Effect of the First Amendment on Off-Label Marketing

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ABA Section of Litigation Regional CLE Workshop : Current Issues in Pharmaceutical, Medical Device, and Biotech Litigation, Bristol-Myers Squibb, Lawrence Township, NJ (October 20, 2017)

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Past 1st Amendment Cases (A Sampling)

Washington Legal Foundation *case – Medical Journal Reprints*

IMS v. Sorrell *– Rx-Level Data used by Pharma Companies to Interact with HCPs*

United States v. Caronia *– Promotion of Off Label Uses Immediately Prior to FDA Approval of New Use*

Gov't's View of Caronia decision . . .

Under 2nd Circuit Caronia decision: truthful & non-misleading speech about an off label use cannot be the sole basis for a misbranding enforcement action.

BUT gov't can still prove misbranding on a theory that promotional speech provides evidence that a drug is intended for a use that is not included on the drug's FDA-approved label.

More Recent 1st Amendment Updates

Amarin & Pacira Case Settlements

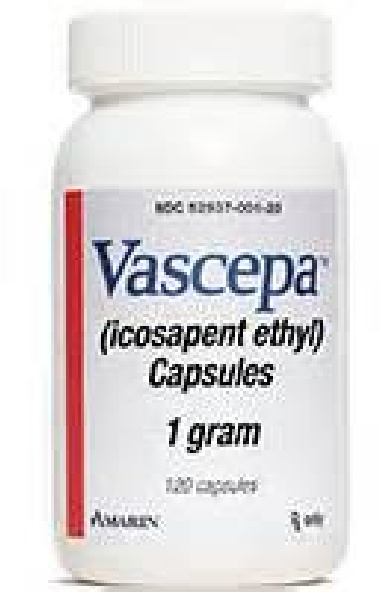
Vascular & Facteau Prosecutions

FDA's **First Amendment Memo**, plus **"Intended Use" Final Rule** (now delayed)

Draft Guidances: "Consistent with Labeling" & Payor-Directed Communications

AMARIN & PACIRA CASES

Amarin Corp.



omega-3 acid EPA

Pacira Pharmaceuticals, Inc.

Non-opioid pain medication

Examples of What Amarin Wanted to Be Able to Say to HCPs (not consumers):

- Double-blind, placebo-controlled clinical trial showed Vascepa® lowered triglycerides in patients with persistently high triglycerides (>200 mg/dL and < 500 mg/dL) not controlled by diet and statin therapy

- Supportive but not conclusive research shows that EPA & DHA omega-3 fatty acids may reduce risk of coronary heart disease

Also, Amarin wanted to share peer-reviewed scientific publications relevant to potential effect of EPA on reduction of risk of coronary heart disease.

Non-Rx Products can say. . .

“Supportive but not conclusive research shows that consumption of EPA & DHA Omega-3 fatty acids may reduce the risk of coronary heart disease.”

Amarin Settlement

Amarin submits proposed marketing materials (that include off label information) to FDA.

FDA can object if, in its view, information is untrue or misleading. If the two parties cannot agree, a federal judge will sort it out.

Pacira Case – "On Label" Promotion

10/28/11 - Exparel approval: "administration into the surgical site to produce postsurgical analgesia"

Pivotal trials addressed pain after bunion and hemorrhoid surgery, but FDA req'd pediatric studies (in other surgeries) & military uses drug for other types of post surgery pain too

9/22/14 – FDA Warning Letter cites: 1) promotion in surgeries other than bunion and hemorrhoid & 2) up to 72 hour pain relief (but only one study). Pacira sends corrective communications.

6/23/15 – Pacira sends 32 page communication (how OPDP's position is inconsistent with scientific evidence, prior precedents, and the FDA's own regulations)
7/24/15 – FDA sends close-out letter & ignores 6/23/15 Pacira submission

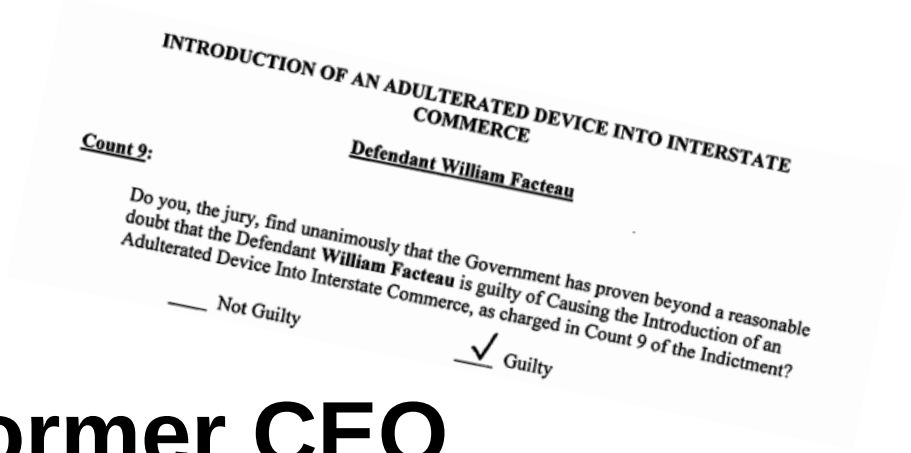
9/8/15 – Pacira files lawsuit, which includes challenge of "subst. evid." 2 study requirement for promotional claims & restrictive view of approved indication despite PI

12/15/15 – Case settles. FDA withdraws warning letter, approves labeling supplement & confirms that indication includes surgeries that were not part of pivotal trials & parties agree to deal with each other in open, forthright and fair manner.

U.S. v. William Facteau & Patrick Fabian

July 20, 2016

Jury convicted two Acclarent executives on 10 misdemeanor counts of introducing misbranded & adulterated product into interstate commerce



INTRODUCTION OF AN ADULTERATED DEVICE INTO INTERSTATE COMMERCE

Count 9: Defendant William Facteau

Do you, the jury, find unanimously that the Government has proven beyond a reasonable doubt that the Defendant **William Facteau** is guilty of Causing the Introduction of an Adulterated Device Into Interstate Commerce, as charged in Count 9 of the Indictment?

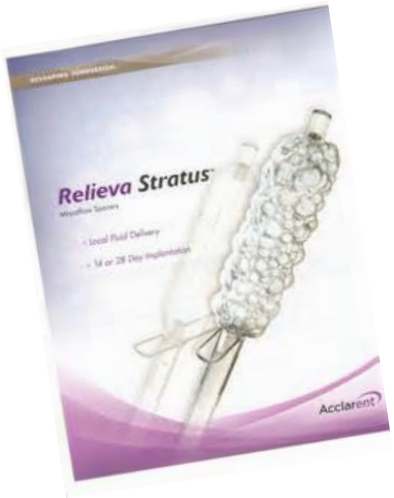
___ Not Guilty

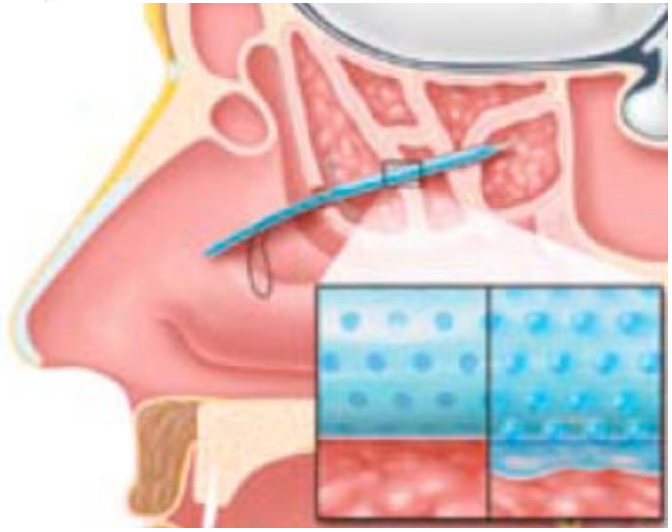
✓ Guilty

- **William Facteau, Former CEO**

- **Patrick Fabian, VP of Sales**

Facteau Case – Relieva Stratus Medical Device

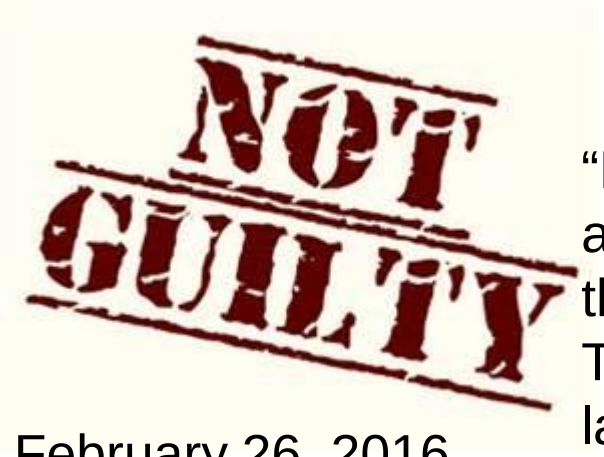




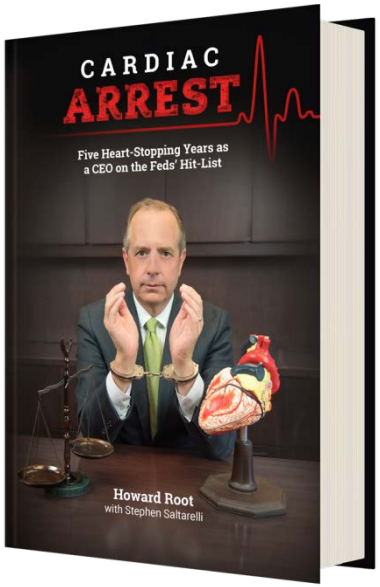
Defendants: convictions violate 1st Amendment & no fair notice of what constitutes crim'l conduct

Gov't: defendants weren't convicted for speech, but rather for their actions – by selling medical devices for intended use that have not rec'd FDA approval. Company's internal speech and that of sales reps provided evidence of device's intended us but was not, itself, the criminal conduct. Also: FDCA's misdemeanor provisions, combined with "intended use" concept are not unconst'lly vague.

U.S. v. Vascular Solutions & Howard Root



February 26, 2016

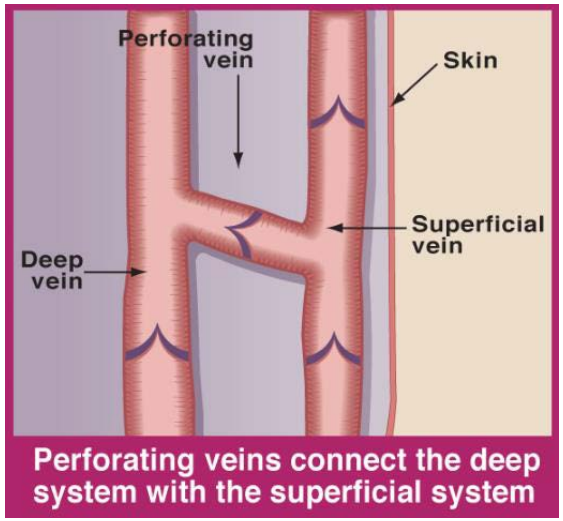


Jury Instruction:

"Doctors may use medical devices that have been approved or cleared for one use for a different use that has not been cleared or approved by the FDA. This is often referred to as unapproved use or off-label use. This is not illegal. ***It 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.*** ***If you find that VSI's promotional speech to doctors was solely truthful and not misleading, then you must find the Defendants not guilty of the misbranding offense."***

U.S. v. Vascular Solutions Case & Howard Root

Gov't: "Vari-Lase" product line only approved for treatment of superficial veins. BUT company promoted product for ablation of "perforator" veins, which connect the superficial vein system to the deep vein system.



Charged company & CEO with 1 count conspiracy & 8 counts of introducing adulterated and misbranded devices into interstate commerce.

Key FDA Documents Released: Jan. 2017

Released two days before:

Memo: FDA's Position on 1st Amendment

"Intended Use" Rule

2 Draft Guidances

First Amendment Memo (Jan. 18, 2017)

Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products

Government Goals in Having Restrictions

"[I]t is intolerable to permit the marketing of worthless products under the rules of a cat-and-mouse game where a firm can fool the public until the [FDA] finally catches up to him"

FN 16 (Sec'y of Health, Education & Welfare statement to Congress; The Drug Industry Antitrust Act of 1962: Hearings before the Antitrust Subcommittee of the Committee on the Judiciary, 87th Congress, 2nd Session 171 (1962)

FDA's 1st Amendment Memo

It's not possible for individuals to conduct same rigorous evaluation that FDA scientists perform. In addition to off label use, need to consider pharmacokinetics, drug disease interactions & other safety considerations.

Few physicians are trained in research & they rely on published literature, which is skewed toward positive results.

No labeling for how to safely use drugs for unapproved uses (e.g. appropriate dosing, contraindications, instructions for use) & therefore, there is a significant risk of harm to patients.

FDA's 1st Amendment Memo

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Marketing & psychological research suggest that marketers are most successful in their messaging due to emotional content, humor & other noninformational techniques (which disengage critical faculties) and possible to influence consumer behavior without consumers being aware of the powerful effect of advertising.

Per 2004 study, a Primary Care Physician would require 627.5 hours/month to keep up with medical literature relevant to primary care practice.

Intended Use

Medical Product Communications That Are Consistent With the FDA-Required Labeling — Questions and Answers

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Catherine Gray at 301-796-1200; (CBER) Office of Communication, Outreach and Development at 800-835-4709 or 240-402-8010; (CDRH) Angela Krueger at 301-796-6380; (CVM) Thomas Moskal at 240-402-6251; or (OC) Kristin Davis at 301-796-0418.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Center for Veterinary Medicine (CVM)
Office of the Commissioner (OC)

January 2017
Procedural

"Consistent with FDA-Required Labeling"

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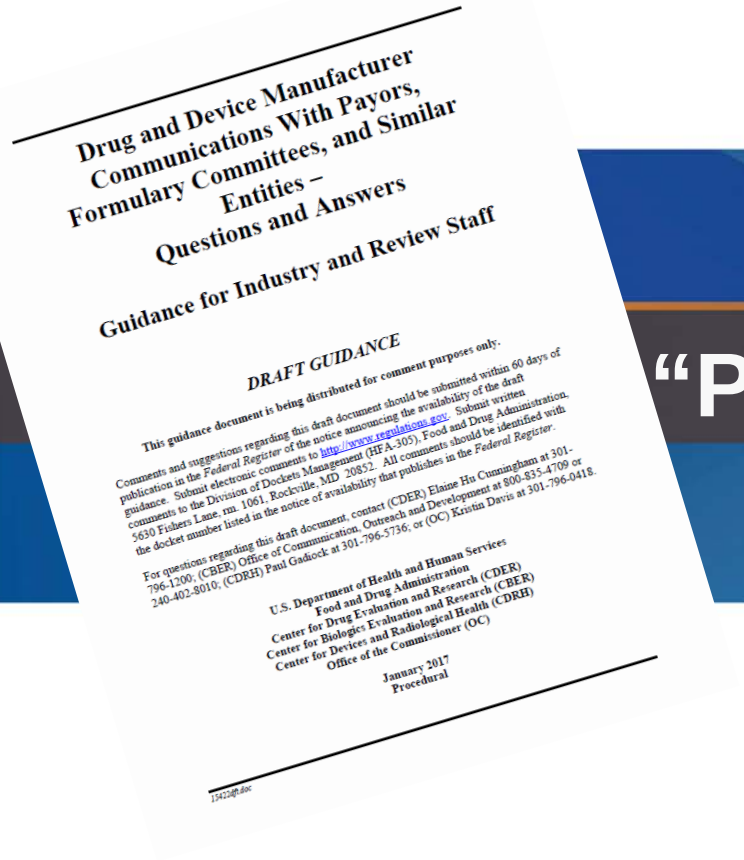
21st Century Cures Act signed into law 12/16



Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers

Guidance for Industry and Review Staff

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"Payor Communications"

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Questions/Comments?