The First Amendment and Off-Label — Caronia and Beyond

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PCC
The First Amendment and Off-Label

- Looking Back
- Where We Are Now
- Looking into the Crystal Ball
Looking Back
First Amendment Evolution: A Look Back at Corporate Speech

Lochner v. New York (1905)


First Amendment Evolution: Putting it into Context

Allergan v. United States (2009)
Sorrell v. IMS Health Inc. (2011)
United States v. Caronia (2012)
Burwell v. Hobby Lobby (2014)
Pom Wonderful v. FTC (2015)
Amarin Pharma Inc. v. FDA (2015)
Pacira v. FDA (2015)
The Trio (Informative, but Fact-Specific)

Caronia
• The 2d Circuit held that the government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for truthful speech promoting the off-label use of an FDA-approved drug

• Citing Sorrell v. IMS Health, Inc., the court began with the principle that “[s]peech in the aid of pharmaceutical marketing … is a form of expression protected by the … 1st Amendment.”

Amarin
• US District Court in NY found that Amarin could distribute off-label information as long as it was “truthful and not misleading”
• Terms of settlement

Pacira
• Case brought in the same jurisdiction where Amarin was heard
• Parties settled
• FDA withdrew Warning Letter
Where We Are Now
The Memo

Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products (Jan. 2017)
“A Complex Task”

“[P]ublic health and safety interests served by FDA’s regulatory approach related to unapproved uses of medical products”

“[O]ngoing developments in science and technology, medicine, healthcare delivery, and constitutional law”
Medical Product Communications that are Consistent with the FDA-Required Labeling—Questions and Answers (Jan. 2017)
On-label or Off-label?

“The purpose of this guidance is to provide clarity for firms regarding FDA’s thinking when examining the consistency of a firm’s communications about a medical product with that product’s own FDA-required labeling. … [F]irm’s communications of information that is not contained in their product’s FDA-required labeling but that are determined to be consistent with the FDA-required labeling are not alone considered evidence of new intended use.” (emphasis added)
Consistent with the FDA-required Labeling

Factors for Consideration

1. Consistent Conditions of Use
   - Indication
   - Patient population
2. Potential for Harm to Health
   - Limitations and directions for handling/use
   - Dosing/administration
   - Affect to overall benefit-risk profile
   - Relative to the labeled benefit-risk profile
3. Adequate Directions for Use
   - Safe and effective use under the represented/suggested conditions
   - Following the labeled directions for use
Considerations when Developing Communications

- Express and implied claims—How is the information understood?
- Have material facts and limitations been disclosed?
- Is the product accurately characterized?
- Is supporting evidence present and accurately represented?
- Is the presentation balanced with disclosures of unfavorable or inconsistent findings?
- Has related data from the FDA-approved label and other contextualizing information been provided?
Evidentiary Support

Even communications consistent with the label require supporting evidence in order to be truthful and not-misleading.

- Reveal material information grounded in fact and science
- Present with appropriate context
- Describe limitations of the strength of evidence
- Support the representations or suggestions made in the communication
- Accurately characterize support in the communication
- Reference scientifically appropriate and statistically sound data, studies, or analyses
The Other New Draft Guidance

Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities—Questions and Answers (Jan. 2017)
### Appropriate HCEI Audience

- Deliberative review process
- Decision-makers on a population basis
- Payors or HCO purchasers

### Inappropriate HCEI Audience

- No deliberative review process
- Decision-makers on an individual basis
- Direct care providers/prescribers or patients/consumers
HCEI won’t be considered false or misleading if:

1. It relates to an approved indication
2. It is based on competent and reliable scientific evidence (CARSE)
3. It includes a conspicuous and prominent statement describing any material differences between the HCEI and the approved labeling
Investigational Products: Covered by the Carve-Out?

FDA does not intend to object to HCEI communications regarding Investigational Products if:

<table>
<thead>
<tr>
<th>HCEI falls into these categories:</th>
<th>HCEI is unbiased, factual, accurate, and non-misleading and is presented with:</th>
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<tbody>
<tr>
<td>Product info (e.g. drug class, device design) or Pricing Info</td>
<td>Clear statement that product is under investigation</td>
</tr>
<tr>
<td>Factual presentations of clinical/preclinical studies</td>
<td>Clear statement that safety and effectiveness has not been established</td>
</tr>
<tr>
<td>Product-related programs or services</td>
<td>Information related to the stage of product development</td>
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<tr>
<td>Info about indication sought (i.e. endpoints and patient population being studied)</td>
<td>Anticipated timeline for approval/clearance</td>
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<tr>
<td>Targeting/marketing strategies</td>
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Key Take-Aways

- FDA will continue to regulate off-label promotion - no green light to promote off-label
- False or misleading speech is not protected
- Truthful and non-misleading speech is protected, but…
  - How does your company determine what is “truthful and non-misleading?”
  - Accurate information can still be misleading
  - Information in isolation can be truthful, but misleading in context
  - Transparency is key – no cherry-picking but full disclosure, the good and the bad
- Internal review committee must be gatekeeper
- Cannot discount other issues – product liability, competitor complaints, state action
Looking in the Crystal Ball
Wait, What Happened in Arizona?

• Arizona, HB 2382, titled The Free Speech in Medicine Act, permits a pharmaceutical manufacturer or its representative to engage in “truthful promotion of an off-label use of a drug, biological product or device.”

• Passed unanimously

• The Goldwater Institute plans to take its “model law” to other state legislatures
This is Certainly Not the End

• Medical Product Communications Act of 2017
  ➢ Rep. Morgan Griffith (R-VA) has introduced a new bill that would allow pharmaceutical companies to discuss off label uses with physicians
  ➢ Provides definition of “scientific exchange”

• New FDA Commissioner?