OPDP letters issued in 2011, 24 (77%) contained allegations that the promotional pieces omitted and/or minimized the risks of the drug. For example, in a December untitled letter, OPDP alleged that an exhibit booth had "de facto" omitted risk information about the drug because such information "was not visible to viewers as a practical matter." Each time that an OPDP representative viewed the booth, the risk information was obscured from view by bags, boxes, and other materials. The booth thus misleadingly suggested that the drug is safer than has been demonstrated by substantial evidence and substantial clinical experience.

2. Overstatement of Efficacy

Eleven letters (35%) alleged that the promotional pieces overstated the efficacy of the drug. For example, a May OPDP untitled letter cited a professional flashcard for overstating the efficacy of the drug. The card listed various symptoms associated with different mood disorders, such as loss of interest in sex, fatigue, and irritability. Although the drug was approved to treat the mood disorders, its effectiveness was demonstrated based on the total scores of the relevant scales evaluated for each mood disorder, which did not measure the effect of treatment on individual symptoms. The card therefore misleadingly implied that the drug was effective in treating these symptoms.

3. Unsubstantiated Claims

Nine letters (29%) addressed unsubstantiated claims. An October untitled letter, for example, cited an exhibit panel that claimed that use of the imaging drug was "simple" and "hassle-free." This claim was misleading and unsubstantiated because the PI for the product describes a "complex" series of steps required for proper preparation, administration, and disposal of the drug.

4. Unsubstantiated Superiority Claims

Eight letters (26%) addressed unsubstantiated superiority claims, such as the one cited in a May untitled letter focusing on a professional detail aid. The promotional piece presented multiple claims regarding the superior efficacy of the ADHD drug in comparison to another drug at "2 hours postdose." The aid referenced two clinical studies, but these studies did not constitute substantial evidence because "[t]reatment for ADHD consists of symptom relief over an extended time period; thus, ADHD medications must control disease symptoms over the entire treatment course." According to OPDP, by focusing on one specific time point, "the studies did not account for the different pharmacokinetic profiles and subsequent efficacy profiles associated" with the two drugs over the entire course of treatment. Moreover, although the studies suggested that the promoted drug may provide greater efficacy at two hours, they also suggested that it could provide less efficacy from hour nine and beyond. Finally, the aid included a claim regarding thinking "first" of the drug "for a fast start." These presentations therefore misleadingly implied that the drug was more effective than other ADHD medicines, which has not been shown by substantial evidence or substantial clinical experience.

5. Broadening of Indication

Seven OPDP letters (23%) addressed presentations that broadened the indication for the drug. A January warning letter, for example, cited a direct mailer for a dental drug, which contained a claim by a dental hygienist that "[a] lot of people won't even let me clean their teeth without" the drug. This claim misleadingly implied that the product is safe and effective for use in any patient undergoing routine dental cleaning. The drug, however, was indicated only for "adults who require localized anesthesia in periodontal pockets during scaling and/or root planing." The promotional piece also featured a statement by another hygienist claiming that she was using the drug "for every patient for scaling and root planing." This claim was misleading because it suggested that the drug was safe in all patients undergoing such procedures. The misleading nature of the presentations was "exacerbated" by the failure to include the complete approved indication.

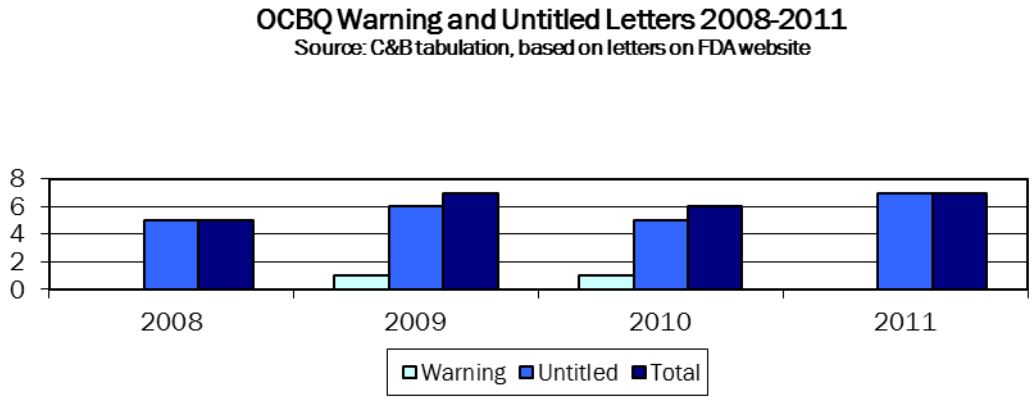
6. Other Allegations

Other, less common allegations that appeared in OPDP letters in 2011 included omission of material facts, promotion of an investigational drug/promotion of unapproved uses, and omission of indication. Other letters contained rare allegations, such as failure to use the required established name and inappropriate reminder labeling.

OCBQ

I. ENFORCEMENT ACTIVITY

In 2011, the Office of Compliance and Biologics Quality (OCBQ) issued seven untitled letters and no warning letters. This is roughly consistent with the total amount of enforcement letters issued by OCBQ over the past several years. One of the untitled letters was issued to the manufacturer of a device that was cleared through FDA's 510(k) process, but that is regulated by CBER because it is used for the preparation of autologous platelet-rich-plasma.



II. CONTENT OF WARNING AND UNTITLED LETTERS

A. Promotional Pieces at Issue

In 2009, OCBQ cited 12 different types of promotional materials (e.g., DTC advertisements, a patient biopsy letter, a company website, a slim jim sales aid, etc.). In 2010, the letters focused on significantly fewer types of materials. This trend continued in 2011, with letters focused on only sales aids/brochures, exhibit booth panels, a website, a print ad, a slide presentation, and a telephone script.

In 2011, OCBQ focused more on promotional pieces directed at healthcare professionals than patient-directed pieces. Five of the seven letters cited only healthcare-directed materials (e.g., a detail aid). One letter cited a healthcare professional-directed sales aid, as well as a print advertisement without a clear indication of the intended audience for the ad. Finally, one letter cited a website that appears to have been readily accessible by both consumers and healthcare professionals.

B. OCBQ's Allegations

OCBQ's 2011 letters contained allegations under seven different subheadings: (1) omission and/or minimization of risk information, (2) false and/or misleading presentation, (3) unsubstantiated efficacy claims, (4) misleading superiority and clinical significance claims, (5) unsubstantiated superiority efficacy and safety claims, (6) failure to provide adequate directions of use, and (7) unsubstantiated comparative claims. The untitled letter issued to the manufacturer of the 510(k) device did not use such subheadings, but the allegations centered around the promotion of the device for uncleared uses.

1. Omission and/or Minimization of Risk Information

Three out of the seven letters (43%) contained allegations of omission and/or minimization of risk information. For example, an October 2011 untitled letter claimed that a visual aid minimized risk information by including a headline on the front page promoting the effectiveness of the product. By "[u]sing this claim as the sole headline on the page," the piece failed to present "a fair balance between risk information and efficacy information on that page spread."

2. False and/or Misleading Presentation

Two of the letters (29%) contained allegations of false and/or misleading presentation. A February 2011 untitled letter, for example, cited a sales aid and print advertisement misstating the influenza immunization recommendations by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP). The materials also misleadingly implied that the vaccine met these recommendations when it had not been demonstrated to be safe and effective for the entire population included in the recommendation (i.e., individuals 6 months and older).

3. Unsubstantiated Efficacy Claims

Two of the letters (29%) also contained allegations of unsubstantiated efficacy claims. A September 2011 untitled letter, for example, discussed professional brochures containing claims that the fibrin sealant product was strong, stable, and secure and provided "added confidence" through "clot integrity." The claims were presented in conjunction with the image of a steel structure, which implied strength and stability. The presentations were misleading because they were not supported by substantial evidence or substantial clinical experience. Clinical studies of the product measured efficacy by time to hemostasis, not by clot integrity or clot stability.

4. Other Allegations

Other allegations that appeared in one letter each were misleading superiority and clinical significance claims, unsubstantiated superiority efficacy and safety claims, failure to provide adequate directions for use, and unsubstantiated comparative claims.

CDRH Office of Compliance

I. PROMOTIONAL ACTIVITY

In 2011, CDRH's Office of Compliance (OC) issued 10 warning letters[6] relating to the promotion of approved or cleared medical devices,[7] a modest increase from the 7 warning letters issued in 2010. OC also issued one form letter in September 2011 to an undisclosed number of eye care professionals relating to promotion of laser eye procedures, including LASIK, that allegedly omitted risk information related to the procedures.

In contrast to the enforcement letters issued by OPDP and OCBQ, 4 (36%) of OC's letters, including the LASIK letter, were sent to entities other than the manufacturer of the device being promoted. For example, one of the letters was sent in December 2011 to numerous surgical centers engaging in misleading promotion of the LapBand gastric banding procedure, as well as a 1-800 number used by the centers to promote the procedure. Similarly, a March 2011 warning letter was sent to a

[6] CDRH has historically not posted any untitled letters that it issues on FDA's website.
[7] This number does not include letters addressing promotional activity for devices that were not cleared or approved for any use.

physician who owned a Natural Health Center and was promoting an infrared camera for uses outside those cleared through the 510(k) process.

II. OC'S ALLEGATIONS

In prior years, OC's allegations had focused almost exclusively on the promotion of devices for uses that were neither approved nor cleared. And the letters typically cited claims made on company websites only. In 2011, however, OC cited numerous additional problems with the promotional pieces, such as omission of risk information and unsubstantiated superiority claims, and cited a broader array of promotional pieces, including billboards, brochures, websites, and a radio spot. For example, a January 2011 warning letter sent to an imaging center claimed that the company's website and a radio spot promoted an infrared camera device for uses beyond those cleared through the 510(k) process. The device's cleared indication stated that the device was "for use as an adjunct to other clinical diagnostic procedures in the diagnosis, quantifying, and screening of differences in skin surface temperature changes." But the website and radio spot included claims such as one stating that the device "[e]ffectively and safely screens breasts with implants." According to OC, these presentations suggested that the device could be used alone to diagnose or screen for various diseases or conditions associated with the breast. The promotional pieces also suggested that the device has greater sensitivity and safety than the use of mammography.

Similarly, the warning letter issued to the LapBand surgery centers and the 1-800 number cited billboards and advertising inserts that OC alleged minimized risk informaion by presenting it in an unreadable font size. According to the agency, the pieces also failed to reveal material facts related to the LapBand procedure, including age and other qualifying requirements for the procedure. The pieces, which included claims such as "The Lap-Band has helped thousands of happy people safely and effectively lose weight and keep it off!" and "Let Your New Life Begin!" also failed to discuss the ongoing need for patients to modify their eating habits.

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