THE OFF-LABEL DEBATE AND FDA’S SHIFTING OUTLOOK

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Agenda

- Legal and Regulatory Landscape
- 2017 FDA Statements
- Recent Trends
- Practical Implications
Legal and Regulatory Landscape

• A drug is “misbranded” if its labeling does not contain “adequate directions for use.” 21 U.S.C. §352(f).

• The FDA defines “adequate directions for use” as “directions under which the lay[person] can use a drug safely and for the purposes for which it is intended.” 21 C.F.R. §201.5.

• FDA position: “Off-label” promotion misbrands a drug because it is evidence of a “new intended use” for which “adequate directions” are lacking.
**United States v. Caronia**

- Sales representative convicted of conspiracy to misbrand for discussing an “unapproved use” of an FDA approved drug with a physician.
- The Court of Appeals held that “the Government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug.”

*U.S. v. Caronia, 703 F.3d 149 (2d Cir. 2012)*
Amarin Pharma, Inc. v. U.S. Food and Drug Admin.

• Amarin sought preliminary injunction to prohibit FDA from bringing a misbranding action related to truthful, accurate, and non-misleading statements about off-label use of Vascepa.

• The court held that “Caronia’s holding was that the FDCA’s misbranding provisions cannot constitutionally criminalize, and therefore do not reach, the act of truthful and non-misleading speech promoting off-label use.”

Vascular Solutions, CEO acquitted of federal charges in off-label case

Minn. CEO calls legal attack "obscene" in berating U.S. prosecutors

By Joe Carlson Star Tribune | FEBRUARY 26, 2016 — 8:26PM

Howard Root, CEO, Vascular Solutions

Maple Grove medical-device maker Vascular Solutions and its CEO Howard Root have been acquitted on all counts in a criminal case that had alleged a

Jury acquits medical-device company execs of felony fraud charges

By Lisa Schensker | July 20, 2016

A federal jury on Wednesday acquitted two former medical-device company executives on more than a dozen felony counts of fraud related to off-label marketing but convicted them of 10 misdemeanor counts on the same issue.

The mixed verdict came less than a year after U.S. Deputy Attorney Sally Quillian Yates issued a memo indicating that the Justice Department was committed to holding individuals, not just companies, accountable for corporate misconduct. It's the second recent case in which healthcare executives escaped serious consequences for alleged corporate misconduct.

The Boston jury convicted former Acclarent CEO William Fadell and former Acclarent Vice President of Sales Patrick Fabian of 10 counts of introducing adulterated and misbranded medical devices into interstate commerce Wednesday, according to the U.S. Attorney's Office for the District of Massachusetts. The trial lasted six weeks.

Fabian's attorney, Frank Libby, praised the jury's acquittal Wednesday.
FDA Definition of “Intended Use”

- **September 2015 Proposed Rule:** FDA will not consider a firm’s knowledge of off-label use as evidence of “new intended use.”

- **January 2017 Final Rule:** Proposed Rule was not intended to eliminate manufacturer knowledge as a relevant source of evidence; “totality of the evidence” standard.

- **April 2017:** FDA delayed rule to allow time for public comment in response to a Citizen Petition filed by pharmaceutical and medical device industry groups.

- **March 2018:** FDA grants industry petition requesting indefinite stay of revisions to intended use guidelines.
January 2017 FDA Draft Guidance:

Medical Product Communications that are Consistent with the FDA-Required Labeling

• “Consistent with”
  • Related to an indication, patient population, or dosing and administration instructions set forth in the approved label, and not inconsistent with any use limitation or direction for handling or using the product
  • Must not increase the potential for patient harm relative to information in the approved labeling or otherwise adversely impact the risk / benefit profile
  • Whether the directions for use in the FDA-required labeling enable the product to be safely and effectively used under the conditions represented or suggested in the communication

• Must not be “false and misleading”
January 2017 FDA Draft Guidance:
Communications with Payors, Formulary Committees and Similar Entities

• Health Care Economic Information (HCEI)
  • Pertains to the economic consequences related to the clinical outcomes of treating a disease or of preventing or diagnosing a disease.

• HCEI can be provided to “a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs for coverage or reimbursement.”
January 2017 FDA Draft Guidance:
Communications with Payors, Formulary Committees and Similar Entities

- HCEI must be “related to” an approved indication.
- HCEI must be accompanied by:
  - Study Design, Methodology, and Limitations
  - Material differences from FDA approved label
  - FDA approved indication
  - Risk Information
  - Financial Affiliation / Bias
January 2017 FDA Draft Guidance:
Drug and Device Manufacturer Communications with Payors, Formulary Committees and Similar Entities

• Investigational Products
  • FDA will not object to providing payors with “unbiased, factual, accurate, and non-misleading” information regarding investigational drugs and medical devices.
  • Information on Investigational Products should also include:

  • Drug Class
  • Indication
  • Factual presentations from clinical or preclinical studies
  • Anticipated timeline for FDA approval / clearance

  • Pricing
  • Targeting / marketing strategies
  • Product-related programs or services
January 2017 FDA Draft Guidance:
Drug and Device Manufacturer Communications with Payors, Formulary Committees and Similar Entities

• Investigational Products
  • Information must be accompanied by clear statements that the product is under investigation and that the safety or effectiveness has not been established as well as information related to the stage of product development.
Recent DOJ Perspective on Enforcement

February 2018

• Key Considerations
  • Was the speech at issue false or misleading, or was it truthful?
  • Did the off-label use injure patients, or did it help patients?
  • Did the company’s actions materially mislead the FDA?
  • Did the company lie or mislead doctors and patients?
  • Did the conduct involve improper inducements or kickbacks?
# Practical Implications

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What We are Watching

- State and Federal legislation
- FDA Commissioner Scott Gottlieb
- FDA next steps on “Intended Use”
- Trends in enforcement and *qui tam* litigation
Questions and Answers
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• Has been with GSK for 11 years
• Handles a variety of commercial and product liability matters, as well as internal and government investigations
• Previously worked in the litigation departments of two Philadelphia law firms – Drinker Biddle and Morgan Lewis
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- Represents clients in the pharmaceutical and medical device industry in connection with civil and criminal investigations by federal, state and municipal authorities
- Has counseled clients on their compliance reporting obligations, recall campaigns, responses to formal inquiries, and compliance with labeling, warranty, advertising and packaging requirements
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• Focuses her practice on the defense of pharmaceutical and medical device manufacturers in products liability litigation, federal civil and criminal investigations, and *qui tam* litigation involving the Anti-Kickback Statute and False Claims Act

• Has experience counseling companies on regulatory compliance and risk avoidance