

# Rx COMPLIANCE REPORT

EXCLUSIVELY DEVOTED TO PHARMACEUTICAL  
SALES AND MARKETING COMPLIANCE

## Lead prosecutor in Pfizer's \$2.3 billion settlement says off-label promotion issues are becoming "broader and more complex"

*Key risk areas include drug samples, social media, and publication strategies*

The off-label promotion enforcement landscape confronting pharmaceutical companies is becoming broader and more complex, according to Assistant U.S. Attorney **Sara Bloom**, the lead federal prosecutor in Pfizer's landmark \$2.3 billion off-label case. Several years ago, says Bloom, she expected to finish up the off-label cases currently in her office before the issue largely went away. "I am, unfortunately, less sanguine now," she told attendees at FDLI's Advertising & Marketing conference last week in Washington, D.C. "particularly because I understand it better than I did when we were just doing the Neurontin case."

According to Bloom, the Neurontin case offered a degree of clarity, because, in that instance, Pfizer had allegedly promoted the drug for pain and other uses when it only had a narrowly approved indication for epilepsy. "What we have seen as the cases have developed is that the issues of off-label are broader and more complex than that," says Bloom. "There are all sorts of ways of going off-label apart from simply asking for a diagnosis that is clearly off-label."

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## FDA announces public hearing on social media

*Experts applaud "long overdue" effort by FDA*

Last week, the FDA announced plans to hold a two-day public hearing in November to discuss the promotion of drugs and devices using the Internet and social media. While the announcement caught many by surprise, all sides view it as long overdue. The agency has not addressed the issue since its public meeting on Internet promotion in October 1996. Since that time, as the agency notes, there has been a "massive explosion" of new tools and technologies.

"This is a huge step in the right direction," says former FDA attorney **Meredith Manning**. "The industry really needs guidance on what it can and cannot do." But the challenge facing the FDA, she says, is to create a regulatory framework that is flexible enough to be "a living document" as the Internet and social media tools undergo changes. In short, she says, the next ten years will likely see as many changes in technology as the last ten years. ► *Cont. on page 7*

► *Cont. from page 1*

## **Lead prosecutor in Pfizer's \$2.3 billion settlement says off-label issues are becoming "broader and more complex"**

The off-label issues present in Bextra case, which represented \$1.8 billion of the \$2.3 billion settlement that covered no fewer than nine different drugs, are more nuanced than those present in the Neurontin case, says Bloom. For example, she says, one of the allegations in the Bextra case revolved around promotion for acute pain when the drug was only approved for chronic arthritis pain (*see p. 4 for an excerpt of the Bextra complaint addressing this allegation*).

Another example of the more nuanced nature of the off-label cases now emerging, as evidenced by the Bextra case, is promoting a larger dosage for a particular use when only a smaller dose is approved by the FDA (*see p. 5 for an excerpt of the Bextra complaint addressing this allegation*).

Bloom also cites superiority claims – or comparative claims with a competitor product – as an example of an off-label issue that is flying under the radar. This typically surfaces when sales reps promote a specific product in place of a competitor product. However, regardless of whether the competitor product is a less expensive generic or an expensive brand product, the approved indications usually do not match up, she says.

### **Understanding the FDCA**

According to Bloom, the challenge for drug companies is that sales reps are "ingrained" with the mindset to capture some portion of the competitor's market. Needless to say, considerable focus is placed on what the FDA deems necessary to make a claim, says Bloom. "If you are outside of that, you may be in the land where the FDA says your statement is false and misleading," she warns, "and we are likely to take the same position."

However, companies should not take any false comfort from the fact that something has not been prosecuted in the past, as she has sometimes experienced, says Bloom.

Rather, she says, legal and compliance executives should make sure not only that they are familiar with the entire Food Drug and Cosmetic Act, but that their sales force understands they must comply with the entire regulation.

This may sound obvious, says Bloom. But the sales force must understand, for example, that it cannot make superiority claims without two double-blind placebo controlled studies simply because their competitors may be doing so, she cautions.

### **Bloom: "Mind the gap"**

One of the key points Bloom emphasized is that prosecutors are now investigating and bringing cases against companies that have what looked, at one point, to be excellent compliance programs. "But when you get out in the field, things are happening that [make] your jaws drop," she says. Bloom refers to this as the "mind the gap" problem.

Often, she says, there is a significant gap between headquarters and the marketing department, as well as between the field marketing department and the sales force – from the managers down to the sales reps. The challenge for compliance officers, she says, is to manage the complexity that exists and translate that to conduct out in the field.

While federal prosecutors now have a greater appreciation for this complexity, she says, the government will still hold the company responsible for what its employees do in the field. "One of the challenges we are seeing is that writing nice policies in headquarters and getting the training programs out is not the same as having it actually change the conduct in the field," she explains, "especially when you are talking about things like superiority claims or a comparison to your competitor's product or making a claim about cost-effectiveness or price or a whole range of things."

"Although everyone knows you are supposed to stay on-label," she says, "if the sales representatives stuck to what was on the label, they would not have very much to say – and that is a real dilemma."

"I think trying to figure out how you deal with that is still a very difficult issue," she adds.

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***"There are all sorts of ways of going off-label apart from simply asking for a diagnosis that is clearly off-label," warns Assistant U.S. Attorney Sara Bloom.***

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Bloom also points out that one of the elements of the Pfizer settlement dealing with Zyvox involves an FDA warning letter. “The settlement actually has agreed upon stated facts that the company continued to promote contrary to what the FDA had objected to in the warning letter,” she points out.

“That is, in some ways, a pretty easy set of facts for us,” says Bloom. “But I wonder how many companies really have in place a system to check when you fix a journal article or an ad whether you actually spoke to your sales representatives,” she says. Correcting the promotional piece is only half the problem, she explains. The other half is actually instructing the sales force not to make those claims anymore.

In other words, she says, it is not just a matter of what gets out of the review committee. “It is that distinction between what is going through review committee and what is happening out in the field,” she says. “That, again, is part of that ‘mine gap problem’.”

### **Risk areas**

According to Bloom, the “pre-PhRMA-type kickbacks” such as fancy trips, are not something prosecutors expect to see any longer. “The world has changed,” she says. “In any major pharmaceutical company, you don’t expect to see that. If we do see it, it really ought to be a rogue employee.”

On the other hand, there is no shortage of more subtle issues that continue to attract attention.

For example:

**Consultant meetings.** Abuse of consultant meetings has “mostly changed” in major companies, says Bloom. “The hundreds of meetings with hundreds of attendees have largely changed,” she says. However, other strategies have become replacements for the use of that money, she cautions.

**Continuing medical education.** “CME issues are still out there,” says Bloom, beginning with making sure that CME is truly independent. In the off-label cases, she says, very often, marketing plans and strategies use CME to get out an off-label message.

“A lot of what we are looking at is really the use of CME to get around restrictions on off-label marketing,” says Bloom. She says this includes whether the CME has fair balance and whether companies have any influence over the content.

Funding legitimate independent CME is not illegal, she points out. “It is the independence that is

important,” she explains. “We don’t expect you to make sure it is fair and balanced.” On the other hand, if companies are using the CME in their marketing strategy, she says, they are probably influencing it, in which case, issues of fair balance and false and misleading information will arise.

**Drug samples.** “Sampling is great evidence,” says Bloom. She says the first question prosecutors ask is: “Who are you giving samples to?”

According to Bloom, some people have questioned whether a case can be made using samples. “But when there is a pattern of abuse along off-label lines, that can be an important element in potential cases,” she explains.

“If a doctor has both on-label and off-label uses for the product, than the mere dropping off of the sample will not, for us, prove that you promoted to him or her off-label,” she explains. However, if the doctor has no on-label use for the product, she says, there is a legal position that the dropping off of a sample is a

promotional act, says Bloom. “Since the doctor is going to use that for an off-label purpose and you know that, it is not that hard to argue that the dropping off of a sample was promoting off-label,” she explains. “In fact, what else could it be?”

“If you are not reviewing your sampling and the actual distribution of your samples to make sure that your sales reps are not giving them to doctors who have no on-label use for them, you are making it easy for us,” she warns. “We know you have those records. We are going to look at them if we have any reason to.”

“Likewise,” she adds, “if you are giving out a lot of samples for something that is one percent of your sales, you are making it easy for us.”

**Social media.** Bloom says companies should not overlook social media, including websites. “We can look at that too,” she says. “We love websites. They are very easy to access. So, if your off-label message

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***“If the sales representatives stuck to what was on the label, they would not have very much to say,” says AUSA Sara Bloom, “and that is a real dilemma.”***

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is on your website, that is awfully kind of you.”

The other group that is looking at websites and using social media is company employees, she points out. “They get it,” she says. “They know you are not supposed to make these claims, because they are trained on what you can and cannot do.”

If something is shows up on Facebook or Twitter, she warns, all an employee has to do is print it out and give prosecutors a database. “We understand that there is some role for employees on their own,” she adds, “but if it is being used for a marketing purpose the company can be held responsible for that.”

**Publication strategies.** One of the areas that pharma companies have struggled with is scientific publication regarding off-label data. “This is a tricky area,” warns Bloom. If a company is seeking a new indication, it would naturally require a strategy regarding the science supporting that indication, she says. “But when you start having publication-only strategies, you are at least at high-risk,” she cautions, especially if documents lend the impression that the purpose is to get out an off-label message.

“That can be a fine line,” says Bloom. “Or you can make it easy for us and put the publication strategy in your marketing department, which makes it not such a fine line.”

“That is not to say you can’t do research in an off-label area,” she adds. “There is a legitimate scientific role for that.” However, prosecutors will carefully examine the evidence in order to distinguish real science from marketing strategy, she says.

To the extent that companies can keep genuine science and research distinct from the sales and marketing department, the more likely they will avoid the creation of bad documents—or worse, says Bloom.

### The OIG weighs in

According to **Mary Riordan**, senior attorney at the HHS OIG, Pfizer’s new

## Excerpts from Third Amended Complaint (Pfizer/Bextra)

*Here is an excerpt of the third amended Bextra complaint filed by qui tam relator John Kopchinski, through his attorneys, Phillips & Cohen and Baertlett Hackett Feinberg, on behalf of the United States, 17 states, and the District of Columbia on December 22, 2008:*

### INTRODUCTION

As alleged herein, Pfizer and Pharmacia caused thousands of false claims to be made on federal and state healthcare programs. Since at least late 2001, Pfizer and Pharmacia systematically and improperly promoted a prescription drug—Bextra—for unapproved, off-label uses. In addition, Pfizer gave substantial and illegal financial inducements to providers to encourage them to prescribe Bextra and/or to switch from competitor products. These false claims cheated the federal and state governments out of funds that should not have been paid, unlawfully enriched Pfizer and Pharmacia and subjected patients to non-approved, non-effective, and unsafe uses and dosages of Bextra.

Through their fraud, Pfizer and Pharmacia:

knowingly disregarded federal Food and Drug Administration (FDA) regulations concerning off-label promotion, and concealed such disregard from the regulatory authorities;

knowingly misrepresented to physicians the evidence regarding the safety and efficacy of off-label usage of Bextra;

knowingly promoted off-label uses of Bextra and dosages that were neither effective nor safe, all for the purpose of significantly increasing Bextra sales;

knowingly created publications concerning Bextra’s off-label uses and that appeared to be written by neutral independent researchers, but, in fact, were created and written by defendants and their agents;

improperly disseminated such publications to physicians, as a result of improper “solicited” requests from such physicians, or with no physician “request” at all;

paid illegal financial inducements to prescribers to attend seminars, ostensibly for “consulting,” but, in fact, to expose physicians to intensive Bextra promotion and influence prescribing practices; and

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corporate integrity agreement specifically addresses the retention of healthcare professionals as authors and publications strategies as part of the company's integrity obligations. "We applaud the science," she says. But when it becomes a marketing tool, it crosses the line and becomes a risk area for the company, as well as an area the government investigates, she cautions.

Riordan encourages compliance departments to look beyond sales and marketing in order to take a broad view of all of the activities that are taking place across the company and how the compliance message is being carried out. Part of that assessment should include the purpose of the publication and research strategies, says Riordan. "I would argue that those areas should be subject to needs assessments and to critical thinking about whether people are crossing a compliance line in those areas," she concludes. ■

## **TAF outlines maze of whistleblowers**

A total of seven whistleblowers and their attorneys will receive payments totaling more than \$102 million from the federal share of the civil recovery in Pfizer's \$2.3 billion settlement, with additional money to flow as a result of parallel False Claims Act cases filed at the state level, notes Taxpayers Against Fraud (TAF).

John Kopchinski brought off-label marketing allegations regarding Bextra, which accounted for \$1.8 billion of the total. He was represented by Erika Kelton of Phillips and Cohen. His relator's share under the federal False Claims Act is \$51.5 million.

Stefan Kruszewski brought allegations regarding the off-label marketing of Geodon. He was represented by Brian Kenney and Tavy Deming of

paid illegal financial inducements to prescribers to participate in "preceptorships," "clinical article review," "journal clubs," "speaker roundtable," and "speaker training," all of which was to expose prescribers to intensive Bextra promotion and to influence their prescribing practices.

## **BACKGROUND**

In November, 2001, Bextra was first approved by the FDA for relief of the symptoms of osteoarthritis and adult rheumatoid arthritis, and for treatment of primary dysmenorrhea. Significantly, Pfizer had also sought approval for several additional indications, including acute pain, pre-operative dosing and opioid sparing, but was rejected by the FDA.

Since Bextra's FDA-approval nearly three years ago, Pfizer has sought to expand its approved indication only once. On or about December 23, 2002, Pfizer submitted a supplemental new drug application to the FDA for approval to market Bextra for the treatment of migraine headache pain in adults. The FDA has not yet approved Bextra for the treatment of adult migraines.

Bextra's narrow FDA-approved indication limits the potential sales growth of the drug, particularly in view of the fact that numerous other approved pain medications are also available to the public. As alleged below, to grow drug sales in a constrained environment, Pfizer and Pharmacia resorted to marketing strategies prohibited by federal law, including kickback schemes and off-label promotion.

As alleged below, Pfizer and Pharmacia circumvented federally mandated FDA-approval processes by aggressively marketing Bextra for numerous unapproved uses – including, but not limited to, treatment for general acute pain; chronic arthritis at doses greater than 10 mg/day; pre-surgical dosing; and post-surgical pain, among many others. Indeed, Pfizer's requests for approval for treatment for acute pain other than dysmenorrhea; chronic arthritis at doses greater than 10 mg/day; and dysmenorrhea at doses greater than two 20 mg doses/day, were specifically rejected by the FDA.

In addition, Pfizer and Pharmacia have violated federal anti-kickback laws by paying and offering to pay financial inducements to physicians and other providers to influence their Bextra prescribing practices. ▶ *Cont.next page*

the law firm of Kenney, Egan McCafferty & Young and W. Scott Simmer and Thomas Poulin of Blank Rome.

Glen Demott brought off-label allegations regarding Geodon, Lyrica, Relpax, Celebrex, Bextra, and Depo-provera. He was represented by Grant & Eisenhofer attorneys Reuben Guttman, John Kairis, and Traci Buschner, as well as Ann Lugbill, Michael Anderson and Mark Hanna of Murphy Anderson.

Blair Collins brought kickback allegations regarding Lipitor, Norvasc, Viagra, Zithromax, and Zyrtec to the government's attention. He was represented by Boston attorneys Suzanne Durrell, Robert Thomas, Jr. and Rory Delaney.

David Farber and Casey Schildhauer brought off-label marketing allegations related to Lyrica, and were represented by W. Scott Simmer and Thomas Poulin of Blank Rome.

Ronald Rainero, represented by Stephen Sheller, James Pepper, and Brian McCormick of Sheller P.C., brought off-label allegations regarding Zyvox.

TAF notes that all of the attorneys involved in this case are members of Taxpayers Against Fraud. TAF's **Patrick Burns** also points out that while only \$1 billion of the total \$2.3 billion settlement will be paid under the False Claims Act, the *qui tam* relators are responsible for setting the entire settlement in motion.

## The Highly Aggressive Marketing Strategy For Bextra Was Driven By Lucrative Off-Label Markets

Pfizer and Pharmacia's aggressive marketing plans for Bextra and Celebrex are set forth in the attached Exhibit 2, a PowerPoint presentation of Pfizer Legal Division, dated March 13, 2002, titled "Bextra Launch Plans." The presentation shows Pfizer's entry into the aggressively growing arthritis and pain market, with sales expected to expand from \$6 billion in 1999, to more than \$15 billion in 2005. See Exhibit 2 at 21. For Bextra alone, Pfizer projected sales of \$350 million in 2002 (the year it was introduced), and sales of at least \$1 billion by 2004. See Exhibit 2 at 26.

These goals were to be achieved by marketing Bextra and Celebrex as a combination portfolio of drugs for all types of pain relief. See generally Exhibit 2. This presentation makes clear that Pfizer intended to circumvent the Food and Drug Administration's (FDA) limited approval of Bextra, discussed more fully below, to fulfill these aggressive plans. The internal presentation acknowledges that, while the FDA only approved Bextra for chronic arthritis and menstrual pain, Pfizer had also sought approval for the use of Bextra for "acute pain," "pre-op[erative] dosing," and "opioid sparing [meaning use of Bextra to reduce narcotic pain relievers]," and the FDA had denied approval for those uses. See Exhibit 2 at 18. Despite this, the presentation makes it clear that Pfizer still intended to market Bextra for "perioperative pain," and that it was pursuing clinical trials on Bextra for many types of acute pain. See *id.* at 17; *id.* at 47-50 (clinical trials on Bextra and acute pain).

It is evident from the FDA's medical review (Exhibit 7) that there were serious concerns over the safety and effectiveness of Bextra if used for other than the indicated purposes at the indicated dosages. For example, the FDA medical reviewer recommended "non-approval" for all acute pain uses other than primary dysmenorrhea. While the reasons for non-approval of other acute pain uses are deleted from the version released to the public, the report indicates that "the extensive safety database at 10-80 mg daily in the arthritis safety database is adequate to support approval of the chronic therapy at 10 mg/day for arthritis and acute dose of 20 mg bid [twice a day] for short-term use in dysmenorrhea." See Exhibit 7 at 3, item 1B. As set forth more fully below, the non-deleted portions of the FDA medical report clearly indicate that the agency's medical review demonstrated concerns about the safety of Bextra, if used at dosages over 10 mg in the long-term, and if used for short-term pain at dosages over 20 mg twice a day.

► *Cont. from page 1*

## **FDA announces public hearing on social media**

The industry faces a similar challenge, says Manning, who co-chairs Hogan & Hartson's FDA practice in Washington, D.C., because the industry must put together comments that will help steer FDA in the right direction.

"Although the agency believes that many issues can be addressed through existing FDA regulations," the FDA said in its announcement, "special characteristics of Web 2.0 and other emerging technologies may require the agency to provide additional guidance to the industry on how the regulations should be applied."

The FDA acknowledges that, the continually evolving nature of the Internet, including Web 2.0

***The challenge facing the FDA, says former FDA attorney Meredith Manning, is to create a regulatory framework for social that is flexible enough to be "a living document."***

product-related information on the Internet and newer technologies.

In the meantime, says Manning, companies have been forced to figure out how to use social media in the absence of guidance. For example, she says, many companies are setting up blogs they monitor and establishing internal SOPs that outline what to do if employees post inappropriate material on their website. In short, she says, they are developing their own internal guidance in the hope that if they receive a warning letter from the FDA they can provide a credible argument for their social media outreach.

and social media tools, as well as their expansion to applications such as mobile technology, have raised questions and concerns over how to apply existing regulations to promotion in these newer media. The agency says it is evaluating how the statutory provisions, regulations, and policies concerning advertising and promotional labeling should be applied to

## **FDA outlines issues for social media discussion**

According to the FDA, questions have arisen regarding the application of the prescription drug and device advertising and labeling provisions, regulations, and policies of promotion on the Internet, especially with regard to the use of emerging technologies such as blogs, microblogs, podcasts, social networks and online communities, video sharing, widgets, and wikis.

Here is a rundown of the questions the agency plans to address at its two-day public hearing in Washington, D.C. on November 12-13, 2009:

### **1. For what online communications are manufacturers, packers, or distributors accountable?**

What parameters or criteria should be applied to determine when third-party communications occurring on the Internet and through social media technologies are subject to substantive influence by companies that market products related to the communication or discussion?

In particular, when should third-party discussions be treated as being performed by, or on behalf of, the companies that market the product, as opposed to being performed independent of the influence of the companies marketing the products?

How should companies disclose their involvement or influence over discussions or material, particularly discussions or material on third-party sites?

Are there different considerations that should be weighed depending on the specific social media platform that is used or based on the intended audience? If so, what are these considerations?

With regard to the potential for company communications to be altered by third parties, what is the experience to date with respect to the unauthorized dissemination of modified product information (originally created by a company) by non-company users of the Internet?

## A tall order for FDA

According to Manning, the FDA clearly wants to avoid a situation where it is regulating largely in response to steps that companies have already proactively taken, as opposed to building a platform for social media that it believes is appropriate. “That’s a tall order,” she says.

Former FDA attorney, **Michael Misocky**, takes a similar view. He applauds the agency for announcing the hearing rather than continuing to set policies on the Internet and social media through enforcement. Misocky, who now heads up his own consulting firm specializing in this area, says he expects to see a “bend but not break” mentality come out of meeting as it pertains to some of the long-standing principles underlying the regulation of advertising and promotion.

In other words, the FDA is not likely to change the underlying regulations or even how they are applied to the Internet, generally speaking, Misocky predicts. But he does expect to see some flexibility in the application of the regulations to accommodate emerging technologies and social media platforms.

For example, he says, the use of links and the recently condemned “one-click away rule” may be resurrected to allow for the provision of certain required information, such as prescribing information or important safety information when a company is faced with character and space limitations in the social media environment.

## No immediate guidance likely

Misocky believes it is unlikely that a guidance document will result from the hearing, at least immediately. Nevertheless, he says, the exchange of information will be helpful to inform the FDA’s current thinking and enforcement practices on these issues in the immediate future.

Manning says the agency is not likely to issue any “podium policy.” Rather, she says, it is likely to be a listening session for the agency. She, likewise, believes the complexity of the issue makes it a safe bet that no guidance will be immediately forthcoming. “Companies are still going to have to wrestle with this issue on an ongoing basis, until the FDA issues something.” ■

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■ **Michael Misocky**, President, Misocky Consulting Group, Hillsborough, NJ, [michael@misocky.com](mailto:michael@misocky.com)

## 2. How can manufacturers, packers, or distributors fulfill regulatory requirements (e.g., fair balance, disclosure of indication and risk information, postmarketing submission requirements) in their Internet and social media promotion, particularly when using tools that are associated with space limitations and tools that allow for real-time communications (e.g., microblogs, mobile technology)?

How should product information be presented using various social media tools to ensure that the user has access to a balanced presentation of both risks and benefits of medical products?

Are there data to support conclusions about whether different types or formats of presentations have a positive or negative impact on the public health?

Are there proposed solutions that may help address regulatory concerns when using social media tools associated with space limitations or tools that allow for real-time communications to present product information?

How should companies address the potential volume of information shared on various social media sites with regard to real-time information that is continuously posted and regulatory requirements to submit promotional materials to FDA as applicable?

## 3. What parameters should apply to the posting of corrective information on Web sites controlled by third parties?

Are there any parameters or criteria that could be used to determine the appropriateness of correcting misinformation and/or scope of information a company can provide when trying to correct misinformation on a Web site outside a company’s control?

Should the parameters differentiate with regard to the prominence of the third-party site (i.e., readership), its intended audience (e.g., general public, health care professionals, patients), its intended purpose (e.g., personal diary, encyclopedia-type reference), and/or the author of the information on the site?



# CEI comments on agency draft guidance highlight concerns over regulation of new media

Comments recently submitted by the Competitive Enterprise Institute (CEI) on the FDA's Draft Guidance for Presenting Risk Information in Prescription Drug and Medical Device Promotion illustrate the industry's concerns with respect to the agency's regulation of advertising and promotion of prescription drugs in new media, such as the Internet.

Here is an excerpt of CEI's comments, prepared with the assistance of veteran attorney **Arnie Friede**:

In principle, CEI disagrees that the current regime for risk disclosure in prescription drug advertising and promotion, no matter what the medium, optimally serves the interests of public health. On the contrary, in our view, encyclopedic disclosure of risk that is incapable of both meaningful comprehension by individuals of ordinary education and intelligence and meaningful cognitive integration in behavioral terms violates the "less is more" tenet that FDA has repeatedly acknowledged to be appropriate and that the agency's own research has repeatedly, albeit perhaps only implicitly, validated.

Moreover, and at least as applied to direct-to-consumer (DTC) advertising, such encyclopedic risk disclosure is not required by the Act, and is inconsistent with it. It also necessarily elevates risks over benefits in the minds of consumers, which in many instances itself works a substantial disservice to the public health. In as much as the "how to" aspects of the Draft Guidance are largely based on this flawed premise, CEI questions the document's overall utility. Nor is it apparent why FDA believes it ought to propose such a "how to" bible without first addressing, let alone resolving (or indeed even discussing meaningfully in the Draft Guidance), the significant issues raised in earlier agency proceedings about the nature and scope of mandatory risk disclosures in FDA-regulated prescription drug advertising and promotion.

At the same time, however, and taking the encyclopedic disclosure premise as a given for analytic purposes, there remain serious concerns about how that premise should be accommodated in the context of FDA's regulation of new media such as the Internet.

## 4. When is the use of links appropriate?

Should parameters be established for links to and from Web sites?

## 5. Questions specific to Internet adverse event reporting

FDA regulations require the submission of postmarketing adverse event reports.

How are entities with postmarketing reporting responsibilities and other stakeholders using the Internet and social media tools with regard to monitoring adverse event information about their products?

How is adverse event information from these sources being received, reviewed, and processed?

What challenges are presented in handling adverse event information from these sources?

What uncertainties are there regarding what should be reported from these sources to meet FDA adverse event reporting obligations?

## Veteran attorney establishes specialized FDA practice

Frequent *Rx Compliance Report* contributor **Arnie Friede** recently established his own firm specializing in FDA-related legal and regulatory matters.

Arnie is a widely respected food and drug law counselor and advocate with significant advertising law, healthcare law, First Amendment, and commercial and transactional experience. He has a long long history of direct involvement in successfully representing clients in FDA-regulated matters, beginning as an Associate Chief Counsel at the FDA. He was senior corporate counselor with Pfizer and Counsel at McDermott Will & Emery.

Arnie can be reached at:  
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## *Individual prosecutions*

# Former InterMune CEO convicted of wire fraud in connection with off-label case

*Jury verdict is only part of the increasing focus on holding individuals accountable*

**W** Scott Harkonen, M.D., the former CEO of InterMune, was convicted of wire fraud this week for the creation and dissemination of false and misleading information about the efficacy of InterMune's drug Actimmune as a treatment for idiopathic pulmonary fibrosis (IPF). The jury, in its third day of deliberations, found Harkonen guilty of wire fraud related to a press release issued on August 28, 2002. He was acquitted of a misbranding charge brought under the Federal Food, Drug, and Cosmetic Act.

"This conviction is for conduct that, in years past, may have warranted a warning letter," says former DOJ attorney **Larry Freedman**. "It shows how turbo-charged off-label enforcement has become," says Freedman, a partner with Patton Boggs in Washington, D.C. He says it is hard to reconcile this prosecution with the many cases that have ended with corporate settlements, and sometimes pleas, for similar conduct. "Once again the danger zone is expanded," says Freedman.

### **The case against Harkonen**

Harkonen, a medical doctor, was the chief executive officer of InterMune from February 1998 through June 30, 2003, and a member of InterMune's Board of Directors. According to the Department of Justice (DOJ), evidence at trial showed that under his direction, InterMune marketed and sold Actimmune to treat the fatal disease IPF, despite the fact that Actimmune was not approved by the FDA as a safe and effective treatment. The cost of Actimmune for one IPF patient for one year was approximately \$50,000 and the vast majority of InterMune's sales of Actimmune were for the unapproved, off-label use of treating IPF.

DOJ says evidence at trial showed that the Harkonen caused InterMune to issue a press release publicly announcing the results of a clinical trial of Actimmune for the treatment of IPF on Aug. 28, 2002. Although the clinical trial in fact failed, says DOJ, Harkonen caused the issuance and distribution of a false and misleading press release to portray

that the results of the trial established that Actimmune helped IPF patients live longer. Specifically, the press release's headline falsely stated that, "InterMune Announces Phase III Data Demonstrating Survival Benefit of Actimmune in IPF," with the subheading "Reduces Mortality by 70% in Patients With Mild to Moderate Disease."

### **Earlier settlement**

In October 2006, InterMune agreed to enter into a deferred prosecution agreement and to pay nearly \$37 million to resolve criminal charges and civil liability in connection with the illegal promotion and marketing of Actimmune.

The case is being prosecuted by Assistant U.S. Attorney Ioana Petrou of the Northern District of California and Trial Attorneys Sondra Mills and Allan Gordus of the Office of Consumer Litigation in the Civil Division in Washington, D.C. ■

■ **Larry Freedman**, Partner, Patton Boggs, Washington, D.C., [lfreedman@pattonboggs.com](mailto:lfreedman@pattonboggs.com)

### **The "democratization of accountability"**

Veteran attorney **Lynn Snyder** of Epstein Becker & Green last week pointed to the "democratization of accountability" as moderator of an FDLI panel that addressed, among other issues, the integrity obligations of Pfizer's new corporate integrity agreement.

Both the HHS OIG's Mary Riordan and Assistant U.S. Attorney Sara Bloom placed considerable emphasis on the government's efforts to expand certification requirements to the managerial level.

The next issue will explore the potential impact of this trend.

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*Former DOJ attorney Larry Freedman says the jury verdict shows how turbo-charged off-label is now.*

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## *Continuing medical education*

# GlaxoSmithKline becomes latest pharma company to discontinue commercial support of CME

GlaxoSmithKline last week became the third major pharma company to discontinue its funding of commercial providers, including medical education and communication companies (MECCs). Beginning next year, the company said it will “raise the bar” and fund only independent medical education programs that are “clearly designed to close gaps in patient care, and that demonstrate support for the optimal performance of healthcare professionals.”

“GSK will not support as many medical education programs, but we will continue funding those with the greatest potential to improve patient health,” said Deirdre Connelly, GSK’s President North America Pharmaceuticals. She characterized the move as “one more step” in the company’s efforts to be more transparent in the way it operates its business and interacts with healthcare providers.

### **New processes**

GSK says it will invite grant applications from approximately 20 medical education providers with a documented track record of developing and delivering high quality medical education programs that have a measurable impact on improved patient health. Potential grant applicants will be limited to academic medical centers and their affiliated teaching and patient care institutions, as well as

national-level professional medical associations that represent healthcare professionals responsible for the delivery of patient care. All selected providers must be directly accredited by a recognized accrediting body.

Funding levels for each grant will depend on the quality, scope and complexity in closing the clinical gap identified by the provider. All proposals must have an objective, well-documented assessment of the need for such a program, clear learning objectives and plans to assess the impact of the educational program on healthcare professional competence, performance, and improved patient health.

All approved grants will continue to be posted on the company’s website, [www.us-gsk.com](http://www.us-gsk.com). Since February 2009, GSK has posted quarterly reports of its educational and charitable grants to US health-related organizations including hospitals, teaching institutions, managed care organizations, professional associations, and patient advocacy groups. ■

Next week, *Rx Compliance Report* will feature the views several medical education providers on the outlook for medical education “The Five Biggest Myths about CME,” according to Brian Lewis.

## Ten steps to develop and implement effective compliance monitoring of CME activities

*By Jane Ruppenkamp*

**P**harmaceutical funding of accredited CME activities is very much in the cross-hairs of the legislative and legal communities. New enforcement mechanisms being touted by the FDA and the Accreditation Council for Continuing Medical Education (ACCME), the recent Senate hearings on CME, and Pfizer’s highly restrictive CIA—requiring expanded levels of monitoring—are challenging current standards of compliance monitoring.

Companies are assessing the effectiveness of current monitoring efforts to ensure compliance

while maintaining required firewalls. Also weighing heavily in this assessment is the increasing need to collect comprehensive objective data and determine if and when a corrective course of action is required for individual activities, as well as for operational policies and procedures.

While auditing of CME activities is a common practice, the operational imperative for medical education compliance has shifted from simply conducting audits to developing a systematic approach to collect comprehensive objective data and determine a corrective course of action for

individual activities, as well as operational policies and procedures.

Independence, conflict of interest, content validation and off-label discussion are just a few of the risks associated with CME activities over which grantors have no control. When developing a monitoring program for the CME activities supported by educational grants, creating a credible process is essential and defining the core criteria is a critical first step.

## Develop the Process

**1. Clarify your purpose.** The purpose of the monitoring process may be to address potential industry criticism, identify necessary changes and/or satisfy regulatory requirements. Perhaps it is to gain insight as to the whether the grant was used as intended (e.g., aligned with needs assessment, or compliant with ACCME Standards and the PhRMA Code.)

**2. Develop a comprehensive assessment tool.** Based on your objectives, establish criteria and develop a tool that auditors will consistently use to evaluate the criteria. The tool may address logistics (e.g., meals, venue), content (e.g., content validity, balance, objectivity), and/or commercial bias.

**3. Develop a training program for the auditors.** The training should be a prerequisite for conducting audits, provide the context of the audit and address all of the elements of the assessment tool.

Will the training be conducted live or on-demand?

How will you assess competence?

Will there be a test?

**4. Define COI for auditors.** The independence and objectivity of the auditors lends credibility to the data collected. Determine what will constitute COI for your auditors – e.g., do internal auditors have a conflict of interest? Require auditors to disclose their pertinent financial relationships.

**5. Determine how activities will be selected for audits.** Some companies set goals to monitor a certain percentage of the activities they fund. They may be selected randomly or based on identification of pre-determined risk factors.

## Select an Auditor

**6. Qualify auditors.** The auditor should be proficient with the subject matter as well as regulatory compliance issues. Define qualification criteria. Consider profession, expertise, and experience.

**7. Vet the auditors for COI.** Just as important as having a process in place to conduct the audits is the responsibility to consider potential conflicts of interest. Require disclosures and apply your definition of conflict of interest (COI).

## Follow up Post-audit

**8. Make changes as a result of the data collected.** Consider what you will do with the data collected. Determine what warrants corrective action and the action to be taken.

Will you report egregious activity to the proper authorities? If so, how will you determine what will be reported?

Will you use the information to make future funding decisions?

**9. Measure effectiveness.** Revisit your purpose for implementing the process and determine how you will know it is successful. Consider how you will monitor results, measure outcomes and continually improve the process. Periodically review the aggregate data to identify trends and information that may strengthen the compliance program (e.g., objective criteria for grant requests.)

**10. Document the process.** It is not enough to have a process in place; it must be consistently monitored and documented. Establish who will oversee the process and keep records of the audits, as well as improvements made as a result of the findings.

By following these steps, an effective CME compliance monitoring process will be in place that will help drive continual improvement and address growing criticism of pharmaceutical funding of accredited CME activities.

■ **Jane Ruppenkamp**, President, CME Peer Review LLC, [jruppenkamp@cmepeerreview.com](mailto:jruppenkamp@cmepeerreview.com)



# Plenary sessions announced for November 11–13 Pharma Congress in Washington, DC

Sponsored by the Pharmaceutical Compliance  
Forum

November 11-13, 2009

JW Marriott Hotel, Washington, DC

[www.PharmaCongress.com](http://www.PharmaCongress.com)

## PLENARY SESSIONS:

### DAY I: Enforcement and Transparency Wednesday, November 11, 2009

1:15 p.m.

#### Regulator Panel on Transparency and Disclosure

Melissa J. Lopes, Esq.  
Deputy General Counsel, Massachusetts  
Department of Public Health, Boston, MA

Shana Kay Phares  
Governor's Pharmaceutical Advocate, Office of  
Governor, West Virginia, Charleston, WV

George Till, MD  
State Legislator, Vermont, Jericho, VT

Cody Wiberg, PharmD, RPh  
Executive Director, Minnesota Board of Pharmacy,  
Minneapolis, MN

John Patrick Oroho, Esq.  
Executive Vice President, Porzio Pharmaceutical  
Services; Principal, Porzio, Bromberg & Newman  
PC, Morristown, NJ (Moderator)

2:15 p.m.

#### Overview: Pfizer CIA Promotional Monitoring Requirements

Lori Alarimo, Esq.  
Senior Corporate Counsel, Promotional Quality  
Assurance, Pfizer Inc., New York, NY

Edward Nowicki, Esq.  
Deputy Compliance Officer-Global Programs,  
Senior Corporate Counsel, Corporate Compliance,  
Pfizer Inc., New York, NY

### Day II: Recent Government Enforcement Thursday, November 12, 2009

8:15 a.m.

#### OIG Update

Mary E. Riordan, Esq.  
Senior Counsel, Office of Counsel to the Inspector  
General, Office of Inspector General, Department  
of Health and Human Services, Washington, DC

9:15 a.m.

#### DOJ Civil Division Update

Tony West, Esq.  
Head, Civil Division, US Department of Justice;  
Former California Special Assistant Attorney  
General; Former Assistant US Attorney, Northern  
California, Washington, DC

9:45 a.m.

#### DOJ Criminal Division Update

Lanny A. Breuer, Esq.  
Head, Criminal Division, US Department of Justice;  
Former Special White House Counsel; Former  
Assistant District Attorney, New York City,  
Washington, DC

10:45 a.m.

#### Making the Case for Compliance: A US Attorney's Perspective

Patrick L. Meehan, Esq.  
Partner, Conrad O'Brien Gellman & Rohn, Former  
United States Attorney, Eastern District of  
Pennsylvania, Philadelphia, PA

11:15 a.m.

#### SEC Enforcement Update

Lorin L. Reisner, Esq.  
Deputy Director of Enforcement, US Securities and  
Exchange Commission; Former Assistant United  
States Attorney, Southern District of New York,  
Washington, DC

**Day III: Friday, November 13, 2009**  
**Policy and Ethics**

**8:15 a.m.**

**Keynote: Health Reform Update**

Representative Mike Ross (D-AR) (Invited)  
Leader, Blue Dog Coalition; Member, House  
Committee on Energy and Commerce and Energy  
and Health Subcommittees, United States House of  
Representatives, Washington, DC

**8:45 a.m.**

**Effective and Compliant Promotion: Best Practice  
Training and Monitoring Techniques, A Personal  
Account on the Effects of a Misbranding Charge**

Mary Holloway  
President - Sales and Marketing, DMH BioPharm  
Advisors, LLC; Former Sales Director, Astellas;  
Former Northeast Regional Sales Manager, Pfizer,  
Somerville, NJ

Dee Mahoney  
President - Operations, DMH BioPharm Advisors,  
LLC; Former Senior Vice President, General  
Manager, US Specialty Markets Business Unit,  
Pfizer, New York, NY

**9:15 a.m.**

**Medical Institution Perspectives on Restrictions  
with Pharmaceutical Companies: Insights on Use of  
HCPs as Speakers/ Consultants, Access for  
Pharmaceutical Sales Reps and MSLs, and  
Transparency**

Ivy Baer, Esq.  
Director and Regulatory Counsel, Association of  
American Medical Colleges, Washington, DC

Pamela J. Grimm, Esq.  
Senior Associate Counsel and Vice President Legal  
Affairs, University of Pittsburgh Medical Center,  
Pittsburgh, PA

Jessica L. Quinn, JD  
Vice President and Chief Compliance Officer, The  
University of Texas M.D. Anderson Cancer Center,  
Houston, TX

Michael Shaw, Esq.  
Global Head, Ethics & Compliance, Novartis

Oncology; Former Senior Counsel, Office of  
Inspector General, US Department of Health and  
Human Services, Florham Park, NJ (Moderator)

**10:30 a.m.**

**The Ethics of Utilizing Unlicensed Drugs and  
Vaccines to Combat H1N1 Flu and Other Public  
Health Challenges in the U.S. and Other Nations**

Arthur Caplan, PhD  
Emanuel and Robert Hart Professor of Bioethics,  
Chair, Department of Medical Ethics; Director,  
Center for Bioethics, University of Pennsylvania,  
Philadelphia, PA

**11:00 a.m.**

**PCF Pharmaceutical Compliance Professional and  
Legal Counsel Roundtable**

Ann Beasley Bacon  
Vice President, Global Integrity and Compliance  
and Compliance Officer-Vaccines, Americas,  
Novartis Vaccines and Diagnostics, Cambridge, MA

Regina Gore Cavaliere, Esq.  
Chief Compliance Officer/Vice President Ethics,  
Quality & Compliance, Otsuka America  
Pharmaceutical, Inc.; Former Vice President and  
Senior Counsel, Alpharma Pharmaceuticals; Former  
Senior Counsel, Bristol-Myers Squibb Company,  
Princeton, NJ

Douglas M. Lankler, Esq.  
Senior Vice President, Associate General Counsel,  
and Chief Compliance Officer, Pfizer; Former  
Assistant US Attorney, Southern District of New  
York, United States Department of Justice, New  
York, NY

Edward Miller, Esq.  
Vice President, Associate General Counsel and  
Chief Compliance Officer, Boehringer Ingelheim  
USA, Inc.; Former Senior Trial Attorney, US  
Department of Justice, Ridgefield, CT

Brian Riewerts  
Partner, Global Pharmaceutical Advisory Services  
Group, PricewaterhouseCoopers LLP, Washington,  
DC (Moderator)

**To review complete agenda, visit:  
[www.pharmacongress.com](http://www.pharmacongress.com)**

## **FDLI's Enforcement and Litigation Conference:**

### ***Enforcement in a Post-Wyeth, New Administration World***

*October 13-14, 2009*

*The Madison Hotel | Washington, DC*

*<http://www.fdpi.org/conf/enforcement/09/>*

FDA Commissioner Dr. Margaret Hamburg delivered a key policy speech at FDLI on August 6, 2009, where she promised a more aggressive posture with respect to enforcement and provided insight into those areas where FDA would focus.

Not only is there likely to be more FDA heat for industry with Commissioner Hamburg at the helm, there is sure to be a surge in whistleblower cases, major criminal investigations, and increasing state prosecutor attention to pharmaceutical and medical device manufacturers and distributors.

In addition, now that the Supreme Court has limited the preemption previously provided to the federal Food, Drug and Cosmetic Act, how will state legislators, health departments, and prosecutors change their enforcement efforts?

The major change in preemption and the huge increase in staff at FDA offices overseas mean that regulated companies need to think more globally (both figuratively and literally) about what FDA enforcement means to them before it is too late.

Come hear FDA enforcement decision makers discuss how FDA will be enforcing the laws that affect your company /client before you face an enforcement action, and hear from leading members of the private food and drug bar about how they are adapting to the new global enforcement environment.

#### **Who Should Attend?**

In-house and outside counsel, compliance officers, regulatory affairs specialists for pharmaceutical, biological, medical device, dietary supplement and food companies.

Non-attorneys who manage government and civil litigation, regulatory compliance matters and other healthcare compliance activities.

*For more information and to register, visit: <http://www.fdpi.org/conf/enforcement/09/>*



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