An Analysis of FDA Untitled and Warning Letters, 2009-2012

Athavale AS, Lokhandwala TT, Datar MV, West-Strum DS

Department of Pharmacy Administration and the Center for Pharmaceutical Marketing and Management, The University of Mississippi, University, MS, USA

Background

- Promotional claims made by pharmaceutical manufacturers are reviewed by the U.S. FDA's Office of Prescription Drug Promotions (OPDP).
- If promotional materials are considered "false, lacking in fair balance or otherwise misleading", an untitled letter of notice of violation or a warning letter is issued to the manufacturer.[1]

Warning Letters[1,2,3]
- More serious or repeated violations
- Reply required within 15 days
- Immediate corrective action required
- Failure to act immediately may lead to criminal prosecution

Untitled Letter of Notice of Violation[1,3]
- Less serious violations
- Reply required within 15 days
- Immediate corrective action required
- Criminal prosecution less likely

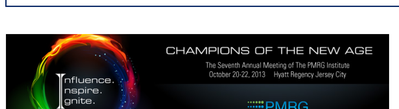
Objectives

- Broad purpose – to gain insight into the changing landscape of the pharmaceutical industry as well as the evolving targets of FDA.
- Specifically, the study has two objectives:
  - To analyze the number of warning and untitled letters issued beginning 2009 through 2012, and the type of claim(s) cited.
  - To demonstrate the use of qualitative data in healthcare to arrive at quantitative results.

Methodology

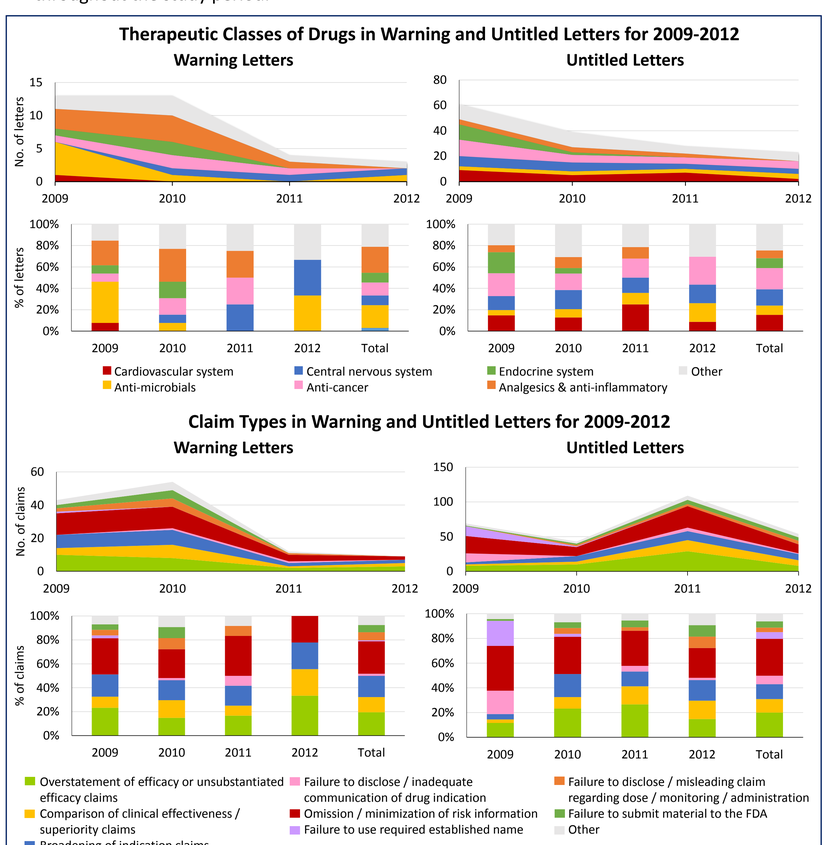
Warning and Untitled Letters from FDA.gov[3] → Relevant data abstracted by researchers → Data for analysis

Variables:
- Drug name
- Company name
- Therapeutic class
- Number of claims
- Type of claims
- Type of promotional material
- Target audience for the promotional material



Results

- A total of 151 letters were reviewed, of which 34 (22.5%) were warning letters.
- On average 38 total letters were issued each year through the study period, of which on average 9 were warning letters.
- The number of claims in each warning letter varied from 1 to 8, summing up to 409 claims throughout the study period.



- There was an increase in the total number of letters issued in 2010 (52) compared to 2009 (41), after which the number declined. The decline was mainly attributable to a decrease in the number of warning letters issued in 2011 and 2012.
- Therapeutic class type: majority of all letters – anti-cancer (18.5%) and cardiovascular (13%). Majority of warning letters – analgesics and anti-inflammatory drugs (24.4%) and anti-microbial drugs (21.2%).
- Claim type: highest number of claims – omission/minimization of risk information (29.6%), followed by overstatement of efficacy or unsubstantiated efficacy claims (20.5%).
- 54.3% of all letters were promotional materials targeting health care practitioners.
- 34.5% of claims were internet-based promotions (websites, sponsored links, etc.).

Conclusions

- Actionable takeaways:
  1. There has been an increase in the intensity of FDA surveillance activities towards protecting general public health.
     - Average number of FDA letters (untitled and warning) increased from 24 in 2002-2008, to 38 in 2009-2012.[2]
  2. There was a decrease in the number of warning letters over the course of the study period → potential decrease in the severity of promotional claim violations.
  3. Most promotional materials targeted by the FDA were directed towards health care practitioners → potentially due to their greater impact on prescribing behavior.
  4. Numerous healthcare qualitative data sources are available free of charge. Researchers can make use of these sources to arrive at valuable quantitative conclusions.

References

1. *Neumann P & Bliss S. FDA actions against health economic promotions, 2002-2011. Value in Health 2012;15:948-953.*
2. *Chatterjee S, Patel HK, Sansgiry SS. An analysis of the warning letters issued by the FDA to pharmaceutical manufacturers regarding misleading health outcomes claims. Pharmacy Practice (Internet) 2012 Oct-Dec;10(4):194-198.*
3. *U.S. Food and Drug Administration. Warning Letters and Notice of Violation Letters to Pharmaceutical Companies. Available at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/default.htm. Last accessed on: May 9, 2013.*