

Morgan Lewis

Life Sciences Summer Series

webcast



Drug and Device Off-Label Promotion

Thursday, June 18, 2009
1:00 pm ET - 2:00 pm ET

- Government enforcement and civil litigation update and trends
- Compliance with new FDA guidance on journal reprints
- Risk management and best practices in training and monitoring

Panelists:

Sarah E. Bouchard
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Enforcement/Statutory Framework and Trends

Presented by:

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Morgan Lewis - Philadelphia

The Legal Framework of Off-Label Promotion

❖ The Off-Label Statute

- The Federal Food, Drug & Cosmetic Act (FFDCA) makes it unlawful to introduce into interstate commerce any food, drug, device or cosmetic that has been adulterated or misbranded (See, e.g., 21 U.S.C. § 331(a), (b), (k))
 - Applies to individuals (corporate officers and employees) and companies
 - The FDA-approved label is the prosecutor’s starting point for assessing off-label promotion activity
- Promotion of drugs or devices for off-label or unapproved uses is a strict liability misdemeanor offense that carries a criminal penalty of up to one year in prison and a \$100,000 fine for individuals and a \$200,000 fine for corporations (21 U.S.C. § 333(a)(1) and 18 U.S.C. § 3571)
- If the off-label promotion activity involves “intent to defraud or mislead,” the criminal penalty is up to three years in prison and a \$250,000 fine for individuals and a \$500,000 fine for corporations (21 U.S.C. § 333(a)(2) and 18 U.S.C. § 3571)
- Under 18 U.S.C. § 3571(d), the fine may be even greater than stated depending on pecuniary gain to company or loss to government

The Legal Framework (cont.)

❖ Other Statutory Considerations

- The False Claims Act (FCA) prohibits knowingly presenting, *or causing to be presented*, a false or fraudulent claim for payment to the government
Healthcare Fraud Statute (31 U.S.C. § 3729)
 - Proof of specific intent is not required
 - Liability attaches to both facially false claims and claims procured through a fraudulent course of conduct
 - Cases often start with a “qui tam” complaint filed by relator
 - \$5,500 - \$11,000 per claim, plus treble (3x) damages to Government
- Mandatory Exclusion (42 U.S.C. § 1320a-7(a))
 - “Conviction of program-related crimes” or “Felony conviction relating to health care fraud”
 - Mandatory minimum five-year exclusion
 - Applies to all federal and state healthcare programs
 - Applies to the entire company

The Legal Framework (cont.)

- Permissive Exclusion (42 U.S.C. § 1320a-7(b))
 - Provides for discretionary exclusion based on broad categories of activities (e.g., “Conviction relating to obstruction of an investigation,” “Claims for excessive charges,” “Fraud, kickbacks, and other prohibited activities”)
 - Shorter exclusionary periods may be applicable and mitigating circumstances may be considered in determining the appropriate length of exclusion

❖ The Sentencing Guidelines

- Fine range is determined by multiplying the base fine against a minimum and maximum multiplier based on a culpability score
- Base fine equals pecuniary gain to the company, loss to government, or amount corresponding to offense level at USSG § 8C2.4
- Culpability score is based on company size, role of management in criminal activity, prior criminal history, existence of compliance/ethics program, cooperation and acceptance of responsibility

Components of a Typical Off-Label Resolution

- Criminal Penalties
- Civil Penalties
- Plea Agreement, Deferred Prosecution Agreement (DPA), or Non-Prosecution Agreement (NPA)
- Corporate Integrity Agreement
- Exclusion (mandatory & permissive)
- Federal Monitoring
- Potential Liability for Corporate Officers and Employees
- Potential Enhancements for Repeat Offenders

Major Off-Label Case Resolutions (last 5 years)

- *Eli Lilly* (E.D. Pa. Jan. 2009) - \$1.4B for Zyprexa
- *Cephalon* (E.D. Pa. Sept. 2008) - \$425M for Actiq, Gabitril, Provigil
- *Bristol-Myers Squibb* (D. Mass. Sept. 2007) - \$515M for Abilify, Serzone (civil only)
- *Purdue Frederick Co., Inc.* (W.D. Va. May 2007) - \$635M for OxyContin
- *Pharmacia* (D. Mass. April 2007) - \$34.7M for Genotropin (criminal only)
- *InterMune* (N.D. Cal. Oct. 2006) - \$37M for Actimmune (civil only)
- *Schering Sales Corporation* (D. Mass. August 2006) - \$435M for Temodar, Intron A
- *Serono* (D. Mass. Oct. 2005) - \$704M for Serostim
- *Warner Lambert* (D. Del. May 2004) - \$430M for Neurontin

Types of Off-Label Conduct Prosecuted

❖ *Eli Lilly (January 2009) - Zyprexa*

- Alleged improper marketing activity of adult schizophrenia/bipolar drug included promoting adverse event of weight loss as a benefit; promoting product to population in which disease rarely occurs (elderly); using medical reprints – where clinical results were mixed – to demonstrate drug’s effectiveness for unapproved indications

❖ *Cephalon (September 2008) – Actiq, Gabitril, Provigil*

- Alleged improper marketing activity included promoting products for unapproved indications; calling on doctors who normally would not prescribe products; training reps to prompt doctors into off-label conversations; encouraging off-label promotion through compensation and bonus structure; explaining to doctors how to document their off-label use so as to receive reimbursement from insurers who did not pay for off-label uses

Types of Off-Label Conduct Prosecuted (cont.)

- ❖ *Bristol-Myers Squibb (September 2007) – Abilify*
 - Alleged improper marketing activity included promoting Abilify (anti-psychotic for adult schizophrenia and bipolar disorder) for pediatric use and dementia; sales reps calling on child psychiatrists and nursing homes

- ❖ *Purdue Frederick Co., Inc. (May 2007) – OxyContin*
 - With intent to defraud, Purdue supervisors and employees marketed and promoted OxyContin as a less addictive pain medication, even though Purdue's own study indicated otherwise; sales reps trained how to significantly downplay abuse issues and addictive qualities of drug when promoting to healthcare providers

Types of Off-Label Conduct Prosecuted (cont.)

❖ *Pharmacia (April 2007) – Genotropin*

- Felony anti-kickback case in which company received DPA for alleged off-label promotion activity that included marketing drug approved for growth failure to anti-aging physician specialists; and marketing growth failure drug for cosmetic use and athletic performance enhancement

❖ *InterMune (October 2006) – Actimmune*

- Company received DPA where malignant osteoporosis drug was promoted for the non-FDA approved indication of idiopathic pulmonary fibrosis (IPF, a fatal lung condition), and Actimmune's own clinical trial failed to establish the drug's efficacy for IPF

Types of Off-Label Conduct Prosecuted (cont.)

- ❖ *Schering-Plough Corporation (August 2006) – Temodar and Intron A*
 - Felony conspiracy case in which company made alleged false statements in response to an FDA inquiry into illegal promotional activities involving the use of Temodar as a first-line treatment for brain cancer, when it was only approved as a second-line treatment; and the use of Intron A, a Hepatitis C drug, in patients being treated for bladder cancer, a non-approved indication

- ❖ *Serono (October 2005) – Serostim*
 - Although Serono's clinical trials used weight loss as the clinical end point for diagnosing AIDS wasting, Serono redefined the indicator of AIDS wasting from weight loss to lost Body Cell Mass (BCM); and to increase use of its drug engaged in an alleged felony conspiracy to market non-FDA approved computer software that used BCM to diagnose AIDS wasting

Types of Off-Label Conduct Prosecuted (cont.)

❖ *Warner Lambert (May 2004) – Neurontin*

- Felony misbranding case due to prior FDCA violations that included allegations that company promoted its adult epilepsy – partial seizure drug for non-approved indications (e.g., pain, bipolar disorder, ALS, migraine, alcohol withdrawal, restless leg syndrome, spinal cord injury, monotherapy for epilepsy), despite lack of supporting clinical data and the FDA’s specific rejection of an application for monotherapy indication; use of organized consultant meetings, advisory boards, teleconferences and purportedly independent medical education programs to promote off-label use

Prosecution Trends

- Healthcare fraud is a priority for new administration in Washington, D.C.
- Significant monetary recoveries for the government will continue
- Prosecutors are not just focusing on “Big Pharma” – smaller companies and medical device companies are at risk
- Executives and employees are at risk for prosecution, especially where the plus factor of patient harm or suppression of clinical evidence exists

Labor and Employment Perspective

Presented by:

Sarah E. Bouchard

Morgan Lewis - Philadelphia

Off-Label Promotion: Employment Law Perspective

- ❖ Off-label promotion claims in the employment context may include:
 - Internal complaint through management, compliance group, with possible Sarbanes-Oxley (SOX) complaint upon adverse action
 - Qui tam claim, a popular choice because of the federal government's role in regulating the pharmaceutical industry – and its role as purchaser of drugs *vis a vis* Medicare/Medicaid programs

Sarbanes-Oxley Complaints: Overview

- ❖ The Sarbanes-Oxley Act of 2002 (SOX) prohibits publicly traded companies from retaliating against an employee because he or she assisted an investigation relating to an alleged violation of mail fraud, wire fraud, bank fraud, or securities fraud, or a violation of SEC rules or regulations or federal laws relating to fraud against shareholders
- ❖ SOX's whistleblower litigation process is administered by the DOL's Occupational Safety & Health Administration (OSHA)
 - Complaints required to be filed in writing within 90 days of a violation
 - **Remember:** OSHA investigates the circumstances of adverse action against employee, **not** the circumstances of the ethics breach for which the whistle sounded...

Sarbanes-Oxley Complaints: Overview

- ❖ In recently published statistics, whistleblowers prevailed in only 17 out of 1,169 complaints filed since 2002

Sarbanes-Oxley Complaints							
	Cases		Complaint Determinations				
	Received	Completed	Withdrawn	Dismissed	Meritorious		Total
					Settled	Merit Findings Issued	
FY 2002	3	1	1	0	0	0	1
FY 2003	146	80	14	56	9	2	81
FY 2004	184	175	24	127	23	6	180
FY 2005	285	250	38	192	27	9	266
FY 2006	223	250	30	182	47	0	259
FY 2007	218	238	31	171	42	0	244
FY 2008*	110	72	14	47	14	0	75
Total	1169	1066	152	775	179		1106
					162	17	
*Through March 30, 2008							

Qui Tam Actions: Overview

- ❖ Provision of the False Claims Act that allows private citizens to file a lawsuit in the name of the U.S. Government charging fraud by government contractors and others who receive or use government funds, and share in any money recovered
 - Statute in place since 1863, with 1986 amendments significantly increasing incentives for private individuals, called qui tam “relators”
- ❖ Qui tam recoveries since 1986 total \$12 billion, with more than half (\$6.6 billion) in the last three years alone

Qui Tam Actions: Rights of the Relator

❖ Relator can:

- Receive 15-30% of government's recovery in a successful case
- Participate in litigation
- Be insulated from retaliation by employers
- Bring a qui tam case even when the government already knows about the fraud, except where there has been a "public disclosure" unless he/she is an "original source"

Qui Tam Actions: Procedure for Filing

- ❖ Relator files a complaint, under seal, in a U.S. district court that has jurisdiction over the case
 - Must also serve written disclosures on DOJ describing “substantially all material evidence and information the person possesses“
 - DOJ has 60 days to investigate and decide whether to intervene in the action (although extensions are liberally granted)
 - Relator is entitled to investigate and prosecute the case, should DOJ decline to intervene and prosecute the case or any individual claims
- ❖ **Key:** The target employer, typically, is unaware of the investigation!

Qui Tam Actions: Off-Label Promotion Claims

- ❖ Fraud Enforcement and Recovery Act of 2009, signed on May 20 by President Obama, is making sweeping changes to the False Claims Act.

Key changes:

- Act overturns the recent Supreme Court decision in *Alison Engine*, 128 S.Ct 2123 (2008), which held that defendant had to intend that his/her false statement (or off-label promotion) would result in the government paying a false claim. Under the new law, liability attaches if the defendant uses a false statement to get a false claim paid or approved.
- Act includes a "relation back" clause that allows the government to take an original claim, add new complaints, but still use the relator's filing date for purposes of the statute of limitations, eliminating an important pharma defense in qui tam cases.
- Whistleblower provisions expanded to include any employee, contractor or agent, effectively overruling a number of cases where certain employees of fiscal intermediaries – like auditors/investigators -- were not allowed to seek relief.

Qui Tam Actions: HHS Fraud Statistics

- ❖ Out of the 375 qui tam matters in 2008, over 60% (228) were HHS related
- ❖ HHS related fraud responsible for over 66% of DOJ's total qui tam and non-qui tam fraud recovery over the past 20 years
- ❖ Increase in enforcement in near future, as Fraud Enforcement and Recovery Act authorizes \$165,000,000 dollars to DOJ for FY 2010 and 2011 for "investigations and prosecutions and civil and administrative proceedings involving Federal assistance programs and financial institutions."

FRAUD STATISTICS - HEALTH & HUMAN SERVICES ¹							
October 1, 1986 - September 30, 2008							
Civil Division, U.S. Department of Justice							
FY	NEW MATTERS ²		SETTLEMENTS AND JUDGMENTS ³				TOTAL QUI TAM AND NON QUI TAM
	NON QUI TAM	QUI TAM	NON QUI TAM ³	QUI TAM		TOTAL QUI TAM AND NON QUI TAM	
			TOTAL	TOTAL	RELATOR SHARE ⁴		
2006	18	223	1,050,520,714	1,241,774,802	166,735,688	2,292,295,516	
2007	24	202	465,052,993	1,065,800,181	155,129,755	1,530,853,174	
2008	60	228	150,808,253	966,568,225	183,528,337	1,117,376,478	
TOTAL	627	3,306	4,187,777,862	10,116,614,364	1,629,603,471	14,304,392,226	

Employment Law Considerations

- ❖ In this economic climate, whistleblowers are a “hot” story
 - Obama Administration and Congress signaled increased attention to whistleblower issues by including protections for whistleblowers in the American Recovery and Reinvestment Act of 2009 (stimulus bill)
 - Anticipate attention from government and press
- ❖ Have procedure in place to handle whistleblower complaints
 - Critical that managers and supervisors appreciate the potential legal risks and liability
 - Critical that managers and supervisors understand the protections of privilege in order to preserve the integrity of the company’s defenses and legal positions
 - What managers do post-incident/complaint may impact that integrity



FDA Developments Concerning Off-Label Promotion

Presented by:

Kathleen M. Sanzo

Morgan Lewis – Washington, D.C.

How Big Is the Issue?

- ❖ 2006 study in Archives of Internal Medicine found:
 - In 2001, 150 million off-label mentions (21% of overall use)
 - Cardiac and anticonvulsant medicines had highest level of off-label mentions
 - Most mentions had little to no scientific support
- ❖ No evidence that practice has decreased

Recent History of FDA Regulation of Off-Label Use Information

- ❖ The Food and Drug Administration Modernization Act of 1997 (FDAMA) contains a provision that allows for dissemination of off-label information, assuming submission to FDA of supplement for use and other burdensome requirements
- ❖ FDAMA provision successfully challenged by WLF and becomes a safe-harbor from FDA enforcement, rarely if ever used by the pharma industry
- ❖ Provision sunsets in 2006

Resurrection of Off-Label Reprint Use

- ❖ November 2007 Congressman Waxman obtains a copy of internal draft of new off-label guidance and writes FDA that he is concerned that even limited distribution of this type of information puts the public at risk for “ineffective and dangerous drugs”
- ❖ February 2008 FDA releases draft Guidance on Reprints and in response to industry comments, makes some minor changes
- ❖ Notwithstanding Waxman concerns, FDA acknowledges the benefit of dissemination of off-label information by publishing Good Reprint Practices Guidance in February 2009

What Are Good Reprint Practices?

- ❖ Set of controls that FDA has identified to allow the distribution of off-label information without its use as promotion
- ❖ Not a safe harbor for other sales and marketing activities that evidence off-label promotion (e.g., dinner speeches, use of homemade bread, improper grants, etc.)

Who Gets to Give and Receive Off-Label Information?

- ❖ The givers—drug and device manufacturers (reps, MLs, others?)
- ❖ The receivers—HCPs, and healthcare entities like PBMs, MCOs, insurers, formulary committees, hospital purchasing agents, state and federal agencies

What Is a Good Reprint?

- ❖ Scientific/medical journal articles, information, reprints, reference publications (“reprints”)
- ❖ Must be on unapproved uses of approved drug products and approved and cleared devices
- ❖ Does not apply to investigational products

What Is a Good Reprint?

❖ Reprints:

- Publisher must have an editorial board that uses qualified and independent experts
- Adheres to full disclosure policy on conflicts of interest
- Peer-reviewed
- Not a manufacturer-funded supplement

What Is a Good Reprint?

❖ Reference publications:

- Should be generally available in bookstores for medical/scientific textbooks
- Not primarily distributed by the manufacturer
- Not edited or otherwise influenced by the manufacturer

What is a Good Reprint?

- ❖ Information in the reprint or journal:
 - Should address scientifically sound adequate and well-controlled clinical trials including historically controlled studies, PK/PD studies, and meta-analyses testing a specific clinical hypothesis; devices can be supported by significant nonclinical research
 - Should not be false and misleading
 - not called “definitive” if inconsistent with weight of credible evidence
 - Cannot involve a study FDA has told the company is not adequate and well-controlled
 - Should not pose a significant risk to public health, if relied upon

What's Out?

- ❖ Letters to editors
- ❖ Abstracts
- ❖ Phase 1 studies of healthy subjects
- ❖ Reference publications that do not discuss study data

What Must Be Given with the Reprint?

- ❖ Approved labeling
- ❖ Comprehensive bibliography (**Note: not sure how often to update?**)
- ❖ Articles with contrary conclusions about the off-label use
- ❖ Disclosures of:
 - Nonapproved status of indication
 - Manufacturer's interest in the drug or device

What Must Be Given with the Reprint?

❖ Disclosures:

- Any authors known to the manufacturer as having a financial interest in the product or the company or who is receiving any compensation from the manufacturer, along with the author's affiliation, and nature and amount of any compensation or financial interest
 - **(Note: how far back must the affiliation be recognized? Is this a reasonable person's standard for knowledge? How detailed must the disclosure be?)**

What Must Be Given with the Reprint?

- ❖ All significant risks known to the manufacturer concerning the unapproved use not discussed in the reprint
 - How does the company monitor what it knows about risks? Is a significant risk the same type that is reportable as an AE?
 - The requirement is not limited to risks that are publicly known

What's Off Limits?

- ❖ Annotations, summaries, excerpts
- ❖ Markings, highlighting
- ❖ Providing promotional pieces with reprints—no carriers, stickers, etc.
- ❖ Discussion of any part of the reprint by the sales reps; all questions to the Medical Affairs or comparable scientific group
- ❖ Handing out reprints at commercial booths at trade shows and conferences

Litigation Trends

Presented by:

Sandra L. Phillips

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Now, More Than Ever, Life Sciences Companies Are Battling a Very Organized Plaintiffs' Bar

- ❖ Plaintiffs' lawyers are coordinating efforts with state and federal governments in bringing civil litigation against life sciences companies arising from the same allegations of off-label promotion [e.g., product liability, consumer fraud (individual and third-party payors), ERISA, securities litigation]
- ❖ “Hydra” litigation – personal and economic injury cases are intertwined with government litigation
- ❖ The plaintiffs' bar is well organized in its assault on the Pharmaceutical/Medical Device Industry (e.g., AAJ, "Pharmaceutical Litigation Packets")

Common Causes of Action Arising from Off-Label Promotion Allegations

❖ **Negligence**

(E.g., failing to seek FDA approval of the marketed off-label use, improper labeling, promotion of an off-label use of an FDA-approved drug)

❖ **Failure to Warn**

(E.g., liability for "foreseeable misuse"/failure to warn generally arises out of actions subsequent to the manufacturer's production of the drug and can develop over time)

❖ **Fraud**

(E.g., individual, collective, third-party payors bring consumer fraud actions (common-law and state statutes); fraud based on the alleged misbranding of product improperly marketed)

❖ **FCA**

(E.g., in qui tam or "whistleblower" actions)

❖ **Securities and ERISA**

(E.g., liability for decline in stock price due to alleged off-label promotion; company executives breached fiduciary duty by inflating earnings through unlawful promotion of off-label use)

❖ **RICO**

(E.g., allege that manufacturers engaged in a pattern of racketeering activity by fraudulently promoting drug for off-label uses through interstate mail and wire communications; allege that manufacturers created a large association-in-fact enterprise consisting of numerous medical marketing firms and physicians, as well as subenterprises engaged in peer-to-peer selling of the drug and publishing ghost-written articles about its off-label uses, and smaller enterprises)

Attacks on Off-Label Promotion Claims

❖ **Learned Intermediary**

- Liability determination hinges on whether the risk of harm was foreseeable by the manufacturer or whether the off-label use is the known standard of care in the medical community

❖ **Off-label is not inherently fraudulent**

- Truthful off-label promotion is, by definition, not fraudulent (*U.S. ex rel. Hess v. Sanofi*); actions based on truthful communications also raise First Amendment concerns

❖ **Preemption**

- Applies in PMA medical device cases (*Riegel v. Medtronic, Inc.*)

❖ **No private right of action**

- The federal government has the exclusive right to enforce federal regulations governing off-label promotion (*In re: Epogen Off-Label Marketing & Sales Practices Litig.*)

❖ **No Causal Connection**

- No reliance on the alleged misstatements in off-label promotion; no injury; no fraud-on-the market

❖ **Not Suitable for Class Certification**

- Common questions will not predominate over issues affecting individual plaintiffs; no common proof

Off-Label Civil Litigation: Update & Trends

❖ Neurontin (AED)

Facts: 2004 \$430M settlement with federal government on off-label promotion claims spun massive product liability and consumer fraud litigation based in large part on off-label promotion claims

Outcome: Earlier this year, Philadelphia State and Massachusetts Federal Courts decertified class actions based on lack of common issues, predominance (e.g., lack of reliance on alleged off-label promotion)

See In re: Neurontin Mktg. Sales Practices and Prods. Liab. Litig., No. 04-10981, 2009 WL 1323835 (D. Mass. May 13, 2009); *Clark v. Pfizer*, No. 2004-1819 (Phila. Ct. Com. Pl. Feb. 9, 2009).

❖ Seroquel (atypical anti-psychotic)

Facts: Union health and welfare benefit funds alleged RICO claims that Astra Zeneca misrepresented the comparative safety of Seroquel and unlawfully marketed the product for off-label uses, leading them to pay millions of dollars to treat unapproved conditions

Outcome: In 2008, Florida federal court ruled that plaintiffs failed to allege a causal connection between the alleged fraudulent marketing scheme and their injuries (no reliance)

See Ironworkers Local Union No. 68 v. AstraZeneca Pharm. LP, 585 F. Supp. 2d 1339 (M.D. Fla. 2008).

Off-Label Civil Litigation: Update & Trends

❖ Actimmune (Biologic)

Facts: Following a settlement with DOJ regarding misbranding claims, a putative class of third-party payors and individuals alleged that the defendants engaged in fraudulent and off-label promotion of Actimmune (approved for treatment of a rare autoimmune disease) for the treatment of idiopathic pulmonary fibrosis; plaintiffs alleged RICO violations claiming consumers unnecessarily paid for drug because of off-label promotion

Outcome: Court dismissed case because plaintiffs failed to plead facts showing an ascertainable loss that was in direct relation to the alleged fraudulent activity; fraud-on-the-market theory cannot plead the necessary elements of causation; off-label marketing of an approved drug is itself not inherently fraudulent

See In re Actimmune Mktg. Litig., No. Co 08-02376, 2009 WL 1139 585 (N.D. Cal. April 28, 2009); *see also District 1199 P Health & Welfare Plan v. Janssen L.P.*, Nos. 06-3044, 07-2224, 07-2608, 07-2860, 2008 WL 5413105 (D. N.J. Dec. 23, 2008) (dismissing RICO claims involving alleged off-label marketing of Risperdal because plaintiffs did not meet requirements of concrete injury).

Off-Label Civil Litigation: Update & Trends

❖ Zyprexa (anti-psychotic)

Facts: Following government investigation into alleged off-label promotion and safety concerns, Lilly faced civil suits alleging, *inter alia*, that Lilly marketed Zyprexa as appropriate for patients who did not meet accepted diagnoses of schizophrenia or bipolar disorder, Zyprexa's only approved uses

Outcome: Lilly has settled a significant portion of product and consumer fraud litigation for more than \$1B; securities litigation dismissed on statute of limitations; in 2009 the Fifth Cir. affirmed a judgment barring claims based on learned intermediary; class certification granted to class of third-party payors claiming that the drug was overpriced due to off-label promotion, holding that plaintiffs could rely on an expert's statistical model in support of price-inflation theory; class certification denied for individuals because of conflict between overpayment and personal injury claims

See Ebel v. Eli Lilly & Co., No. 08-40170, 2009 WL 837325 (5th Cir. 2009); *In re Zyprexa Prods. Liab. Litig.*, 549 F. Supp. 2d 496 (E.D.N.Y. 2008); *In re Zyprexa Prods. Liab. Litig.*, 253 F.R.D. 69 (E.D.N.Y. 2008).

Off-Label Civil Litigation: Update & Trends

❖ Paxil (anti-depressant)

Facts: Consumers and third-party payors alleged that GSK promoted Paxil for depressed teenagers and children despite clinical trials showing the drug may be ineffective and unsafe, seeking reimbursement for the cost of the drug

Outcome: In October 2008 a federal judge approved a \$40M class action settlement with third-party payors; in 2006 GSK settled with consumers for \$63.8M

See Carpenters & Joiners Welfare Fund v. SmithKline Beecham Corp., No. CV 04-3500 MJD/SRN, 2008 WL 4435734 (D. Minn. 2008).

Off-Label Civil Litigation: Update & Trends

❖ Infuse Bone Graft

Facts: Plaintiffs alleged that Medtronic did not disclose that most of its revenue from Infuse Bone Grafts came from off-label uses, that off-label uses were causing major complications, that Medtronic adopted unlawful marketing practices to promote its use, and that these practices resulted in artificial inflation of the stock; also alleged that Medtronic illegally promoted the product by paying physicians to endorse and teach off-label uses for the product

Outcome: In May 2009 a federal court threw out a putative ERISA class action alleging that Medtronic and its executives breached their fiduciary duties because the named class representative lacked standing (he sold his shares during the price inflation period)

See Brown v. Medtronic, Inc., No. 08-4904 (RHK/AJB), 2009 WL 1458259 (D. Minn. 2009).

❖ Serostim (AIDS)

Facts: Plaintiffs alleged that Serono promoted the use of a medical device that was not approved by the FDA and improperly diagnosed people as having AIDS wasting; provided doctors with travel stipends if they would prescribe Serostim; marketed the drug for unapproved uses

Outcome: In February 2007 the company settled a class action lawsuit with plaintiffs, including a nationwide coalition of health advocacy groups, for \$24M



Best Practices to Manage the Risks of Off-Label Activities

Best Practices to Manage the Risks of Off-Label Activities

- ❖ Adequately train sales reps and managers as to what is off-label promotion and how to avoid promoting off-label; test effectiveness of materials and training
- ❖ For device reps, make sure they understand how to provide technical assistance and support without promoting off-label uses; consider policies for the OR and clinics
- ❖ Compensate reps and managers in a way that does not incentivize off-label sales; monitor sales levels, review business and strategic plans

Best Practices to Manage the Risks of Off-Label Activities

- ❖ Audit sales reps and managers frequently and creatively to determine compliance
- ❖ Review CME grants to ensure properly independent and not a tool for off-label promotion
- ❖ Ensure internal communications are consistent with approved promotion

Best Practices to Manage the Risks of Off-Label Activities

- ❖ Fully follow FDA Good Reprint Practices—being partially compliant likely will create significant exposure
- ❖ Ensure the company has adequate controls and infrastructure to manage off-label reprints
 - Company resources to oversee publication requirements, disclosure requirements
 - Mechanism to assess whether the benefits from off-label reprints outweigh the risks resulting from the required disclosures
 - Auditing to ensure compliance with controls

Best Practices to Mitigate Civil Litigation

- ❖ Marketing material should not be viewed as a permissible way to communicate an otherwise impermissible message to physicians and the market
- ❖ Efforts should be made to avoid the appearance that “scientific publications” are serving as vehicles for marketing messages
- ❖ In the medical device context, balance the risk of providing technical support to physicians on off-label uses with the risk of not providing technical support.

See Davenport v. Medtronic, Inc., 302 F. Supp. 2d 419 (E.D. Pa. 2004) (holding that manufacturer's knowing participation in implant procedure for off-label use was permissible).

– CLE –

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Life Sciences Summer Series: Drug and Device Off-Label Promotion

Q&A

Thank You