

Regulation of Sales and Marketing Activities

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Issues for Discussion

- Fraud & Abuse Issues
 - ▶ Anti-kickback Statute
 - ▶ False Claims Act
- FDA Advertising & Promotion standards
 - ▶ Off-Label Promotion
- Support for Independent Medical Education
- State Law Compliance
 - ▶ Reporting Gifts/Payments to HCPs
 - ▶ Other reporting requirements
 - ▶ Compliance Program/Code mandates

Other Issues to Consider (not discussed here)

- Government price reporting (Best Price, AMP)
- Sample Accountability (PDMA)
- Drug Safety Monitoring and Product Liability
- Patient Privacy - sponsored communications
- DTC Advertising and other special advertising considerations (e.g., reminder ads)

Fraud & Abuse Laws affecting Pharmaceutical Industry

- Refers to laws designed to:
 - ▶ protect govt healthcare programs against excess costs due to overutilization and/or fraud, and
 - ▶ prevent distortion of healthcare decisions due to financial incentives
- Primary Fraud & Abuse laws:
 - ▶ Anti-kickback Statute
 - ▶ False Claims Act

Anti-Kickback Statute 42 U.S.C. §1320a-7b(b)

- Makes it a felony to provide or seek something of value as an inducement to select a product paid for by a federal healthcare program
- Violations of the statute may lead to both criminal and civil penalties
- Very actively enforced (by HHS OIG) against the pharmaceutical industry in recent years
- Law and HHS regulations provide for several “safe harbors” relating to financial arrangements with referral sources or prescribers

False Claims Act 31 U.S.C. §3729

- Provides for treble damages and civil penalties of up to \$10,000 per claim for any person who knowingly presents *or causes to be presented* a false or fraudulent claim for payment to the federal government
- Under the *qui tam* (whistleblower) provisions of the statute, private citizens may bring an action under the FCA and collect up to 30% of any resulting recovery
- FCA, under a variety of theories, has been the primary basis for most of the largest F & A recoveries from pharma companies

Major Fraud & Abuse Cases in Pharma Industry

- 2001 - TAP Pharmaceuticals (\$875 million)
- 2002 – [PhRMA Code adopted]
- 2003 - AstraZeneca (\$355 million)
- 2003 - Bayer (\$257 million)
- 2004 - Neurontin - Pfizer/P-D (\$430 million)
- 2004 - Schering-Plough II (\$345 million)
- 2005 - Serono (\$705 million)
- 2007 – Schering-Plough III (\$435 million)
- Small companies, too: InterMune, Jazz, CTI, Medicis
- **Many** pending investigations

TAP Case (2001)

- **\$875 million** in criminal and civil fines
- Criminal indictments of managers, sales personnel, and physicians
- Allegations included use of samples to enrich prescribers, marketing the “spread,” free trips, and improper grants
- Government found evidence of a “culture” that condoned improper inducements

PhRMA Code on Interactions with HCPs

- Adopted by PhRMA in 2002 in response to negative publicity and enforcement activity re industry sales tactics
- Focused mainly on activities presenting anti-kickback risks (gifts, entertainment, consulting)
- Primary prohibitions:
 - ▶ Gifts with value >\$100 or unrelated to practice
 - ▶ Entertainment of any kind
 - ▶ Business meals without an educational activity
 - ▶ Spouse attendance at meetings/programs
 - ▶ Program at an inappropriate venue
 - ▶ Any kind of “quid pro quo” arrangement

HHS OIG Compliance Program Guidance for Pharma Companies

- Issued in 2003 to identify compliance issues on which pharma companies should focus
- One in a series of compliance guidances for sectors of the healthcare industry – advice re compliance program structure is similar
- Specific risk areas identified for pharma co’s:
 - ▶ Integrity of data used for gov’t reimbursement
 - ▶ Kickbacks and other illegal remuneration
 - Arrangements with purchasers
 - Relationships with physicians and other HCPs
 - ▶ Arrangements with sales agents
 - ▶ Drug samples

OIG Compliance Guidance Specific “Advice”

- Any price reporting that drives gov’t reimbursement or purchasing cost must be complete and accurate
- Discount arrangements with purchasers should be structured to meet a safe harbor if possible
- Educational and research grant making should be separate from sales and marketing function
- Service arrangements with HCPs should be structured to meet safe harbor standards
- Relationships with sales agents should not be structured in a way that may encourage misconduct
- Adhere strictly to PDMA when providing samples

Promotional Communications

- “Promotion” is not defined in FDA regs - essentially means communications that are intended to encourage selection or utilization of a product – context is important
- FDA regulates all promotional communications as “labeling” – any product-specific communications that “accompany” the product
- Examples: Details aids, brochures, presentations, journal reprints
- Advertisements are a special type of labeling, with special rules (21 CFR §202.1)

Non-promotional Communications

- Scientific Interchange
 - ▶ Presentations at Scientific/Medical Meetings
 - ▶ Medical information in response to unsolicited request
 - ▶ Publication of data in peer-reviewed journals
- Independent (of industry) medical education
- Investor Communications
 - ▶ Communications clearly intended solely/primarily for investors, based on context and content
- Private communications with contracted consultants or advisors
- Communications relating to clinical research

Support for CME Activities

- Industry support for continuing medical education (CME) programs continues to receive scrutiny – see Senate Finance Committee report April 2007
- Independent medical education should be just that - **independent**
- Follow ACCME Standards for Commercial Support and FDA Guidance (ISSEA)
 - ▶ Education provider controls all program details – by written agreement and in fact
 - ▶ Ensure education provider performs due diligence and addresses/discloses conflicts of interest

FDA Standards for Advertising & Promotion

- All promotional claims must be:
 - ▶ consistent with the FDA-approved label (PI)
 - ▶ based in fact and/or supported by substantial evidence
 - ▶ accurate and balanced – not false or misleading
- Claims may be made that are not expressly included in PI, as long as they meet the above standards
- “Claims” are the messages that are stated or implied by the promotional piece – not just the literal text
- All promotional materials must be submitted to FDA at time of first use

“False or Misleading”

- See 21 CFR 202.1(e)(6) & (7) for “laundry list” of false or misleading communications (33 examples)
- Statements that are true on their face can still be false or misleading
- Depends on whether the statement tells the full story – contextual information may be critical (e.g., placebo rate, study population, study design)
- Images or graphics can convey a misleading impression, even if the words of the piece do not (e.g., image of arthritis patient with perfectly normal joints)

Fair Balance

- All promotional materials must include “fair balance” – a balanced emphasis of safety/risk information relative to efficacy/benefit claims
- Fair balance is more than a safety statement at the end of a piece – required safety info (content and placement) depends on the specific benefit claims or statements made in the piece
- Minimizing or failing to disclose risk information is the most frequent subject of FDA enforcement action

Comparative Claims

- Comparative claims (those claiming superior efficacy or safety) are generally not favored by FDA, and must be substantiated
- Typical standard is two adequate and well-controlled head-to-head studies (limited comparisons based on inherent qualities)
- Comparisons may not be based on data from separate studies or from inadequately designed head-to-head studies
- This is the second most frequent subject of FDA enforcement action

Off-Label Promotion

- FDA rules prohibit a manufacturer from promoting a product for indications beyond those contained in the approved PI
- “Promotion” here means claiming in a promotional context that the product is safe and/or effective for the investigational use, or encouraging the prescriber to use the product in a manner not consistent with the PI (21 CFR §312.7)
- Promotion of a drug for an unapproved use causes the drug to be “misbranded”

Off-Label Promotion

- A company (through its Medical function) may engage in scientific dialogue with physicians – “safe harbor” for response to unsolicited questions (1994 FDA guidance)
- Resolution of WLF cases left the standards for dissemination of off-label information unclear – any dissemination may be used as evidence in FDA enforcement action
- Physicians are free to prescribe drugs for any use they deem medically appropriate (FDA does not regulate the practice of medicine)

Neurontin Background

- The Neurontin case is the “biggie” in off-label promotion – signaled a major enforcement focus in this area
- Sales of Neurontin grew from \$97.5 million in 1995 to \$2.9 billion in 2003 – majority of use was off-label
- DOJ alleged that Warner-Lambert aggressively marketed Neurontin for a variety of off-label uses

Neurontin Settlement

- Warner-Lambert (now owned by Pfizer) agreed in May, 2004 to plead guilty to criminal violations and pay \$430 million to settle fraud allegations
- Guilty plea related to two violations of the FD&C Act:
 - ▶ Misbranding (failure to provide adequate instructions for use)
 - ▶ Introducing an unapproved new drug in commerce
- Criminal fine was \$240 million (second largest ever in a healthcare fraud case)

Government Allegations

- Activities by Warner-Lambert constituted off-label promotion in violation of FD&C Act
- Warner-Lambert violated the anti-kickback statute by providing financial inducements to physicians
- Claims (submitted by pharmacies) for gov't payment for prescriptions "tainted" by kickbacks and off-label marketing violated the False Claims Act

Learning from Enforcement Actions Mistakes to be Avoided

- Consulting meetings with more attendees than needed, and more talking than listening
- Excessive involvement in details of independent medical education, or undisclosed relationships with CME providers
- Making off-label use happen, as opposed to letting it happen as appropriate
- Use of educational grants as a sales tool
- Sham service arrangements and/or compensation in excess of FMV
- Any financial arrangement involving a perceived "quid pro quo" relating to product use

Enforcement Trends

- *Qui tam* cases under the FCA (federal and state)
 - many cases pending, and no end in sight
- New “creative” theories of liability under the FCA
 - drug safety issues, off-label or misleading promotion “causing” false claims
- Off-label promotion continues to be a major focus
- Watch for developments from NY Medicaid Fraud enforcement team
- Legislative focus on CME support and disclosure of financial relationships with HCPs

State Laws Focused on Pharma Companies

- State law compliance is becoming an increasing burden for pharma/biotech companies
- Types of state laws that have been enacted:
 - ▶ All-payor anti-kickback laws (Several)
 - ▶ Pricing/discount disclosure requirements (VT)
 - ▶ Promotional expenditure reporting (ME, WV, DC)
 - ▶ HCP gift limits and/or reporting (MN, CA, ME, etc.)
 - ▶ Clinical trial data disclosure requirements (ME)
 - ▶ Mandatory compliance program/code laws (CA, NV)

Disclaimer

These slides and accompanying discussion provide a general overview of selected legal and regulatory issues. They are not intended to be, and should not be relied upon, as legal advice.

The views expressed herein are those of the author and not those of ZymoGenetics or the author's boss or colleagues.

References/Resources

- HHS OIG Compliance Program Guidance for Pharmaceutical Manufacturers
(<http://oig.hhs.gov/authorities/docs/03/050503FRCPGPharmac.pdf>)
- PhRMA Code on Interactions with Healthcare Professionals
(<http://www.phrma.org/files/PhRMA%20Code.pdf>)
- DDMAC (FDA) Enforcement Letters
(<http://www.fda.gov/cder/warn/index.htm>)
- FDA Guidance – Industry-Supported CME
(<http://www.fda.gov/cder/guidance/isse.pdf>)
- ACCME Standards for Commercial Support
(<http://www.accme.org>)