FDA's Evolving Approach to Comparative Claims

Dara Katcher Levy, Director, Hyman, Phelps & McNamara, PC

Justin Drinkwine, Corporate Counsel, Jazz Pharmaceuticals, Inc.

Coleen E. Klasmeier, Partner, Sidley Austin LLP

FDLI

Final Guidance: Communications Consistent with FDA-Required Labeling ("CFL")

- **Intended to "provide clarity" in response to frequently asked questions**
- **Addresses two key issues:**

Evidence of "Off-Label" Promotion

FDA "does not intend to rely on" a CFL communication "to establish a new intended use" or "as evidence of a firm's failure to comply with" the section 502(f)(1) requirement "that a medical product's labeling bear adequate directions for use"

But, the communication "may be part of the overall material that is evaluated when assessing [a] firm's conduct" if there is other evidence of a new intended use

Basis for Other FDCA Violations

"FDA would not consider representations or suggestions in a CFL promotional communication to be false or misleading based only on the lack of evidence sufficient to satisfy the applicable approval/clearance standard" (e.g., "substantial evidence" for drugs)

But, "the communication could be false or misleading for other reasons"

Determining when a Communication is CFL

- **Guidance articulates a clinically oriented, risk-based framework based on 3 factors:**
  - How information in communication compares to information about certain conditions of use in FDA-required labeling
  - Whether representations/suggestions in communication increase potential for harm relative to information reflected in FDA-required labeling
  - Whether directions for use in the FDA-required labeling enable safe and effective use under conditions represented/suggested

Relevant Conditions of Use in the FDA-Required Labeling

- *Indication*
- *Patient population*
- *Use limitations*
- *Directions for handling/use*
- *Dosing/administration*

A communication is consistent with FDA-required labeling if it satisfies **all three** factors

Recent OPDP Enforcement – Comparative Claims

- **2 OPDP Letters in September 2019**
  - Warning Letter to Galt
    - September 13, 2019
    - Includes Allegations that Comparisons Created
      - False or Misleading Risk Presentations
      - False or Misleading Efficacy Presentations
  - Untitled Letter to Kowa
    - September 24, 2019
      - Includes Allegations that Comparisons Created
      - False or Misleading Risk Presentations

Warning Letter

- The subject email included claims and a presentation related to the relative abuse potential of Doral v. other sleep medications. FDA cited the following:
  - Header that stated, “Concerned about Abuse potential of sleep medications?”
  - “Doral’s relative likelihood of abuse is considerably lower than some of the widely used sleep aids (i.e. Zolpidem & Temazepam)*”
  - “Doral was ranked even lower than OTC product Diphenhydramine for relative abuse potential*”
  - A figure comparing the “Relative Likelihood of Abuse” of 19 drugs, with Quazepam shown as having a score lower than 16 of the drugs depicted
  - “Doral’s abuse potential is 1/2 of Zolpidem & 1/3 of Temazepam”

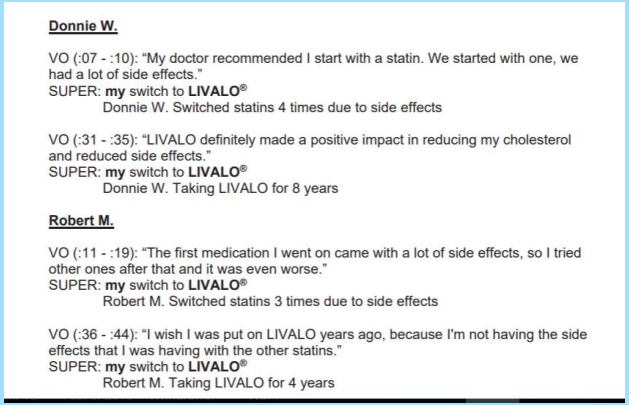
- Is the Comparison Consistent with FDA required labeling?
  - How does it compare with conditions of use? (Indication, Patient Population, Limitations, Dosing)
  - Does it Increase Potential for Harm?
  - Do the existing directions for use in the FDA-Required Labeling allow for the safe and effective use of the product under the conditions described?
- Is the Comparison Truthful and Non-Misleading?

Warning Letter

- “These claims and presentation are misleading because they minimize the risks of abuse and dependence associated with Doral and suggest that this C-IV scheduled drug is superior in safety to other prescription and over-the-counter (OTC) products. . . .While we acknowledge the figure includes the following statement, ‘*Please see complete prescribing information for detailed information on each product. The above chart is not intended for efficacy comparison. The authors algorithm, while comprehensive, does lack prospective abuse data in human subjects and had not been validated in subsequent research,’ this statement does not mitigate the overwhelming impression that Doral is superior in safety to other prescription and OTC products.”

Untitled Letter

- DTC You Tube video with a montage of patient testimonials about Livalo and switching from other statins due to side effects.



Donnie W.

VO (:07 - :10): "My doctor recommended I start with a statin. We started with one, we had a lot of side effects."
SUPER: **my** switch to **LIVALO®**
Donnie W. Switched statins 4 times due to side effects

VO (:31 - :35): "LIVALO definitely made a positive impact in reducing my cholesterol and reduced side effects."
SUPER: **my** switch to **LIVALO®**
Donnie W. Taking LIVALO for 8 years

Robert M.

VO (:11 - :19): "The first medication I went on came with a lot of side effects, so I tried other ones after that and it was even worse."
SUPER: **my** switch to **LIVALO®**
Robert M. Switched statins 3 times due to side effects

VO (:36 - :44): "I wish I was put on LIVALO years ago, because I'm not having the side effects that I was having with the other statins."
SUPER: **my** switch to **LIVALO®**
Robert M. Taking LIVALO for 4 years

- Is the Comparison Consistent with FDA required labeling?
  - How does it compare with conditions of use? (Indication, Patient Population, Limitations, Dosing)
  - Does it Increase Potential for Harm?
  - Do the existing directions for use in the FDA-Required Labeling allow for the safe and effective use of the product under the conditions described?
- Is the Comparison Truthful and Non-Misleading?

Untitled Letter

- “This presentation misleadingly suggests that Livalo is safer than its competitors by implying that patients switching to Livalo from other statins will experience a reduction in side effects compared to other statins, or no side effects at all. While the patient testimonials in this presentation may be an accurate reflection of these patients' own personal experiences with Livalo, the testimonials do not adequately support the suggestion in the presentation that other patients switching to Livalo from other statins will experience a similar reduction in side effects compared to other statins, or no side effects at all.”

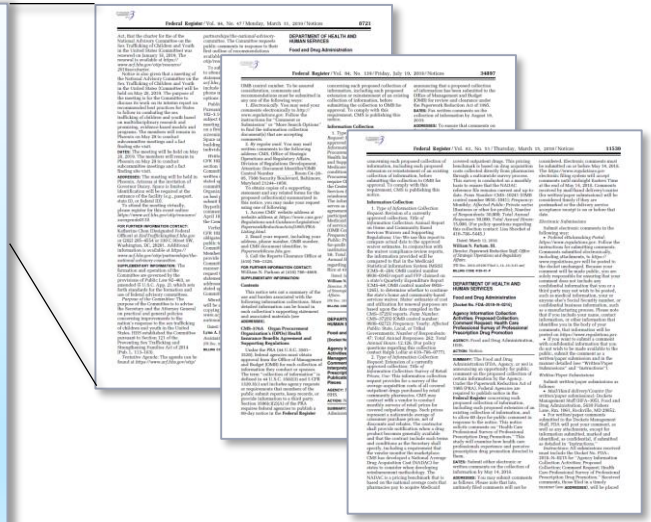
OPDP Research Agenda Statements

“FDA’s regulatory policies are aligned with the principles of free speech and due process in the U.S. Constitution.”

84 Fed. Reg. 34,897 (July 19, 2019); 84 Fed. Reg. 8,721 (Mar. 11, 2019).

“FDA regulates within the framework of free speech and due process principles of the United States Constitution.”

83 Fed. Reg. 11,539 (Mar. 15, 2018).



“From a legal perspective, care must be taken to consider how the government may, in the future, use such data in the different setting of an enforcement matter premised on a false or misleading statement.”

There are challenging questions regarding the “interplay between the First Amendment and audience comprehension when evaluating whether a promotional statement will be viewed as false or misleading.” –FDA Chief Counsel address on March 8, 2018

FDA's Evolving Approach to Comparative Claims

Dara Katcher Levy, Director, Hyman, Phelps & McNamara, PC

Justin Drinkwine, Corporate Counsel, Jazz Pharmaceuticals, Inc.

Coleen E. Klasmeier, Partner, Sidley Austin LLP

FDLI