



Off-label Marketing of Prescription Drugs and Devices, the False Claims Act and the Impact of Medicare Part D

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OUTLINE

- **OIG and Industry Guidance**
- **Fraud and Abuse Enforcement Activity**
- **Medicare Part D**

OIG Compliance

➤ Compliance Guidance

- The OIG has solicited comments on and has finalized a series of 11 compliance guidance documents each applicable to a different component of the health care delivery system. These guidance offer valuable assistance and provide the OIG's insight. Examples:
 - Pharmaceutical Manufacturers (2003)
 - Physicians (2000)
 - Hospitals (1998) – due to be reissued in updated form soon
- Compliance guidance being developed for researchers

OIG Guidance for Pharmaceutical Manufacturers

- In April 2003, the OIG issued its final Compliance Program Guidance for Pharmaceutical Manufacturers (the “Pharma Guidance”). While the Pharma Guidance is for pharmaceutical manufacturers, and is intended to assist them with their compliance activities, it provides valuable insight for any provider.
- Purchasers, benefit managers, formulary committee members, and GPOs (among others) are persons or entities in a position to generate Federal health care business.

OIG Guidance for Pharmaceutical Manufacturers (*cont.*)

- Data collection service agreements, as well as other agreements, between pharmaceutical manufacturers and purchasers should be structured, whenever possible, to fit within the personal services safe harbor; Pharma Guidance notes that any remuneration from a pharmaceutical manufacturer to a purchaser could implicate the kickback provisions and should be carefully reviewed.

OIG Guidance for Pharmaceutical Manufacturers (*cont.*)

- Rebates or payments that are based on, or otherwise related to, customers' purchases could implicate the kickback provisions.
- Pharmaceutical manufacturers may provide funding for communications with physicians and patients and notes that, while these communications indirectly benefit the manufacturer, “the primary economic beneficiary is typically the formulary sponsor.”

OIG Guidance for Pharmaceutical Manufacturers (*cont.*)

- Educational grants and research funding could raise issues under the kickback provisions if they are conditioned in whole or in part on the “purchase of product” even if the purpose of the program is legitimate.
- “Grant making functions” should be separated from “sales and marketing functions.” To the extent the manufacturer has any influence over the substance of an educational program or a presenter, there is a risk it will be used for inappropriate marketing purposes.

FDA Guidance on Industry-Supported Scientific and Educational Activities

- Issued in 1997
- Programs performed by, or on behalf of, companies that market pharmaceuticals are subject to FDA's requirements on advertising and labeling
- FDA does not regulate independent and non-promotional industry-supported activities
- Determination of independence includes:
 - Control of content
 - Inclusion of promotional material
 - Single-product marketing vs treatment options
 - Source of invitation lists

PhRMA Code on Interactions with Healthcare Professionals

The Main Points of the Code are:

- **General Interaction**: Interaction should focus on informing the professional about scientific and educational information and supporting scientific medical research and education to maximize patient benefits.
- **Entertainment**: Interaction should not include entertainment. Interaction should occur at a venue conducive to providing scientific or educational information. Specifically, this means no “dine and dash,” no entertainment, and no recreational events (e.g., sporting events or spa visits).

PhRMA Code on Interactions with Healthcare Professionals (*cont.*)

- **Continuing Education**: Companies can provide support to the conference sponsor but should not fund individual participants. Sponsor may in turn provide grants to individuals to participate, or to reduce the overall registration fees for all attendees.

PhRMA Code on Interactions with Healthcare Professionals (*cont.*)

- **Consultants:** Legitimate consulting or advisory arrangements are appropriate if retention of professionals are based on their expertise and retention is made for no more than needed for the specific program. However, token consulting arrangements should not be used to justify payments to professionals.
- **Educational and Healthcare Practice-Related Items:** Educational and practice-related items may be provided to professionals, but should be for the health care benefit of patients and of less than substantial value (\$100 or less). Items for the personal benefit of the professional should not be offered or distributed.
- **The Code became effective on July 2002.**

AdvaMed Code of Ethics for Interactions with Health Care Professionals

Key points:

- Defines “Health Care Professionals” as:
 - *“...individuals or entities that purchase, lease, recommend, use, arrange for purchase or lease of, or prescribe Members’ medical technology products in the United States”*
- **Member-Sponsored Product Training and Education** – Must be held in settings conducive to education and training; moderate/low value meals and receptions; no other entertainment for HCP attendees; reasonable travel and lodging for HCP attendees; cannot pay for guests of HCPs or others without *bona fide* professional interest in the meeting.

AdvaMed Code of Ethics for Interactions with Health Care Professionals (*cont.*)

- **Supporting Third Party Educational Conferences** – Members may provide funds to conference sponsor to reduce costs or allow HCPs-in-training to attend **if** meeting promotes scientific, educational or policy activities, **and** training institution or conference sponsors selects attendees. Such funds may be provided for modest meal and hospitality of HCP attendees, HCP *bona fide* faculty expenses, advertisements and booth space.
- **Sales and Promotional Meetings** – Meetings with HCPs on product features, contract negotiations, sales terms; occasional/infrequent meals and receptions for HCP attendees; reasonable travel costs for HCP attendees; not appropriate to pay for meals or other hospitality for guests of HCPs.

AdvaMed Code of Ethics for Interactions with Health Care Professionals (*cont.*)

- **Arrangements with Consultants** – Members may pay for reasonable compensation for services, and reasonable/actual expenses incurred;
 - *Bona fide* consulting arrangements are:
 - In writing, with services specified, and must be signed;
 - Compensation is consistent with fair market value;
 - Legitimate purpose and need for services identified in advance;
 - Selection based on consultant's qualifications and expertise;
 - Venues of meetings are modest;
 - Written protocol for research services

AdvaMed Code of Ethics for Interactions with Health Care Professionals (*cont.*)

- **Gifts** – Modest, occasional gifts allowed if gift benefits patients or serves genuine education function **and** gift has fair market value of less than \$100 (exceptions: text books and anatomical models). May occasionally provide branded promotional items of minimal value; no cash or cash equivalents; legitimate practice of providing samples and product evaluations.
- **Grants and Charitable Donations** – Members may make donations for charitable purpose if made to charitable organization in support of: independent medical research, indigent care, patient education and public education, sponsorship of events where proceeds are charitable; all donations must be documented.
- AdvaMed Code became effective January 2004.

AMA Guidelines

- Ethical Opinion and Guidelines Related to CME
- AMA Cautions Physicians to:
 - Assess educational value of the program and attend program on that basis
 - Choose programs offered by accredited sponsors
 - Don't accept direct subsidies (vs. through sponsor) to attend program or for travel
- Became effective June 2002

OUTLINE

- **OIG and Industry Guidance**
- **Fraud and Abuse Enforcement Activity**
- **Medicare Part D**

Allegations Involving Pharmaceutical Manufacturers/Benefit Managers

- Price concessions, including volume discounts, prompt pay discounts, cash discounts, rebates, up-front payments, short-dated product discounts, and nominally priced or free products
- Educational, clinical, research or unrestricted grants or sponsorships
- Sponsorship of speaking engagements, honoraria, meetings, symposia, case study programs, exhibits and other similar events
- Paid consultancies, advisory boards or research panels

Allegations Involving Pharmaceutical Manufacturers/PBMs (*cont.*)

- Inducements structured to avoid new best price of drugs
- Free or low-cost continuing medical education programs or tuition payments
- Gifts, luxury trips, parties, and entertainment
- Free or low cost practice-support services, such as reimbursement guarantees, audit, accounting, third-party payor, billing assistance services
- Compensation for detailing, time and travel, marketing, switching, or converting from a competitor's product

Allegations Involving Pharmaceutical Manufacturers/PBMs (*cont.*)

- Items to gain access to physician's offices, such as meals and refreshments (often called "access tools") and preceptors
- Free medical and office equipment, including computers
- Charitable contributions
- Marketing of off-label uses
- Ghost-written papers
- Professional courtesies or debt forgiveness
- Equity in new enterprises or in new products

Allegations Involving Pharmaceutical Manufacturers/PBMs (*cont.*)

- Educational grants
- Free or heavily underwritten disease management programs
- Payment for switching
- Various forms of inducements related to formulary status

Pfizer/Parke-Davis/Warner Lambert

United States ex rel. Franklin v. Parke-Davis, 147 F.Supp.2d 39
(D.Mass 2001) (Attached) – allegations:

- “Medical liaisons” employed by sales division of predecessor Warner Lambert
 - misrepresented credentials
 - made off-label claims related to indications and dosing
- Physicians coached to hide off-label nature of prescription
- Sham clinical studies with no scientific value
- Payments for consultants, preceptors, speakers bureau, access to patient records, gifts (Olympic tickets)

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

United States ex rel. Franklin v. Parke-Davis (cont.)

- Decision on 9(b) motion to dismiss by Parke-Davis for failure to plead fraud with particularity
- Neurontin– has many recognized off-label uses (pain, epilepsy) – 50% of sales
- Accupril – approved for hypertension
- Note: Amended Complaint subsequently filed, and unsealed in April 2002

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

United States ex rel. Franklin v. Parke-Davis (cont.)

Court found that scheme to promote off-label uses is actionable under the False Claims Act (“FCA”)

- Company concedes that off-label prescriptions are not reimbursable by Medicaid
- Complaint sufficiently alleges “a fraudulent marketing campaign in which kickbacks and unlawful and misleading marketing were allegedly used to encourage doctors to **increase their use** of Neurontin for unapproved purposes.” (Emphasis added)
- Material misrepresentation to obtain a benefit – false statements regarding these drugs and use of kickbacks

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

United States ex rel. Franklin v. Parke-Davis (cont.)

- Theory that kickback violation is actionable under FCA requires a showing that Parke-Davis caused or induced doctors and/or pharmacists to file a false or fraudulent certification regarding compliance with the Anti-Kickback Statute
- Court rejects allegation under FCA that Parke-Davis engaged physicians to perform clinical trials where drugs were charged in violation of § 312.7
 - Regulatory violation not actionable under the FCA
 - No allegation that Parke-Davis caused the submission of false claims

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

- Pfizer/Warner Lambert Settlement (2004)
 - Resolution: \$430 million to settle federal criminal and civil cases as well as state civil cases
 - Criminal plea by Warner Lambert for two counts of distribution for unapproved uses (off-label) & misbranding (Attached)
 - \$240,000,000 criminal fine
 - \$190,000,000 (plus interest) civil fine to federal and state governments
 - Whistleblower was a Ph.D. microbiologist employed as Parke-Davis medical liaison -- \$26.4 million, plus attorneys fees.

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

- As part of this settlement, Pfizer agreed to an updated CIA (May 2004) available on the OIG's website at:

www.oig.hhs.gov/fraud/cia/index.html

- Specific requirements related to off-label promotion
 - Policies and Procedures
 - Specific Training
 - Independent Review Organization specific engagement for “Promotional and Product Services Systems Review” (Attachment C).
 - “Promotional and Product Services Transactional Review” by IRO (Attachment D)

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Parke-Davis/Warner Lambert/Pfizer (cont.)

➤ Warner Lambert Sentencing Memorandum (June 2, 2004)
(Attached)

- 53 pages
- Inadequate directions for use
- Distribution for unapproved use
- Misbranding/false or misleading labeling or advertising
- Encouraging off-label prescribing

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.)

“Medical Liaisons, this is [the northeast Associate Medical Director]. I am calling in regard to the-- you know, there’s a Neurontin push that’s supposed to be on. ...So, what we need to do is focus on Neurontin. When we get out there, we want to kick some ass on Neurontin, we want to sell Neurontin on pain.

All right? And monotherapy and everything that we can talk about, that’s what we want to do. ‘Cause I’m embarrassed. I don’t know if you guys are embarrassed. But I’m embarrassed about where we are with Neurontin. We’ve got to take it into our own hands and really kick some ass on it, all right? Let’s do it up.” *At 11*

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.)

“...off-label uses grew from approximately 15% of all uses in 1994, the first year Neurontin was marketed, to 94% in 2002.” *At 13*

“...the 1997 Neurontin Strategic Plan references ‘increase in emerging uses’ as both an issue and an opportunity. ... ‘Primary marketing objectives for Neurontin in 1997 will be to grow the use of the brand of epilepsy indications and to maximize Neurontin opportunities in emerging applications’ (emphasis supplied).” *At 15*

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.)

“...Parke-Davis’ management considered whether it should seek FDA approval [but decided not to seek such approval] of additional uses for Neurontin beyond adjunctive anti-seizure treatment. These uses included such areas as pain, pediatric use, psychological disorders, ALS (amyotrophic lateral sclerosis or Lou Gehrig’s disease) and, especially, monotherapy for epilepsy. Among the factors considered were the potential market value of the use both with and without FDA approval, the likelihood of obtaining FDA approval, the short patent life of Neurontin and the impact of broader Neurontin indications on a new drug being developed.” *At 17*

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.)

“Parke-Davis promoted Neurontin for a variety of pain types, including painful diabetic neuropathy, post-herpetic neuropathy, reflex sympathetic dystrophy and migraine headaches, among others.” *At 20*

“Parke-Davis also promoted Neurontin for a variety of psychiatric conditions, including bipolar disorder, anxiety, social phobia and general mood stabilization...” *At 22*

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.)

“All claims by Parke-Davis as to the *effectiveness* of Neurontin at doses above 1800 mg./day were off-label and constituted misbranding under the FD&C Act. The evidence shows that Parke-Davis made such claims as part of a concerted effort to get doctors to increase the level of Neurontin prescribed, even as the company unsuccessfully sought approval for a higher dose.” *At 25*

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.)

“Among the key tactics Parke-Davis set out in its planning documents and which it used to achieve its goal of increasing off-label use of Neurontin were the following:

- “(1) Encouraging sales representatives to provide one-on-one sales pitches (‘details’) to physicians about off-label uses of Neurontin;**
- “(2) Utilizing medical liaisons, who represented themselves, often falsely, as neutral scientific experts in the area of a particular drug, to promote off-label uses for Neurontin, working in tandem with the sales representatives to directly sell Neurontin to physicians for off-label uses;**

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.) *(cont.)*

- “(3) Paying physicians to allow a sales representative to see patients with the doctor and to participate in discussing the treatment plan;
- “(4) Paying physicians, through both direct payments, and the provision of trips, hotel rooms, dinners and other benefits, to attend a variety of meetings termed ‘consultant’ or ‘advisory’ meetings or ‘speaker bureau trainings’ in which doctors received presentations about off-label uses of Neurontin;

Pfizer/Parke-Davis/Warner Lambert (*cont.*)

Warner Lambert Sentencing Memorandum (cont.) (cont.)

- “(5) Implementing frequent teleconferences in which doctors were paid by Parke-Davis to speak about Neurontin on off-label topics to other doctors; and**
- “(6) Sponsoring ostensibly independent ‘medical education’ events on off-label Neurontin uses where there was actually extensive input from Parke-Davis regarding topics, speakers, content, and participants.” *At 26-27***

Intermune, Inc. Settlement

October 26, 2006 settlement N.D. Cal.

- Criminal Information
- Deferred Prosecution Agreement
- \$36.9 million civil settlement
- Five year Corporate Integrity Agreement

Intermune, Inc. *cont.*

- Uncontested facts -- Deferred Prosecution Agreement
 - Actimune (interferon drug) approved for severe malignant osteopetrosis and one other condition
 - Vast majority of sales were for ideopathic pulmonary fibrosis (IPF)
 - Company conducted a phase III clinical trial for IPF indication, but results were not statistically significant.
 - Results presented to FDA → FDA needed more work
 - Company went ahead and marketed Actimune for IPF making claims using statistical comparisons

Intermune, Inc. *cont.*

Obligations under Deferred Prosecution Agreement

- Past cooperation, including
 - disclosed results of internal investigation and
 - made employees available, etc.
- Compliance changes instituted prior to investigation
- Full cooperation for two years
 - Disclosure of information
 - Documents
 - Reasonable access to facilities and employees
- Not make statements contradicting stipulated facts

Intermune, Inc. *cont.*

- In civil settlement, government alleges that the use of Actimmune for IPF was not a “medically accepted indication”
- CIA provisions of interest related to off-label
 - Policies and procedures
 - Specific training
 - IRO Promotional and Product Services Engagement

OUTLINE

- **OIG and Industry Guidance**
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- **Medicare Part D**

Medicare Part D

Regulatory Authority and Guidance

- Section 1860D-2(e)(1) of the Social Security Act defines a Part D covered drug as:
 - A drug that may be dispensed only upon a prescription and that is
 - Approved for safety and effectiveness as a prescription drug under the Federal Food, Drug, and Cosmetic Act
 - Commercially used or sold in the United States ...or which is identical, similar, or related to such a drug, and which has not been the subject of a final determination that it is a “new drug”
 - Described in section 107(c)(3) of the Drug Amendments of 1962 and for which there is a compelling justification for its medical need, and for which it has not been determined that the drug is less than effective for some or all conditions of use prescribed, recommended, or suggested in its labeling

Medicare Part D (*cont.*)

OR

- A biological product ...or insulin ... and medical supplies associated with the injection of insulin (as defined in regulations of the Secretary), and such term includes a vaccine licensed under section 351 of the Public Health Service Act and any use of a covered part D drug for a medically accepted indication (as defined in section 1927(k)(6)).

Medicare Part D (*cont.*)

- 42 C.F.R. § 423.100: Covered Part D drug means a Part D drug that is included in a Part D plan's formulary as a result of a coverage determination or appeal and obtained in a network pharmacy.
- The Preamble to 42 C.F.R. § 423 declares:

“We recognize the value of off label prescribing, particularly with regard to certain medical conditions...physicians and other prescribers [are not precluded] from prescribing drugs for off label indications, provided the drug is prescribed for a “medically accepted indication” as defined in section 1927(k)(6) of the Act.”

Medicare Part D (*cont.*)

➤ Medically Accepted Indication:

“Any use for a covered outpatient drug which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included or approved for inclusion in any of the [following] compendia: [(a) American Hospital Formulary Service Drug Information, (b) United States Pharmacopeia-Drug Information; or (c) the DRUGDEX Information System.”

Medicare Part D (*cont.*)

AHFS's website (<http://www.ashp.org/ahfs/print/ahfs-di.cfm>) describes the Drug Information book as follows:

“[Contains information from medical literature and expert advice from over 500 medical scientists, physicians, pharmacists, pharmacologists, and other professionally qualified individuals that goes beyond FDA-approved labeling.

“Inside find:

- Expert advice and peer reviewed by over 500 medical scientists, physicians, pharmacists, pharmacologists, and other professionally qualified individuals
- Over 40,000 represented medicines and over 100,000 drug products
- Off-label and labeled uses”

Medicare Part D (*cont.*)

- There are a substantial number of other authorities to support additional clinical indications that do not make it into any of the three approved sources. These include:
 - Peer review articles in medical journals
 - Clinical trial data
- These sources do not qualify as medically accepted indications
- There is no realistic way to monitor such off-label prescribing.

Medicare Part D (*cont.*)

- The Preamble to 42 C.F.R. § 423 states:
 - “Plans have the flexibility to decide how to monitor whether a drug is prescribed for a medically accepted indication, as well as to determine whether the statutory definition of “medically accepted indication” is met with regard to the particular use of a drug.”
- If a Part D plan makes an adverse coverage decision, a beneficiary may appeal

Medicare Part D (*cont.*)

➤ 42 C.F.R. § 423.505(h)(1):

The Part D plan sponsor agrees to comply with Federal laws and regulations designed to prevent fraud, waste, and abuse, including, but not limited to applicable provisions of Federal criminal law, the False Claims Act (32 U.S.C. §§ 3729 et seq.), and the anti-kickback statute (section 1128B(b) of the Act).

Medicare Part D (*cont.*)

- **Chapter 9: Part D Program to Control Fraud, Waste and Abuse**
 - Section 70 provides examples of potential schemes, risks, and vulnerabilities to the Part D benefit. Given that Sponsors maintain ultimate responsibility for delivery of the benefit, Sponsors are encouraged to develop their program to control fraud, waste and abuse to address identified risks.

Medicare Part D (*cont.*)

- **Chapter 9: Part D Program to Control Fraud, Waste and Abuse**
 - Section 70.1.6: Examples of Pharmaceutical Manufacturer Fraud, Waste and Abuse:
 - Kickbacks, inducements, and other illegal remuneration, including inappropriate marketing and/or promotion of products.
 - Illegal off-label promotion: Illegal promotion of off-label drug usage through marketing, financial incentives, or other promotional campaigns.

Medicare Part D (*cont.*)

- Prescription drugs prescribed for off-label indications may be covered Part D drugs, provided the drug is prescribed for a “medically accepted indication”
- Guidance on off-label promotion in Part D is sparse
- Government will rely on Part D plan sponsors to monitor for indications of off-label promotion
- Medicare Drug Integrity Contractors (MEDICs) will also monitor for indications of off-label promotion
 - Indications of off-label promotion would initiate an immediate referral to the Office of the Inspector General

Look for additional guidance in the future as schemes are identified (either in Part D or in other programs)



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