Background

- Promotion in the United States is closely regulated by the Food and Drug Administration (FDA):
  - Office of Prescription Drug Promotion (OPDP) for prescription products
  - Advertising and Promotional Labeling Branch (APLB) for licensed biological products
- Advertising and promotion required to be truthful and non-misleading and enforced through untitled letters and, for more serious offenses, warning letters
- Guidance published by FDA provide greater insight into the Agency’s interpretation of regulations
- United States v. Caronia (December 2012) – US Court of Appeals for the Second Circuit rules that manufacturers cannot be prosecuted for promotion of an off-label use of an approved product
- Amarin Pharma, Inc. v. FDA (August 2015) – FDA withdraws warning letter to Amarin for preliminary relief asserting that the FDA cannot bring action solely based on the truthful and non-misleading promotion of an off-label use for their approved product
- Pacira Pharmaceuticals, Inc. v. FDA (October 2015) – FDA withdraws warning letter to Pacira following the company’s September 2015 lawsuit in the Southern District of New York stating that truthful and non-misleading promotion of off-label material for their approved product is protected by the First Amendment

Methods

- Enforcement letters published from 2008-2018 on the OPDP and APLB websites were recorded and categorized by type of letter
- Enforcement letters published from 2011-2013 on the OPDP and APLB websites were placed in categories including violations cited and team issuing the letter
- Guidance publications were also tracked from the OPDP website
- Dates of letter publications were compared with the dates of guidance publications and selected FDA First Amendment court cases

Results

- Number of Enforcement Letters
  - Warning Letters
  - Untitled Letters
  - Total Letters

Table 1: 2018 Violations Cited in Enforcement Letters

<table>
<thead>
<tr>
<th>Year</th>
<th>Unsubstantiated Superiority/Efficacy Claims</th>
<th>Lack of Adequate Directions For Use</th>
<th>Overstated Efficacy</th>
<th>Mislabeled Claims and Presentation</th>
<th>Unsubstantiated Claims</th>
<th>Broadening of Patient Population or Condition</th>
<th>Inadequate Communication of Indication</th>
<th>False or Misleading Benefit Presentation</th>
<th>Unsubstantiated Mechanism of Action Claims</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
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<td>2</td>
</tr>
</tbody>
</table>

Figure 1. Frequency of Enforcement Letter Publication in 2008-2018

Table 2: 2018 Violations Cited in Citations

<table>
<thead>
<tr>
<th>Year</th>
<th>Efficacy-Related</th>
<th>Risk Communication-Related</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
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<td>1</td>
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<td>2</td>
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</table>

Figure 2. Frequency of Citations in 2013-2018

Table 3: 2018 Violations Cited in Citations

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Table 4: 2018 Violations Cited in Citations

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<th>Year</th>
<th>Efficacy-Related</th>
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<th>Other</th>
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<tbody>
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<td>2</td>
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Trends in FDA OPDP and APLB Enforcement Letters Before and After First Amendment Cases and FDA Guidance Publications

Kenneth Hu, Pharm.D., Evelyn Hermes-DeSantis, Pharm.D., BCPS, Michael Toscani, Pharm.D., Joseph A. Barone, Pharm.D., FCCP

Rutgers Institute for Pharmaceutical Industry Fellowships, Ernest Mario School of Pharmacy, Rutgers University, Piscataway, NJ

Limitations

- Study not designed to determine causation from correlation in data
- Data only collected from a select period of time
- Violations cited were subjectively categorized during data collection

Conclusions

- Seventeen draft and final guidances published in 2008-2018 with 14 published in the past six years
- Increase in draft guidance publication from November 2013 to June 2014 (six of the 14 published in the past six years) coincides with the reduced number of enforcement letters following 2013
- Four of eight letters in 2018 included a “False or Misleading Risk Presentation” citation, with this as the sole violation in three letters
- Continued enforcement in 2018:
  - FDA monitoring exhibits at scientific congresses
  - Promotion of a Investigational New Drug
  - Direct-to-consumer promotion, internet promotion, social media
  - OPDP Bad Ad Program
- Generally consistent frequency in enforcement from OPDP Teams over six years (average of 1.53 each year), with following exceptions:
  - Anti-Infective, Cardiovascular, Medical Imaging, Ophthalmology, Renal, and Transplant Team: eight letters in 2011 to average of 0.8 each year following
  - Three Oncology Teams: five letters in 2013 to average of 0.4 each year following
- Fewer APLB enforcement letters than OPDP with only two untitled letters written in six years in 2015 and 2018 and four in 2011

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Please see references below.
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References