

# 2017 End-of-Year Summary of FDA Advertising and Promotion Enforcement Activity

February 2, 2018<sup>1</sup>

Food, Drugs, and Devices

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This e-alert reviews trends emerging from warning letters and untitled letters concerning therapeutic product advertising and promotion issued in 2017 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). OCBQ did not issue any advertising and promotion enforcement letters in 2017. However, we examined the seven advertising and promotion letters issued by OPDP and the CDRH OC, and tabulated the most frequently cited allegations. This alert summarizes our tabulation of all of the letters and other enforcement trends.

## OFFICE OF PRESCRIPTION DRUG PROMOTION (OPDP)

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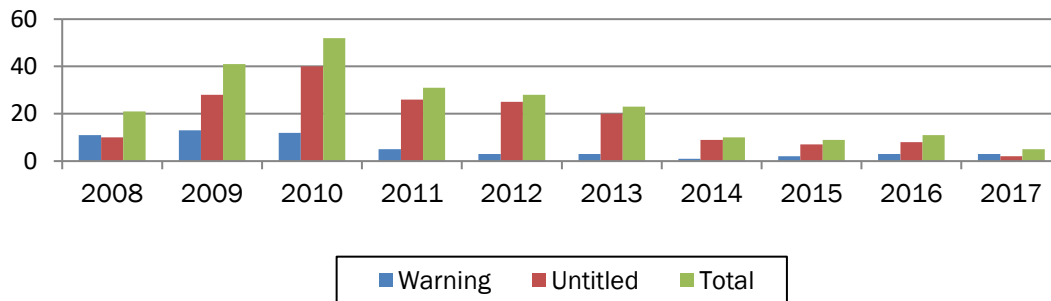
### ENFORCEMENT ACTIVITY

In 2017, OPDP issued five advertising and promotion enforcement letters, six fewer than the number issued in 2016. This is consistent with the overall trend of fewer issued enforcement letters since 2010.

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<sup>1</sup> This revised alert replaces an alert dated January 26, 2017 and includes a late-posted letter issued in 2017.

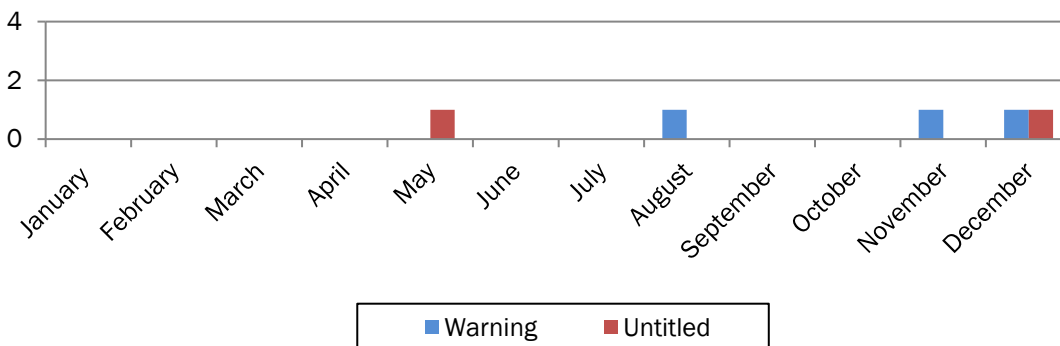
**OPDP Warning and Untitled Letters (2008-2017)**  
**Source: C&B tabulation, based on letters on FDA website**



In a departure from past practice, OPDP issued more warning letters than untitled letters. Of the five letters OPDP issued in 2017, three were warning letters. The average number of allegations in each letter was 1.8 (counted by the number of headings in each letter).

OPDP’s enforcement letters generally were issued in the second half of the year, with one letter being issued in each of May, August, and November, and two letters issued in December. This is similar to the pattern in 2016 in which nine of eleven of OPDP’s enforcement letters were issued in the second half of the year.

**OPDP Letters Issued by Month (2017)**  
**Source: C&B tabulation, based on letters on FDA website**



OPDP has not articulated a reason for its overall decline in enforcement activity, but the downward trend in enforcement aligns with the timing of significant First Amendment litigation

against the agency. *U.S. v. Caronia* was argued before the Second Circuit in 2010.<sup>2</sup> In 2011 the Supreme Court held in *Sorrell v. IMS Health* that “speech in aid of pharmaceutical marketing . . . is a form of expression protected by the Free Speech Clause of the First Amendment,” and therefore, certain restrictions on such speech are subjected to “heightened judicial scrutiny.”<sup>3</sup> The timing of these two cases aligns with the beginning of the decline in enforcement letters in 2011. In 2012, the Second Circuit decided *Caronia*, and “construe[d] the misbranding provisions of the [Federal Food, Drug and Cosmetic Act] as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs.”<sup>4</sup> This decision likewise tracks the next big drop in enforcement activity after 2013. Consistent with this trend, enforcement activity again declined after the decisions in *Amarin* and *Vascular Solutions* in 2015 and 2016, respectively.<sup>5</sup>

In November 2016, FDA held a public meeting on off-label communications,<sup>6</sup> and in January 2017, the agency issued a final rule, two guidance documents, and a memorandum on issues related to off-label communications.<sup>7</sup> This somewhat unusual release of a white paper and guidance on the eve of inauguration suggests an effort on the part of FDA to stake out its policy position at the end of the Obama administration and to draw boundaries around the evolving case law. Both outgoing Commissioner Califf and incoming Commissioner Gottlieb have underscored the need to balance the commercial speech implications of regulating promotion with FDA’s mission to protect the public health.

## CONTENT OF ENFORCEMENT LETTERS

### Approved Products vs. Unapproved Products

In 2016, OPDP sent four letters addressing promotional activity of an unapproved product, a relative spike compared to historical norms. This led some to speculate that unapproved product

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<sup>2</sup> *U.S. v. Caronia*, 703 F.3d 149 (2nd Cir. 2012).

<sup>3</sup> *Sorrell v. IMS Health Inc.*, 564 U.S. 552 (2011).

<sup>4</sup> *Caronia*, 703 F.3d at 168.

<sup>5</sup> See *Amarin Pharma, Inc. v. FDA*, 119 F.Supp.3d 196 (S.D.N.Y. 2015) (holding *Amarin* could engage in truthful and non-misleading speech promoting the off-label use of its drug, *Vascepa*); *United States v. Vascular Solutions, Inc.*, Cr. No. 14-926 at 12 (W.D. Tex. Feb. 25, 2016) (instructing jury members that “[i]t is also not a crime for a device company or its representatives to give doctors wholly truthful and non-misleading information about the unapproved use of a device”).

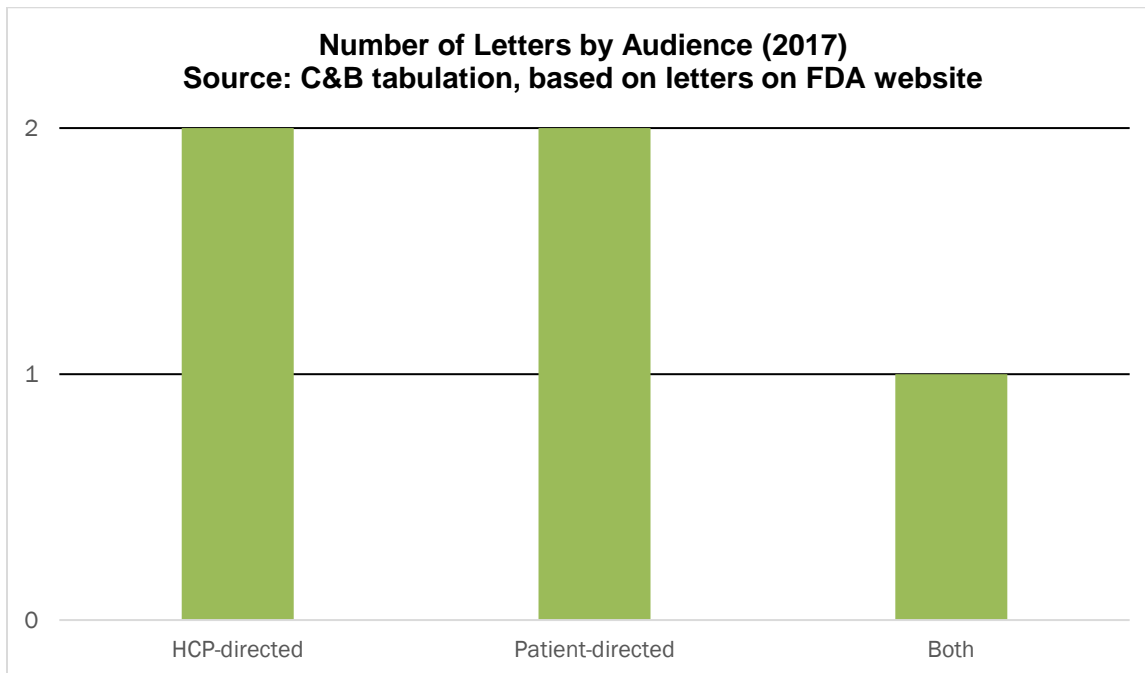
<sup>6</sup> See FDA, Notification of Public Hearing; Request for Comments, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, 81 Fed. Reg. 60299 (Sept. 1, 2016).

<sup>7</sup> See Final Rule, Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding “Intended Uses”, 82 Fed. Reg. 2193 (Jan. 9, 2017); FDA, Draft Guidance, Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities—Questions and Answers (Jan. 2017); FDA, Draft Guidance, Medical Product Communications That Are Consistent With FDA-Required Labeling—Questions and Answers (Jan. 2017); FDA, Memorandum, Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products (Jan. 2017). FDA has proposed delaying indefinitely the effective date of the final rule amending regulations regarding “intended uses,” however. See Proposed Rule, Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding “Intended Uses”; Proposed Partial Delay of Effective Date, 83 Fed. Reg. 2092 (Jan. 16, 2018).

promotion may be a new area of emphasis for FDA. OPDP's activity in 2017 does not support this theory, however, as OPDP issued only one letter addressing promotional activity for unapproved products. Nevertheless, because 2017 is just one data point, it likely is too early to tell whether 2016 was a random spike or the emergence of a new trend.

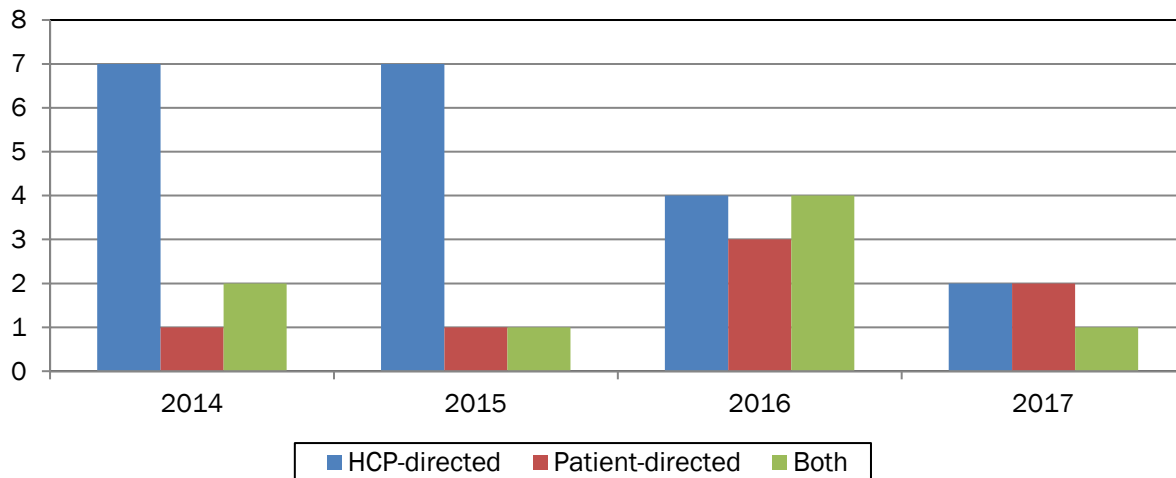
Nature of Promotional Pieces

Similar to 2016, there generally was an even distribution of letters addressing materials directed at health care professionals (HCPs) and patients. In 2017, OPDP sent two letters based on HCP-directed materials, two letters based on patient-directed materials, and one letter based on materials that targeted both HCPs and patients.

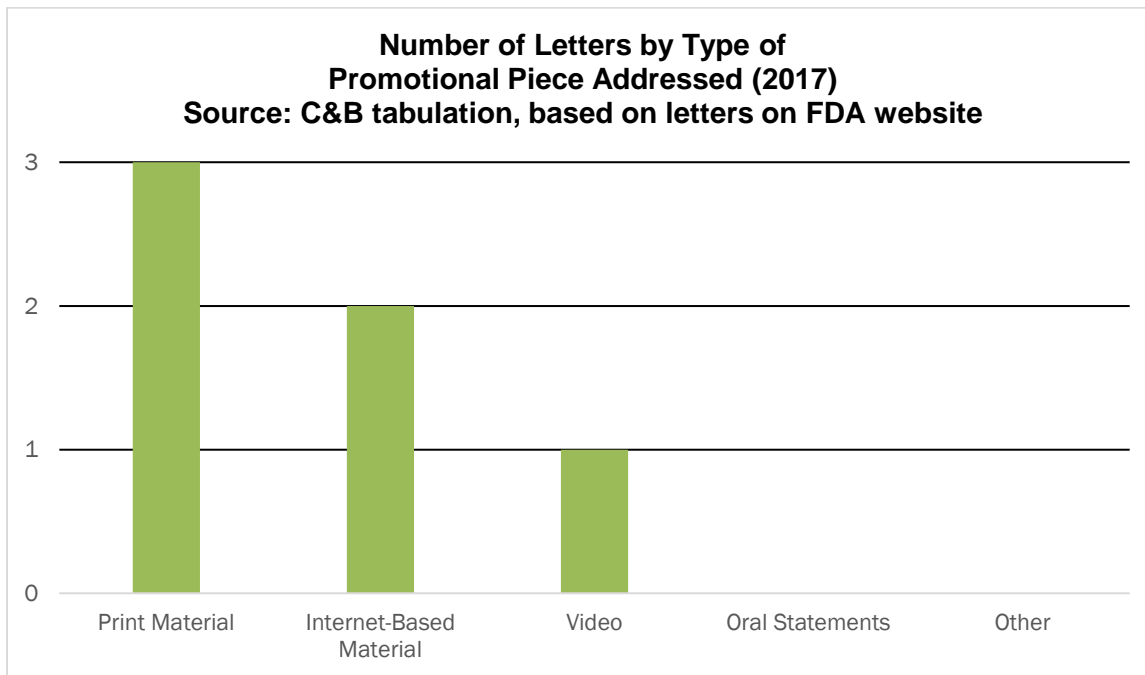


This is similar to the trend from 2016, when there was also a relatively even distribution of letters addressing materials directed at HCPs and patients. By contrast, in 2015, approximately 80% of OPDP enforcement letters addressed materials directed at HCPs. There was a similar distribution in 2014, when promotional materials directed at HCPs comprised 70% of the materials discussed in OPDP enforcement letters.

**Number of Letters by Audience (2014-2017)**  
 Source: C&B tabulation, based on letters on FDA website

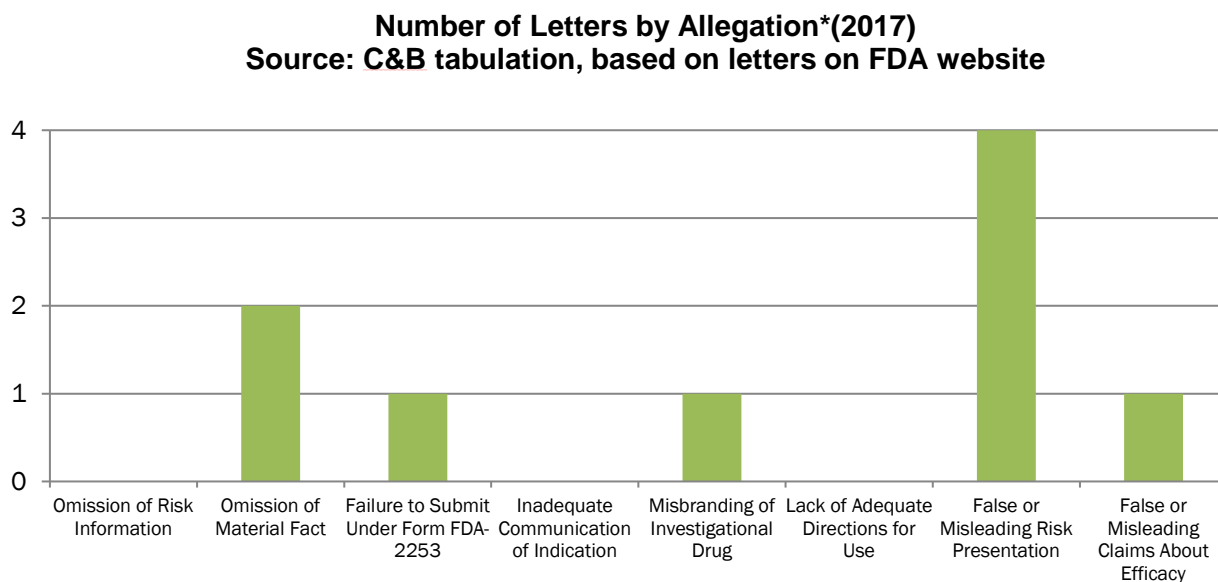


In 2017, OPDP’s letters addressed three types of promotional materials: print materials (professional detail aid and exhibit panels), Internet-based materials (website and online brochures), and video materials (direct-to-consumer broadcast television advertisement). Two of the letters addressed print materials only, one letter addressed internet-based materials only, one letter addressed print and internet-based materials, and one letter addressed video materials. For comparison, over half of the letters issued in 2016 cited video materials. Similar to 2016, however, none of the letters addressed oral statements made by company representatives.



**OPDP’s Allegations**

Four out of five of OPDP’s letters contained allegations of false or misleading risk presentation. Two of those letters additionally cited omission of material facts. One letter included allegations of false or misleading efficacy claims and failure to submit under Form FDA-2253 upon first use. One letter alleged misbranding of an investigational drug.



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

### 1. False or Misleading Risk Presentation

Four out of five letters alleged that promotional materials contained false or misleading risk information. In three warning letters, OPDP alleged that the promotional materials contained efficacy claims but failed to communicate any risk information. In previous years, OPDP typically categorized allegations of this type as “Minimization of Risk Information” (or “Omission and Minimization of Risk Information”). Recasting these allegations as “False or Misleading Risk Presentation” is noteworthy and perhaps reflects a response to court decisions holding that truthful and non-misleading communications are constitutionally protected.

Of particular note, in a May 2017 untitled letter to Contrave, OPDP cited a television advertisement that disclosed certain risk information in the visual portion of the TV ad while simultaneously disclosing different risk information in an overlapping voiceover. According to FDA’s untitled letter, presenting risk information in this fashion “undermines the communication of important risk information and thereby misleadingly minimizes the risks” associated with using the drug. OPDP made similar allegations in two letters issued in December 2016 relating to competing audio and video in TV ads. Those letters were discussed in a [previous client alert](#).

### 2. Omission of Material Facts

In two warning letters, OPDP contended that promotional material was misleading because it failed to provide material information regarding the full FDA-approved indication. For example, in an August 2017 warning letter to Cipher Pharmaceuticals, FDA alleged that promotional material described the indications for ConZip without including “Limitation of Use” information.

### 3. False or Misleading Claims About Efficacy

In a November 2017 warning letter to Amherst Pharmaceuticals, LLC, and Magna Pharmaceuticals, Inc., OPDP alleged that promotional material was misleading because it made unsupported claims regarding the efficacy of Zolpimist and the superiority of Zolpimist compared to other products. For example, FDA’s letter noted that the website for Zolpimist stated that it was “engineered to outperform the oral tablets,” but OPDP was not aware of data to support this claim.

### 4. Failure to Submit Under Form FDA-2253

FDA regulations require companies to submit any labeling or advertising devised for promotion of the drug product at the time of first use. Each submission must be accompanied by a completed transmittal Form FDA-2253. In the November 2017 warning letter to Amherst Pharmaceuticals, LLC and Magna Pharmaceuticals, Inc., OPDP stated that publication of the promotional materials violated these regulations because the materials were not submitted to FDA under cover of Form FDA-2253 at the time of initial dissemination.

### 5. Misbranding of Investigational Drug

In a late December 2017 untitled letter to the University of California Los Angeles (UCLA), OPDP alleged that a webpage and online brochure misbranded the investigational drug Gallium-68 (68Ga-PSMA) by suggesting it was safe and effective for the use for which it was being investigated and by otherwise promoting the drug. For example, although there was no United States marketing authorization for 68Ga-PSMA, the brochure was titled, “New imaging test accurately detects prostate-cancer cells throughout the body.”

## **CBER OFFICE OF COMPLIANCE AND BIOLOGICS QUALITY (OCBQ)**

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### **ENFORCEMENT ACTIVITY**

FDA's Office of Compliance and Biologics Quality (OCBQ) did not issue any enforcement letters in 2017 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. In 2015, OCBQ posted only one untitled letter, related to an influenza vaccine.<sup>8</sup> Covington discussed the letter in a [previous client alert](#).

## **CDRH OFFICE OF COMPLIANCE (OC)**

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### **ENFORCEMENT ACTIVITY**

The Office of Compliance (OC) in FDA's CDRH posted two enforcement letters relating to advertising and promotion in 2017, both in July.

One letter, addressed to QLRAD, alleged that the company's website and its brochures, distributed at conferences in 2015 and 2016, misbranded the RectalPro Endorectal Balloon because they promoted the product for intended uses different from those uses legally marketed under an exemption from the requirement to obtain clearance of a premarket notification (commonly referred to as 510(k)) that might apply to that device. Under 21 CFR § 876.4730, manual gastroenterology-urology surgical instruments and accessories are 510(k)-exempt if they are intended to be used for gastroenterological urological procedures. FDA stated that QLRAD's website and brochures marketed the RectalPro ERB "to immobilize the prostate in patients undergoing radiation therapy." FDA implied that the RectalPro ERB required a cleared 510(k) for this use.

The other letter, addressed to SyncThink, alleged that the company's website misbranded EYE-SYNC because it promoted the product for uses outside the scope of its 510(k) clearance. EYE-SYNC was cleared as a prescription device with indications for use of recording, viewing, and analyzing eye movements in support of identifying visual tracking impairment in human subjects. FDA stated that SyncThink promoted EYE-SYNC on its website for use in "cognitive assessment/testing of concussions and head trauma, including in injured athletes and soldiers." FDA alleged that this promoted use would constitute a major change or modification to the intended use of EYE-SYNC and implied that marketing the device with this use required submission of a new premarket notification to FDA under FDCA § 510(k) and 21 CFR § 807.81(a)(3)(ii).

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<sup>8</sup> Untitled Letter to Protein Sciences Corporation re: Flublok (Influenza Vaccine) BLA STN # 125285 (March 12, 2015), available [here](#).



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While CDRH posted only two letters in 2017, this nonetheless constitutes an increase in warning letters arising from routine surveillance compared to 2015 and 2016, during which CDRH OC did not post any letters.<sup>9</sup>

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:

<b><u>Scott Cunningham</u></b>	+1 415 591 7089	<a href="mailto:scunningham@cov.com">scunningham@cov.com</a>
<b><u>Scott Danzis</u></b>	+1 202 662 5209	<a href="mailto:sdanzis@cov.com">sdanzis@cov.com</a>
<b><u>Stefanie Doebler</u></b>	+1 202 662 5271	<a href="mailto:sdoebler@cov.com">sdoebler@cov.com</a>
<b><u>Michael Labson</u></b>	+1 202 662 5220	<a href="mailto:mlabson@cov.com">mlabson@cov.com</a>
<b><u>Amy Leiser</u></b>	+1 202 662 5916	<a href="mailto:aleiser@cov.com">aleiser@cov.com</a>

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<sup>9</sup> We note that FDA did cite promotional issues, in addition to quality system issues, in several warning letters issued in 2015 and 2016 arising from inspections of device establishments. In addition, CDRH does not routinely post untitled letters issued to device companies.