Asymmetry in the Ability to Communicate CER Findings

CER and the First Amendment

Gerald Masoudi

National Pharmaceutical Council
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Overview

- Off-Label Legal Theories
- Healthcare Economic Information Exception
- Citizen Petition
- Unsolicited Requests Draft Guidance
- *Sorrell v. IMS Health*, 131 S. Ct. 2653 (2011)
- *United States v. Caronia* (2d Cir. 2011)

Promotional Legal Theories

- Promotion of approved product for unapproved use can misbrand product -- lack of adequate directions for use
- Promotion of approved product for unapproved use in labeling can create unapproved new drug
- Dissemination of false/misleading labeling can misbrand product

Off-Label Conduct -- Theories

- "Advertis[ing] or represent[ing]" a "purpose" other than those set forth in FDA-approved labeling. (21 CFR § 201.100(c), 21 USC § 352(f)(1))
- Labeling with "conditions prescribed, recommended or suggested" that vary from those for which approved. (21 USC § 321(p))

On- or Off-Label Conduct

- Claims, including comparative claims, that are false or misleading (21 USC § 352(a)).
- Substantiation FDA expects in promotion
  - 2011 Warning Letter: "Generally, claims of superiority must be supported by two adequate and well-controlled head-to-head clinical trials comparing the appropriate doses and dose regimens of a drug and a comparator drug."
  - 2007 Warning Letter: "First….the active comparison was not clearly planned….Second, the study was not replicated."

Healthcare Economic Information

- In 1997, Section 114 of FDAMA created exception from misbranding under 21 USC § 352(a) for:
  - healthcare economic information
    - that "directly relates" to an approved indication
    - based on "competent and reliable scientific evidence"
  - provided to a formulary committee, or other similar entity, in the course of it carrying out its responsibilities for the selection of drugs for managed care or other similar organizations.

Citizen Petition

- Filed in July 2011 by seven manufacturers requesting that FDA clarify its policies regarding promotion of off-label uses of marketed products.
- Petition requested clarity on:
  - Responses to unsolicited requests for information
  - Scientific exchange
  - Interactions with formulary committees and payors
  - Dissemination of third-party clinical practice guidelines

Citizen Petition – Health Care Economic Data

- Seeks guidance that provision of information by manufacturer to payors is scientific exchange if:
  - Not misleading
  - Delivered by representatives of manufacturer with appropriate expertise
  - Provided to payors carrying out responsibility for selection/coverage of products/therapies
  - Health care economic information directly related to approved indication OR published health care economic information

Unsolicited Requests Draft Guidance

- Prior to the December 2011 draft guidance, policy on unsolicited requests set forth in policy statements, but FDA provided few details regarding the policy.
- First FDA statement on responding to unsolicited requests posted on the Internet and in other public forums such as a speaker program.
- FDA recognizes that health care professionals can lawfully use or prescribe a product for off-label uses and that "off-label uses or treatment regimens may be important therapeutic options and may even constitute a medically recognized standard of care."

Unsolicited Requests Draft Guidance

- "FDA recognizes that firms are capable of responding to requests about their own named products in a truthful, non-misleading, and accurate manner. Furthermore, as these firms … have robust and current information about their products, FDA recognizes that it can be in the best interest of the public health for a firm to respond to unsolicited requests for information about off-label uses."

Sorrell v. IMS Health

- Vermont statute prevented sale, disclosure or use of information on prescribing practices of individual physicians for prescription drug marketing.
- Stated purpose of the law was to safeguard privacy, lower health costs and to protect the integrity of the doctor-patient relationship.
- Vermont data mining companies and PhRMA filed suit alleging the law violated their First Amendment rights.
- Similar laws in Maine and New Hampshire were also challenged through litigation.

Sorrell v. IMS Health: Holding

- Court found the Vermont law imposed content- and speaker-based restrictions. Disfavored only certain speakers (pharmaceutical manufacturers) and certain types of speech (pharmaceutical marketing).
- Court noted that explicit purpose of the law was to inhibit "detailing" and to reduce the effectiveness of marketing by brand name manufactures. Court noted that the State did not contend that detailing is false or misleading or that the law would have prevented false or misleading speech.
- Court therefore subjected the law to "heightened judicial scrutiny" to find the law unconstitutional.

Sorrell v. IMS Health: Dissent

- Would have applied the *Central Hudson* "intermediate" commercial speech standard or standard appropriate for review of economic regulation.
- Noted that "the same First Amendment standards that apply to Vermont here would apply to similar regulatory actions taken … through Food and Drug Administration … regulation."

Sorrell v. IMS Health: Of Note

- "Speech in aid of pharmaceutical marketing . . . is a form of expression protected by the Free Speech Clause of the First Amendment."
- "The more benign and, many would say, beneficial speech of pharmaceutical marketing is also entitled to the protection of the First Amendment. If pharmaceutical marketing affects treatment decisions, it does so because doctors find it persuasive. Absent circumstances far from those present here, the fear that speech might persuade provides no lawful basis for quieting it."

Sorrell v. IMS Health: Of Note

- "[T]he fear that people would make bad decisions if given truthful information cannot justify content-based burdens on speech. The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good. These precepts apply with full force when the audience, in this case prescribing physicians, consists of sophisticated and experienced consumers."
- "A consumer's concern for the free flow of commercial speech often may be far keener than his concern for urgent political dialogue."

United States v. Caronia

- Caronia, a sales rep for Jazz Pharmaceuticals, had arranged a meeting between a prescribing doctor (a confidential government informant) and a physician Jazz used as a promotional speaker, who spoke about off-label uses of Xyrem.
- Caronia was convicted of conspiring to misbrand Xyrem by promoting Xyrem off-label to combat excessive daytime sleepiness. That use was the subject of a sNDA at the time of the conversation and FDA approved the drug for that use shortly thereafter.

United States v. Caronia

- Appealed to Second Circuit before *Sorrell v. IMS Health*, but the court called for supplemental briefing on applicability of *Sorrell* to Caronia's appeal.
- Decision expected shortly.
- First case to address application of *Sorrell* to FDA regulatory system.
- Caronia argued that the FDA regime engages in content and speaker discrimination in that it prohibits manufacturers (but not others) from speaking in favor of off-label uses (but not against), and therefore his conviction was unconstitutional.

United States v. Caronia

- Government argued:
  - The speech merely played an "evidentiary role:" the promotion was evidence of an intended use, for which the drug was not appropriately labeled.
  - "Caronia was not convicted for conspiring to promote off-label uses of Xyrem, but instead for conspiring to distribute Xyrem without adequate directions for use."
  - *Sorrell* does not address disclosure statutes, and the FDCA *requires* information (adequate directions for use) rather than *prohibiting* it.

Questions from Changing Legal Landscape

- How does *Sorrell* apply to participation by manufacturers in discussions over CER?
- Is exception to misbranding for health care economic information narrower than what Constitution requires?
- Is health care economic information provided to payors by manufacturers appropriate evidence of intent that products be used off-label?

Questions?