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Off-Label Liability: Legal and Compliance Issues

Statutory Provisions

- Three Theories
  - FDCA § 502(a), 21 U.S.C. § 352(a): A drug shall be deemed to be misbranded if its labeling is false or misleading in any particular
  - FDCA § 502(f)(1), 21 U.S.C. § 352(f)(1): A drug shall be deemed to be misbranded unless its labeling contains adequate directions for use
  - FDCA § 505(a), 21 U.S.C. § 355(a): No new drug may be introduced or delivered for introduction into interstate commerce without a new drug application (NDA) or abbreviated NDA

"Safe Harbors"

- FDA Policies
  - "Scientific exchange" (21 C.F.R. § 312.7)
    - Example: dissemination of scientific findings in scientific or lay media
  - Responses to unsolicited requests
  - Dissemination in accordance with the CME guidance
  - Dissemination in accordance with reprints guidance

Federal Prosecutors are Pursuing the Dissemination of Off-Label Information as Criminal and Civil Misconduct

- The following major pharmaceutical manufacturers among others have disclosed that they currently are being or have been investigated for alleged off-label promotion of their drugs:

Abbott Labs	Johnson & Johnson
Amgen	Eli Lilly
AstraZeneca	Novartis
Cell Therapeutics	Pfizer
Forest	Sanofi-Aventis
Genentech	Schering-Plough
GlaxoSmithKline	Wyeth
Intermune	

- There are numerous other drugs under investigation.

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- In these cases and investigations, the government has pursued criminal off-label charges that do not require a showing of false or misleading representations or other inherently wrongful conduct

- Instead, the government focuses on all off-label dissemination, including conduct that FDA generally permits
  - Scientific exchange
  - Responses to unsolicited requests
  - Dissemination of enduring materials
  - Continuing Medical Education

Federal Prosecutors are Pursuing the Dissemination of Off-Label Information as Criminal and Civil Misconduct

	On-label	Off-label
Truthful, Non-Misleading		
Untruthful or Misleading		

Federal Prosecutors are Pursuing the Dissemination of Off-Label Information as Criminal and Civil Misconduct

- Government also pursuing alleged off-label promotion under the civil False Claims Act
  - See United States' Statement of Interest in United States v. Rost

- Government's theory cast into doubt by Supreme Court's decision in Allison Engine Co. v. United States ex rel. Sanders (June 9, 2008)

A Few Guiding Principles for Compliance

- FDA is the least of your problems
- One size does not fit all
- All information dissemination has risk
- Consider a portfolio approach to risk
- Be thoughtful about the risks you take

The Future

- Clarity from the courts?
- The future of the reprint guidance and further action by FDA
- Possible clarity from the Department of Justice?
  - Was the communication truthful and not misleading?
  - Were patients harmed?
  - Was FDA approval pursued and\or secured?