

Disclosure of Affiliations: Lessons from the Rofecoxib Litigation

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Overview

- Outline of product
- History
- Litigation(s)
- Lessons learned

Rofecoxib: The product

- Rofecoxib, formerly marketed under brand names including Vioxx, a nonsteroidal anti-inflammatory, a selective cyclooxygenase-2 (COX-2) inhibitor.
- COX-2 mediates the synthesis of prostaglandins responsible for pain and inflammation. Rofecoxib inhibits only COX-2 (not COX-1), greatly reduced risk of fatal or debilitating peptic ulcers.
- FDA approved in 2000, & widely accepted by physicians treating patients with arthritis and other chronic or acute pain conditions.
- 2003: Annual sales revenue of \$2.5 billion.
- 2004: Adverse reactions (primarily cardiovascular and neurological events) and related litigation, Merck voluntarily withdrew rofecoxib from the market on September 30, 2004.

Seeding Trials: Definition

- “Clinical studies conducted by pharmaceutical companies that are designed to seem as if they answer a scientific question, but primarily fulfill marketing objectives.”

Hill et al:

ADVANTAGE Trial: **A**ssessment of **D**ifferences between **VIOXX** and **N**aproxen to **A**scertain **G**astrointestinal **T**olerability and **E**ffectiveness

- Litigations related to VIOXX
 - *Cona v. Merck and Co. Inc
 - *McDarby v. Merck and Co. Inc
- Litigation related court ordered discovery information, Merck internal and external correspondence, reports and presentations
- Created between 1998 to 2006

ADVANTAGE Trial

- 3 issues emerge:

1. Trial was designed by the marketing division to fulfill marketing objectives

2. Marketing head handled both marketing and scientific data, including collection, analysis and dissemination

3. Marketing nature of the trial was not made known to participants, investigators, institutional review boards

Vioxx Settlement: the Highlights

- November 9, 2007: Merck & Co., Inc., and plaintiffs' counsel entered into a no fault Settlement Agreement (the "Master Settlement Agreement" - MSA)
- MSA: addressed resolution and closure of a number of rofecoxib claims (together with additional global rofecoxib claims, the "Vioxx litigation").
- Master Settlement Agreement: Merck reserved \$970 million for related legal expenses through 2007, and reserved \$4.85 billion for settlement of Consolidated Proceedings.

Key Settlement Terms

- Acceptance of at least 85% of Vioxx plaintiffs before settlement goes into effect.
- \$4.85 billion on a multiparty basis works out to \$100,000 to \$200,000 per plaintiff, less attorneys' fees (between 33% to 40%).
- Law firms in the Steering Committees are required to recommend enrollment to their MI or ischemic stroke clients.
- Such firms may not represent nonparticipating plaintiffs.

A Winning Proposition: For Whom?

- A try-every-case approach → lower than anticipated liability exposure.
- Share price rose on announcement; liability had been reasonably estimated at up to \$30 billion.
- Adverse litigation continued after the withdrawal: the Master Settlement Agreement addressed co-pending class actions (the “Coordinated Proceedings”) brought by both U.S. and foreign plaintiffs.
- The Consolidated Proceedings covered 95% of claims brought in four U.S. federal and state courts and comprised of 47,000 claimant groups together with 14,500 additional claimants.
- Litigation expanded along global & shareholder vectors.

Vioxx Litigation Goes Global

- March 2010: Australian court held that Merck, Sharpe & Dohme (Aust) Pty. Ltd. had breached the Trade Practices Act by selling a drug which was unfit for sale and entered a judgment in favor plaintiff for US\$ 287,000.
- In response, Merck noted the court “dismissed all claims against Merck, specifically finding that Merck was not negligent in its development, scientific study and sale of Vioxx.
- Merck and MSD Australia disagree with the limited portions of the court’s findings that were against MSD Australia and intend to appeal them. The companies are in the process of reviewing the full judgment.

Why Australia?

- The “Australasian Journal of Bone & Joint Medicine”
- Single-sponsor journal.
- Published by Elsevier; industry funded.
- Peer review remains disputed.
- Elsevier is revisiting “unacceptable” practices in all Australasian journals.

U.S.: Shareholder Rights Without An End in Sight

US Supreme Court: Rule Announced in *Merck & Co. v. Reynolds* (2010)

Under the applicable statute of limitations, cases by private plaintiffs under § 10(b) of the Securities Exchange Act must be brought no later than the earlier of “2 years after the discovery of the facts constituting the violation,” or 5 years after the violation. *See* 28 U.S.C. § 1658(b).

The Court concluded that the 2-year clock starts to run either when a plaintiff actually discovers *or* when a “reasonably diligent plaintiff” discovers “facts constituting the violation,” including facts giving rise to a strong inference of scienter (*i.e.*, fraudulent intent).

U.S.: Shareholder Rights Without An End in Sight

The Court holding: the word “discovery” in the statute includes not only the *actual* discovery of the facts constituting the violation, but also the *constructive* discovery of such facts.

To establish a statute of limitations defense, a defendant need not establish that a particular plaintiff itself knew facts constituting a violation; it is enough that “a reasonably diligent plaintiff” would have discovered them. (*Merck & Co.*, slip op. at pp. 8-12.)

Shareholder Rights

The Court holding: “the facts constituting the violation” include the fact of scienter, an essential element of a § 10(b) claim (Slip op. @ pp. 12-14).

Court rationale: because a plaintiff must allege facts giving rise to a strong inference of scienter merely to survive a motion to dismiss, a contrary holding would prevent plaintiffs from bringing any claims if the defendant was able to conceal for two years that it had made a misstatement with an intent to deceive. (Slip Op. at p. 13.)

Shareholder Rights

The Court rejected the concept of “inquiry notice” in § 10(b) claims.

The Supreme Court in *Merck* held that sufficient information suggestive of wrongdoing to trigger investigation is inconsistent with the language of the statute. A cause of action accrues only upon actual or constructive “discovery” of the facts of the violation.

- Here, the *Merck* plaintiffs had not actually or constructively discovered facts indicating Merck’s alleged scienter more than 2 years before the case was filed through (a) filing of a tort claim or (b) a FDA notice letter.
- Long story short: litigation continues!

Lessons Learned

- Shareholder litigation proceeds at home, and plaintiff claims continue overseas,
- In light of research and marketing practices common throughout the industry, the Vioxx litigation presents a number of valuable lessons learned for regulatory agencies, manufacturer companies, marketing firms, and counsel active in the drug and device markets throughout the world.

Questions Presented

Ethics or Industrial Conflict?

- Merck/ Vioxx case: existence of a state of ethical conflict.
- Pharmaceutical companies : seek to develop drugs, generate profits from these drugs while causing no harm to consumers.
- FDA mission: protection of consumers & timely approval of beneficial drugs.
- The practices adhering to one set of goals can conflict with another set of goals

Research, Marketing, or Both?

- The Marketing & Sales mandate: maximize sales
- Research Labs: developing profitable new drugs.
- Harm to consumer: ? Can either division be called to account for harm
- Result: individuals working in each division could fulfill roles as excellent workers without any clear reference to the goal of ensuring consumer safety.¹⁷

Questions Presented

- Consider the relationship between the Merck's Defense Medical Standards Board (DSMB), Merck's Human Health Product Approval Committee (HHPAC), and the Merck research and Merck marketing divisions.
- Was the relationship among these entities too intertwined?
- Or were they not sufficiently integrated?
- Should HHPACs (Merck's Human Health Product Approval Committee) be stand-alone entities?

Questions Presented

- Conflicts of Interest: Can mass tort plaintiffs' counsel fully or entirely represent their clients' interest?
- Risk disclosure: All products contain a risk threshold. Where do we draw the line?
- Defense: Merck produced a desirable and effective product; known risks were disseminated through reasonable and timely warnings.

Seeding Trials

- Is there a role for seeding trials?
- Who should be informed and what information provided?
- What should be reported?
- Should there be a public repository of all clinical trials?
- Should all data “collected” from all trials be made available in a public repository?
- Would these measures ensure that “seeding “ trials answer meaningful questions?
- Would these measures ensure that the information collected is made known to the public regardless of outcomes?

Law and Medicine

- Complex questions grounded in science and medicine.
- Causation, causation, causation.
- Role of marketing practices – but does marketing *cause* injury?
- And there was nothing wrong with Merck's marketing. See Debevoise & Plimpton LLP 2006 Management Report.

Law and Ethics

- A lawyer's duty extends beyond theory and to practical knowledge, with an obligation to serve the public good.

Harry Edwards, *A Lawyer's Duty to Serve the Public Good*, 65 N.Y.U. L. Rev. 1148 (1990).

- Merck serves fiduciary duties to present shareholders.

- Medicolegal professionals should better promote practitioner and consumer awareness.

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References

- Hill KP et al: The ADVANTAGE seeding trial: A review of internal documents. *Annals of Int. Med.* 149: 251-58, 2008
- Kessler DA, et al: Therapeutic-class wars—drug promotion in a competitive marketplace. *N Engl J Med.* 1994;331:1350-3.
- Andersen M, et al: How conducting a clinical trial affects physicians' guideline adherence and drug preferences. *JAMA.* 2006;295:2759-64.
- Lisse JR, et al. ADVANTAGE Study Group. Gastrointestinal tolerability and effectiveness of rofecoxib versus naproxen in the treatment of osteoarthritis: a randomized, controlled trial. *Ann Intern Med.* 2003;139:539-46.

Thank you!