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RX COMPLIANCE REPORT

EXCLUSIVELY DEVOTED TO PHARMACEUTICAL SALES AND MARKETING COMPLIANCE

OIG seeks to increase individual accountability for compliance through expanded certifications

Federal prosecutor says certifications could facilitate application of Park Doctrine

The HHS Office of Inspector General (OIG) is seeking to expand accountability as a way to increase the effectiveness of compliance programs throughout pharmaceutical companies. Not surprisingly, the agency is seeking to accomplish this largely through corporate integrity agreements (CIA), as evidenced by the new CIA that was part of Pfizer's landmark $2.3 billion off-label settlement announced last month. "There is nothing like signing one's name to get somebody to really pay attention and take something seriously," says HHS OIG Senior Attorney **Mary Riordan**.

Assistant U.S. Attorney **Sara Bloom**, the lead prosecutor in the Pfizer investigation, takes a similar view. "I have to confess, we are looking forward to having these certifications," Bloom told attendees at FDLI's advertising and promotion conference on September 22 in Washington, D.C. "One of the difficulties of holding people responsible when the conduct has been widespread across the company and acquiesced in is, 'Who do you hold responsible?'"

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OIG's new Work Plan keeps spotlight on pharma

For the second year in a row, the pharmaceutical industry has surfaced as a prime focus of the HHS Office of Inspector General (OIG) in the agency's annual Work Plan. Last year's Work Plan was "pivotal," says drug pricing expert **Bill Sarraille**, because it marked the first time that pharma became *the* single largest focus of the agency's scrutiny. The agency's Work Plan for FY 2010 continues that trend. "This represents a huge shift in the Work Plan as it has historically been designed and used," he says.

▶ *Cont. on page 7*

Allergan sues FDA over off-label policy

Allergan filed suit in U.S. District Court October 1, alleging that FDA's ban on off-label promotion violates its First Amendment rights. However, leading First Amendment attorney, **Bert Rein**, says it remains to be seen how broadly Allergan attempts to make its case. He says that could range from a narrow exception to provide safety-related information to a much broader challenge of current off-label restrictions.

▶ *Cont. on page 12*

▸ *Cont. from page 1*

OIG seeks to increase individual accountability for compliance through expanded certification requirements

Like Riordan, Bloom believes that having individuals attest that they made a risk assessment and mitigated any problems will be very helpful. One specific area where it may prove useful, she says, is in the application of the Park Doctrine—otherwise known as the responsible corporate official doctrine. The standard for the Park Doctrine is essentially that the official must have had responsibility for the area in which the conduct occurred, she says. Under this doctrine, responsible corporate officials can be held criminally liable even if they lack direct knowledge of the conduct in question or any intent to defraud and mislead, she explains.

The Park Doctrine is not a novel theory to the pharmaceutical industry. As Bloom points out, it was recently used in the prosecution of the executives in Purdue Pharma's Oxycontin case. She says the certifications now being required could help make similar prosecutions, as well as the assignment of responsibility to individuals, somewhat easier.

"It is a very rarely used but powerful doctrine," says Bloom. One possible defense is for the official to prove that he or she exercised utmost care and vigilance to prevent the conduct. "But that is a pretty tough standard," she cautions.

OIG seeks increased accountability

According to Riordan, increased accountability is a theme that has been included in several recent CIAs. It is consistent with the OIG's message, she says, that Boards of Directors need to be involved in the compliance process by directly overseeing that process and making sure it is effective.

The Pfizer CIA includes a specific requirement that the Audit Committee of the Board be briefed on the compliance program. A resolution must then be signed by each member of the Audit Committee either indicating that the compliance program is deemed effective or explaining why that certification is impossible.

"We hope that nobody will sign these certifications blindly or without giving due consideration to the underlying facts to which they are certifying," says Riordan. If this means that members of Boards of Directors require more specific information about the compliance program, the OIG believes that is a positive development, she says. "They need to have all the information necessary to be comfortable signing that certification," she says, "because they are going to be attesting that the compliance program is an effective one."

What it takes to get the Board comfortable to make those certifications will likely vary in every instance, says Riordan. The OIG has seen some companies where compliance officers have had direct access and regular interactions with the Board (or a committee of the Board), she reports.

The Park Doctrine is a "powerful doctrine" that could be made easier by the individual certifications required by the OIG, says federal prosecutor Sara Bloom.

In some instances, the Board may feel the need to retain an outside consultant or expert to represent its interests by making an independent assessment of the compliance program, says Riordan. Regardless, she says, each Board of Directors will have to determine what information they require to be comfortable making the certification.

Managers included in certifications

The OIG also believes the certification process is important for managers within the company, says Riordan. That belief is illustrated by a requirement in Pfizer's CIA that the presidents of certain business units and the finance directors within those units certify that they have examined their area of responsibility. The certification must indicate that no problems exist or that any problems have been reported.

In addition, the Pfizer CIA includes a requirement for "sub-certifications" from other managers that business unit presidents and financial directors rely on, says Riordan. "This is a way for people to be held personally accountable for compliance in their area," she says. "I suspect that is a trend that we will continue to see in corporate integrity agreements." ■

See the next issue of Rx Compliance Report for more on this issue.

Corporate integrity agreements

Pfizer's new CIA highlights continued emphasis on effective monitoring and auditing

Senior OIG Attorney says risk assessment and mitigation process marks key change

Pfizer's new corporate integrity agreement (CIA) represents the latest step in an ongoing evolution that places increasing emphasis on effective auditing and monitoring, says HHS OIG Senior Attorney **Mary Riordan**, who has been responsible for CIAs since they emerged as a significant issue for pharma a number of years ago.

According to Riordan, the single biggest difference between Pfizer's new CIA and those that have preceded it is that it includes an explicit requirement for a risk assessment and mitigation process (RAMP), which Pfizer was in the process of establishing (*see excerpt. p. 4*). While this represents a novel requirement in the CIA process, other companies are developing similar processes, she points out.

Riordan says there is a danger of compliance executives becoming overly focused on a particular area, such as speaker programs. While that type of narrow focus is both necessary and useful, she says, it is also important for companies to step back and consider the "big picture compliance message."

In short, she says, companies must ensure that useful policies and procedures developed at headquarters are actually put into practice in the field and carried through in a variety of different ways. "You really have to think about how the field force is hearing the compliance message," she explains. "How are they implementing it? Are you creating conflicting incentives for them by the way you set up your incentive compensation system? Are you rewarding them for calling on doctors who can only write for off-label uses?"

"If you are," she says, "that's a problem."

According to Riordan, the Pfizer CIA requires the company to continue its process of identifying risks associated with products that have field force support. Twice a year, she says, the risks associated with these products will be examined and a risk mitigation plan will be developed and implemented.

"We hope that other companies will continue to do this too," says Riordan. The broader objective, she says, is to have compliance translated from headquarters into the field where it can be implemented "in a very practical way" in the business operations of the company.

Increased transparency

Another key trend highlighted by the Pfizer CIA is increased transparency, says Riordan. Specifically, she says, it includes a requirement that the company contact all the doctors detailed by sales reps to notify them about the settlement. It also creates a mechanism for those doctors to call the company and report any questionable conduct, she points out.

"We in the government know it is difficult for people in headquarters to always know what is going on in the field," says Riordan. The OIG hopes this notification process and reporting mechanism will help companies identify problems earlier. It may also help the government identify problems earlier, she adds, because doctors will be given the option of reporting their concerns directly to the FDA. "The FDA may well be hearing about some questionable conduct," she cautions.

The biggest difference between Pfizer's new CIA and earlier ones is an explicit requirement for a risk assessment and mitigation process, says OIG Senior Attorney Mary Riordan.

Lastly, she notes, the Pfizer CIA continues the requirement that companies post information regarding payments to physicians. The OIG thinks transparency is "a good thing," she says.

Shifting the focus of audits

According to Riordan, the OIG believes that auditing may be even more effective when the focus of audits is subject to some variation each year. For this reason, the Pfizer CIA continues a requirement

which was included in several recent CIAs that allows the OIG to identify up to three additional areas each year as subject to review by the independent review organization (IRO). This flexibility will allow the OIG to direct reviews to particular areas or issues that may represent emerging areas of risk, she says.

Shifting the focus of audits also serves to keep the company on its toes, she says. "If the same people every year believe they are going to be audited, they will run a very clean shop," she explains. "That may give a false sense of security to people who are working in another area, so we want to have some flexibility in the audit provisions."

One of the biggest compliance challenges facing large companies is to figure out what is taking place across a company, says Riordan. The Pfizer CIA includes requirements that field sales activities, including activities largely initiated in the field, such as speaker programs, are monitored, she notes.

Shifting the focus of audits also serves to keep the company on its toes, says the OIG's Mary Riordan.

Likewise, it continues a requirement that compliance or legal personnel ride along with sales reps, because the OIG believes it is critical for the legal and compliance functions to know what is taking place in the field, says Riordan.

Finally, it requires audits of certain types of records that reflect the interactions that sales reps are having with doctors, she says.

Monitoring activities

According to Riordan, the Pfizer CIA also specifically requires the monitoring of activities that are initiated, budgeted, and handled at the headquarters level, such as consulting arrangements and advisory boards.

There is also a requirement for the review of publication activities, says Riordan. In fact, she says, the OIG has started to focus on publication and research activities. "That is part of the internal auditing of headquarters activities in the Pfizer CIA," says Riordan.

Appendix C: Risk Assessment and Mitigation Planning (RAMP) Review

I. General Description of RAMP

The risk assessment and mitigation planning (RAMP) process was developed by Pfizer as a tool to assess risks associated with many of its Government Reimbursed Products and develop a customized risk mitigation plan for each product. For each Government Reimbursed Product subject to RAMP, a Pfizer Attorney (hereafter "Attorney") completes an electronic risk assessment questionnaire. The questionnaire covers a broad range of potential risks, including promotional risk issues. Each question must be answered from a menu of possible responses. Each answer is given a proposed risk score risk areas addressed by (green, yellow, or red) based on pre-determined assessments of each question. Based on the responses to the questionnaire, the reviewed product is given an overall risk score. A "red" risk score represents a product with Heightened Risk.

After completion of the questionnaire, the Attorney is provided with a set of automated risk mitigation options for the reviewed product based on the risk scores for the questionnaire responses. Proposed mitigation options are broken into categories based on the identified risks.

Many of the mitigation options fall within Pfizer's customary practices with regard to its Government Reimbursed Products. However, certain of the mitigation steps identified for those products identified as having a Heightened Risk are mandatory rather than optional, and they entail enhanced monitoring and evaluation activities. These activities are referred to as "Required Monitoring Activities."

After reviewing all proposed risk mitigation options, the Attorney develops a risk mitigation plan for the product. For each identified risk area, the risk mitigation plan must specify: (i) the risk mitigation approach; (ii) the party who is primarily accountable for implementing the mitigation; (iii) the parties who must be consulted, if any; and (iv) the expected date of completion. The Attorney then reviews the completed risk mitigation plan with other Pfizer personnel, including Pfizer Legal and

In addition, the CIA requires Pfizer to look at certain kinds of medical education grants and certain types of charitable contributions, notes Riordan.

All of these items are explicitly highlighted in the CIA as headquarters-based activities that need to be scrutinized through the auditing process, she says.

Reporting to the GC versus the CEO

According to Riordan, the OIG has long believed it is a useful best practice to separate the compliance officer and the compliance function from the legal counsel's office and the chief financial officer of the company. "That has been a longstanding best practice recommendation from the OIG," she says. "We think that by having the compliance officer report to either the General Counsel or the Chief Financial Officer creates the possibility of a conflict of interest."

The Pfizer CIA specifically requires the monitoring of activities that are initiated, budgeted, and handled at the headquarters level.

"We want the compliance officer to be fully focused on compliance and not have any conflicting interests that could come from sitting in either of those other two parts of the organization," she explains.

Under Pfizer's previous CIA entered in 2004, the OIG permitted Pfizer's then-existing structure to continue, she says. "But there has been an evolution in thinking in my office," she reports, "and we have come to believe even more strongly that there needs to be a clear separation of the compliance function from the financial function and the legal function."

Under Pfizer's new CIA, the compliance officer is prohibited from reporting to either the General Counsel or the Chief Financial Officer, says Riordan.

"We also believe that it's important for compliance to be at a very high-level within the company," says Riordan. In the Pfizer CIA, as well as several others, the OIG requires that the compliance officer actually report to the CEO. "We think that is a very clear way to illustrate the importance of compliance within the organization." ■

See back-page for information on a timely audioconference addressing the emerging compliance techniques addressed in this article.

personnel within the applicable Business Unit for the product.

Following mitigation plan development, those designated as "primarily accountable" in the plan are responsible for completing the specified risk mitigation activities. Remedial actions completed during the specified period are entered into the RAMP online system under "Remedial Actions Taken." The Attorney must provide a documented explanation for any mitigation plan activities that were not completed during the period specified in the finalized mitigation plan.

Among other mitigation options, for all Government Reimbursed Products having a yellow or red risk score for applicable questions in the Promotion Category, the assigned Attorney shall review the incentive compensation available for field sales representatives who promote such products and shall review the call plans and Sample Distribution Plans associated with the each product. More specifically, where appropriate to mitigate and minimize risk, incentive compensation for a product shall be modified to: 1) exclude specified physician specialties from the credit and quota system for a product; 2) base incentive compensation on both individual and group performance goals; and/or 3) base incentive compensation on non-sales activities (such as the completion of data collection activities or other non-traditional performance goals). Where appropriate to mitigate and minimize risk of improper promotion, Pfizer shall modify call plans to ensure that field sales representatives promote Government Reimbursed Products in a manner that is consistent with the FDA-approved label for the product and with all Federal health care program and FDA requirements. Similarly, where appropriate to mitigate and minimize risk relating to the distribution of samples, Pfizer shall modify Sample Distribution Plans to ensure that samples are distributed in a manner consistent with Federal health care program and FDA requirements, including, where appropriate, requiring that samples be distributed from a central location rather than permitting field sales representatives to provide the samples.

To view the entire CIA, visit: http://www.oig.hhs.gov/fraud/cia/agreements/pfizer_inc.pdf

Individual prosecutions

Defense counsel blasts fraud prosecution and conviction of former InterMune CEO

Earlier this month, a jury convicted W. Scott Harkonen, the former CEO of InterMune, of wire fraud for the creation and dissemination of false and misleading statements about Acctimune's effectiveness in fighting idiopathic pulmonary fibrosis (IPF), a fatal lung disease. The jury found Harkonen guilty of wire fraud related to a press release issued by InterMune. However, he was acquitted of a misbranding charge brought under the Federal Food, Drug, and Cosmetic Act.

Harkonen's attorney, **Marcus Topel** of Kasowitz, Benson, Torres & Friedman in San Francisco, says the jury verdict was inconsistent, because it acquitted him of the "quasi-off-label" charges. But his overriding objection is that the government had no business criminalizing a scientific issue in the first place. "I find it astonishing that you would posit criminal liability on a scientific interpretation that was backed by InterMune and backed by their chief biostatistician at the time," he says.

Criminalizing scientific interpretation

DOJ says evidence at trial showed that Harkonen caused InterMune to issue a press release publicly announcing the results of a clinical trial of Actimmune for the treatment of IPF on August 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.

"I find it astonishing that you would posit criminal liability on a scientific interpretation," says defense counsel Marcus Topel.

According to Topel, however, there was no question during the trial that the data in question was accurately presented. For example, he says, the number of incidents attributable to Acctimune versus those of a placebo was accurately portayed for the various groups. "It was very clear in the trial that InterMune's chief biostatistician, at the time, acknowledged the P values that were associated with the subgroup analyses and said that they were strongly significant," he says.

In light of these factors, what the government did was basically criminalize an interpretation of the data that it did not like, Topel contends. "As we pointed out at the trial, there are no set rules and regulations about how to interpret data from clinical trials," he told *Rx Compliance Report*.

According to Topel, the statute requires that experts involved in clinical trials use their educated judgment in making assessments. That is called the substantial evidence rule, he says. "There are no rules that say if you miss your primary endpoints you can't make assertions of efficacy as to subgroup analyses," says Topel. "That is just the FDA's on-label current thinking and their current thinking, by their very strict definition is not binding on anybody – including themselves."

Topel says he hopes the District Court judge, on post-trial motions, and/or the Appellate Court of the Ninth Circuit throws the conviction out. "The fact that a jury jumped on the CEO of a pharmaceutical company where patients had to pay $50,000 for the medicine is hardly surprising," he concludes. "I am just very offended at the whole idea that you could have a fraud case in this type of scientific dialogue."

The government's view

Needless to say, the government took a decidedly different view of the case. "[This] verdict demonstrates that pharmaceutical executives will not be able to hide behind a corporate shield when they promote drugs using false or fraudulent information," said Thomas Doyle, Special Agent in Charge of FDA's Office of Criminal Investigations, Metro Washington Field Office. "Pharmaceutical companies do not run themselves, and those who engage in criminal conduct will be held personally accountable." ■

■ **Marcus Topel**, Kasowitz, Benson, Torres & Friedman, San Francisco, mtopel@kasowitz.com

▸ *Cont. from page 1*

OIG Work plan keeps spotlight on pharma

Sarraille says the industry can expect to see the fulfillment of many of the reviews the OIG initiated last year within the next 18 months. Meanwhile, he says, the new Work Plan has added a number of important new initiatives. "This poses added risk," he says, "because many of the new items are significant."

Here is a rundown of some of the items highlighted by Sarraille:

Focus on high-cost anti-cancer and HIV drugs. Notably, says Sarraille, the OIG plans to review high-cost HIV drugs, which shows a willingness on the part of the agency to challenge high drug costs, even among patient populations that have traditionally enjoyed considerable sympathy. Similarly, the new Work Plan includes a review of anti-cancer off-label uses, he points out. Specifically, the OIG says it will review Medicare payments for drugs and biologics used on an off-label basis in anti-cancer chemotherapeutic regimins *(see sidebar, this page)*.

The OIG's scrutiny of off-label use of cancer drugs shows how aggressive the government has become on the off-label issue, says Bill Sarraille.

Here, too, says Sarraille, the focus on drugs with sympathetic populations shows a more aggressive OIG, even in areas where there has been political sensitivity. "I think these are probably the most important items in the Work Plan from a pharmaceutical perspective," he says. "The anti-cancer item, in particular, shows how aggressive the government is on the off-label issue, even in its most sensitive and easily defendable context, which is off-label use of cancer drugs."

Drug pricing. Not surprisingly, says Sarraille, the new Work Plan anticipates a strong ongoing focus on the relationships between Average Sales Price (ASP), Average Manufacturer Price (AMP), and widely available market prices (WAMP), as well as hospital outpatient department reimbursement.

In keeping with the Medicare Modernization Act, the Work Plan says the agency will periodically review WAMP for selected prescription drugs covered by Part B and compare them to ASPs for those drugs. In addition, it will periodically review drug prices by comparing ASPs to AMPs.

OIG targets high-cost drugs

Here is one of the items from the OIG's FY 2010 Work Plan targeting high-cost drugs:

Payments for Off-Label Anti-cancer Pharmaceuticals and Biologicals

We will review Medicare payments for drugs and biologicals used on an off-label basis in anti-cancer chemotherapeutic regimens. The Social Security Act, § 1861(t)(2), provides coverage of FDA-approved drugs used for off-label indications in anti-cancer chemotherapeutic regimens where such uses are supported in authoritative compendia identified by the Secretary of HHS. Federal regulations at 42 CFR § 414.930(b) established a process for identifying authoritative sources of information. The DrugDex, which is a drug compendium, defines drugs in the class we will review as being medically accepted even though the given tests or treatments are indicated in only some cases and even where evidence and/or expert opinions argue against efficacy. In CY 2007, Medicare payments for anti-cancer drugs totaled approximately $2.7 billion. We will determine whether patients with particular indications were prescribed anti-cancer drugs approved by FDA for such indications before resorting to anticancer drugs not approved for those indications and, if so, whether there were improvements in the patients' medical conditions prior to use of off-label drugs. If the beneficiaries' medical conditions improved prior to use of off-label drugs, we will determine how much Medicare could have saved had anticancer drugs continued to be used within indicated usage.

To view the OIG's FY 2010 Work Plan in its entirety, visit:

http://oig.hhs.gov/publications/docs/workplan/2010/Work_Plan_FY_2010.pdf

According to Sarraille, the Work Plan is further evidence of the OIG's efforts to play a role in policy and legislative debates. For example, he points to a review of base date AMPs, which parallels consideration of the same issue in Congress as part of healthcare reform. Likewise, he says, the Work Plan highlights numerous issues regarding Medicaid rebate claims and Medicare Part D pricing. "You see one policy issue after another that are part of the legislative debate being reflected in the OIG Work Plan," he explains.

Late-filed AMPs and ASPs. The new Work Plan includes a focus on late-filed AMPs and late-filed ASPs, an issue with which a number of companies have had problems, according to Sarraille. The agency says it plans to review the impact on Medicare Part B payments when drug manufacturers do not submit their ASP data and AMPs to CMS promptly. "That is an item of some sensitivity," reports Sarraille, "as the Centers for Medicare and Medicaid Centers have increased their referrals of these problems to the OIG."

State's use of AMP. The new Work Plan also calls for continued study of a state's use of AMP for pharmacy reimbursement. Sarraille says this is part of the "ongoing saga" in the development of an alternative to Average Wholesale Price (AWP). "You see that issue, with its enormous consequences for the industry, working its way through this Work Plan once again," he says.

Part D. The FY 2010 Work Plan also continues a strong focus on Part D bid submissions and the reporting of concessions within Part D, as well as oversight of PBMs involvement in Part D. According to Sarraille, many of these items are, at least in part, "stalking horses" for multiple reviews of how manufacturers interact with PBMs and Part D plans in the context of the Part D program. He says this could create risk for manufacturers in terms of whether their contracting strategies raise fraud and abuse issues – namely whether they are in compliance with the Part D transparency guidance – and whether or not they constitute kickbacks. Even though these items seem to be directed at Part D plans or PBMs, these inquiries necessarily will involve an examination of manufacturer contracting strategies that will put manufacturers at some risk, he cautions.

Medicaid 340B issues. The new Work Plan also includes a review of the relationship between Medicaid and 340B issues, notes Sarraille. "With 340B reform being a hot item in all the healthcare reform bills in Congress, that is a significant issue to watch," he says.

HIPAA, privacy and security. The new Work Plan also includes a heavy focus on Information Technology, HIPAA, privacy, and security issues. According to Sarraille, the host of review items cited in this area shows "a fundamentally more aggressive attitude" about privacy-related issues on the part of the new Administration.

Even in 2009, he says, it was clear the OIG was already beginning to reflect the outlook and focus of an incoming Democratic Administration in this regard. However, the new Work Plan includes a whole separate section that deals exclusively with these issues. "This shows how important these issues have become to the OIG," he says.

According to Bill Sarraille, the Work Plan is further evidence of the OIG's efforts to play a role in policy and legislative debates.

Authorized generics. Sarraille also points to an interesting provision regarding authorized generics. There has been considerable uncertainty and difficulty in understanding how to apply the authorized generic guidance in individual circumstances, he says, where the maker of the authorized generic does not have all the data that involves the manufacturer to which it is selling the authorized generic.

"This is a troubling area for a review," he explains, "because manufacturers are not entirely sure how to handle situations where they have incomplete data and the guidance in this area has just been inadequate."

Compounded drugs. The new Work Plan also puts a focus on compounded drugs, which is an ongoing source of concern for many manufacturers, reports Sarraille. "That is a welcome item for some manufacturers," he says, "and an unwelcome item

for other stakeholders that are involved in compounding."

ESRD reimbursement. According to Sarraille, the OIG also puts the spotlight on end-stage renal disease (ESRD) reimbursement, which is going through a transition to a bundling reimbursement mechanism. "That is the wave of the future and this is really the test case for a fundamental shift in the way that reimbursement is likely to evolve," he says.

Sarraille says the OIG's review of those drugs as they undertake their transition to a bundling mechanism could be very important, not only for ESRD drugs, but for many other drugs, as well.

Adverse events. The new Work Plan also places considerable emphasis on medication errors and adverse events. "This shows the OIG is paying attention to drug safety and quality issues," says Sarraille, "which shows an increasing sensitivity in the Work Plan to FDA issues."

Therapy management. The OIG also plans to review of medication therapy management programs. Sarraille says this could have broad impact, in light of healthcare reform, which envisions managing patients more effectively, placing an added emphasis on compliance, persistency, and healthcare disparities.

Foreign clinical trials. The new Work Plan also includes an important review of foreign clinical trials, says Sarraille. "We have already seen the FDA, the EMEA, and the EU express repeated concerns about foreign clinical trials," he observes. "Here, we now have the OIG injecting itself into this issue."

Data Safety Monitoring Boards. Finally, Sarraille highlights a review of the use of Data Safety Monitoring Boards (DSMB), which, once again, reflects the agency's effort to insert itself more fully in issues affecting clinical trials. ■

■ **Bill Sarraille**, Partner, Sidley Austin, Washington, DC. wsarraille@sidley.com

Legislation

Senate Finance Committee bill includes enhanced fraud and abuse provisions

The Senate Finance Committee approved its much anticipated healthcare reform bill this week. Compliance executives have been largely focused on the disclosure provisions adopted from the Physician Payments Sunshine Act *(see next page)*. However, Epstein Becker & Green attorneys **Wendy Goldstein** and **Kathleen Peterson**, point out that several fraud and abuse provisions included in the final measure could potentially have broad implications, as well.

Notably, says Goldstein, the bill would make several changes to so-called "fraud, waste and abuse" provisions, including the federal health care anti-kickback statute, various civil monetary penalty (CMP) provisions, and the HHS Office of Inspector General's federal health care program exclusion authority.

Specifically, says Goldstein, the bill would amend

the federal health care anti-kickback statute to define "willfully" as "a person who acted voluntarily and purposefully to do what the law forbids *and the person need not have actual knowledge of the law or specific intent to violate that law"* [*emphasis added*].

Goldstein says the revised kickback definition would make prosecution under the federal health care anti-kickback statute easier for enforcement agencies, because they would no longer be required to prove the more strenuous "knowledge" requirement.

According to Goldstein, changes to CMP and exclusion authorities could have significant impact on pharmaceutical manufacturers, depending on the final legislative language adopted by Congress. However, the bill does not provide much detail regarding the possible changes to the CMP and exclusion laws, she says.

Additional changes

Peterson says the bill would permit "hardship waivers" of federal health care program exclusion based on hardship imposed on beneficiaries of any federal health care program (not just Medicare Part A or B, as is the case under current law). However, the bill does not specify who may request or authorize a hardship waiver, she notes.

In addition, says Peterson, Medicare Part D plan sponsors would be exempt from the CMP provisions with respect to beneficiary inducements for the limited purposes of waiving copayments for "first fills" of generic drugs. But the generic copayment waiver change does not modify the federal health care program anti-kickback statute, she notes.

Sunshine Act provisions retained in final Senate Finance bill

The healthcare final bill approved by the Senate Finance Committee also incorporates the Physician Payments Sunshine Act provisions. According to attorneys **Wendy Goldstein** and **Kathleen Peterson** these provisions generally require, among other things, that manufacturers report electronically payments and transfers of value greater than $10 (unless annual aggregate exceeds $100) to a physician, a physician medical practice, a physician group practice, or hospital with an approved medical residency training program, according. The reports must identify recipients.

According to Goldstein, the Senate Finance bill also includes the following:

- The provision also would require reporting of certain physician ownership and investment interests in manufacturers.
- "Delayed" reporting would be required for certain development and research payments.
- Recipients will be permitted to submit corrections under a process to be established by the Secretary.
- The legislation would establish CMPs for failure to report up to $1 million annually.
- The Secretary of Health and Human Services would be required to establish procedures by October 1, 2010 (with reporting effective March 31, 2012, and public Internet availability of such information by September 30, 2012).

Limited preemption

There would be limited preemption of state laws, notes Goldstein. But what the Senate Finance bill does not propose in this area is equally important, she says.

For example, she says, there is *no preemption* of any "state (or political subdivision of a state) law or regulation that requires the disclosure or reporting of: 1) any information not required under this provision; 2) the types of information excluded from reporting requirements under this provision, with the exception of the $10 *de minimis*/$100 aggregate

The sunshine provisions included in the Senate Finance bill do not address the logistics of reporting payments, says attorney Wendy Goldstein.

reporting requirement; 3) information by any person or entity other than an applicable manufacturer or covered recipient described above; and 4) information reported to a Federal, state, or local government for public health purposes."

Without preemption, says Goldstein, there is the possibility of duplicate reporting requirements under the federal and state laws that are not generally consistent.

What is not included

According to Peterson, payments to pharmacies, health plans, pharmacy benefit managers, non-physician prescribers, CME program sponsors, patient advocacy groups are not addressed in the Senate Finance bill.

Moreover, she notes, no reporting is required for the following:

- samples intended for patient use;
- patient educational materials;
- loan of a covered device for a short-term time period;
- discounts and rebates;
- payments made to a physician for the provision of health care to employees;
- payments to a physician who is also a licensed, non-medical professional if the payment is solely related to non-medical services;
- payments to a physician solely for services related to a civil or criminal action or an administrative proceeding; and
- in-kind items used for charity care."

In addition, says Peterson, the bill does not specify that the HHS Secretary's process will be subject to notice and comment rulemaking. "Notice and comment rulemaking will be critical to clarify the open issues to mitigate the potential for manufacturers to assume CMP liability under the new CMP provisions," she says.

Moreover, the sunshine provisions included in the Senate Finance bill do not address the logistics of reporting payments, she says. While many manufacturers already have established – or are in the process of establishing – payment tracking systems, the payment required to be tracked under the federal law is more extensive than many state requirements. For example, she cites the "deferred" reporting of research and clinical expenses for unapproved products, which will likely require systems expenses and policy and training updates to implement.

PDMA reporting requirements

The Senate Finance bill would also require manufacturers to provide the drug sample distribution records they maintain under the Prescription Drug Marketing Act (PDMA) to the Secretary of HHS, notes Peterson. However, the legislation offers no reason for the provision of this information and no explanation what will be done with it once it is supplied to HHS, she points out. "Manufacturers are already required to maintain records of drug sample distribution for PDMA compliance purposes," she explains. "However, those records are not generally or routinely made available to the government."

According to Goldstein, there this requirement could potentially increase exposure under health regulatory laws, including kickback, false claims, and diversion theories. "Arguably, there could be a false claim or false certification case based on the payment reports," she cautions. As a result, manufacturers will want to review their PDMA systems and ensure that their field force is adequately trained to avoid falsifying or missing physician requests for samples, says Goldstein.

The Senate Finance bill offers no explanation what the HHS Secretary will do with the drug sample distribution records companies would be required to provide, says attorney Kathleen Peterson.

Finally, the legislation also fails to include any confidentiality provisions or Freedom of Information Act (FOIA) protection, notes Goldstein. "The publicity of the payment data may implicate manufacturer proprietary concerns," she says. ■

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▸ *Cont. from page 1*

Allergan sues FDA over off-label policy

The preliminary injunction for immediate relief Allergan is seeking would enable the company to proactively share truthful and relevant information with the medical community to assist physicians in evaluating the risks and benefits of Botox for certain off-label therapeutic uses, says Allergan spokeswoman **Caroline Van Hove**.

Botox is approved in the United States for four medical uses and one cosmetic indication, notes Van Hove. But it is approved around the world for 21 different uses, she points out. "We are aware that physicians are using the drug for off-label indications to treat serious debilitating ailments," she says. "What we are asking for is the ability to proactively provide those physicians with scientific data and information on dosing guidelines, patient selection criteria, and proper injection technique that would be helpful to them in making a proper risk-benefit assessment."

Without judicial relief, Allergan maintains it is unable to engage in a truthful and relevant information exchange with the medical community for fear of prosecution. Moreover, it says the government's sweeping off-label restrictions violate the First Amendment and are inconsistent with the Food Drug and Cosmetic Act (FDCA).

Why now?

The reason Allergan is taking this action at this juncture, says Van Hove, is that last month the FDA required safety updates to the prescribing labels and a Risk Evaluation and Mitigation Strategies (REMS) program for all botulinum toxin products approved in the United States, including Botox.

The REMS program for Botox presents a unique challenge, argues Allergan, because the safety updates and REMS program require the company to speak in general terms about certain off-label uses of Botox. Allergan says that makes it important for the company to proactively provide comprehensive and up-to-date information about these off-label uses.

Far from seeking freedom from regulation, Allergan says it hopes this suit will lead to clear regulatory guidance on how it can lawfully provide accurate and relevant information on the full range of issues that physicians should consider in determining the best therapies for their patients.

First Amendment expert weighs in

According to **Bert Rein**, of Wiley Rein in Washington, D.C., the case can be viewed very narrowly or very broadly. Viewed narrowly, he says, the case raises this question: If a company is required to start relaying safety-related information about a drug to users who may determine to use it off-label, can the company be restricted if the information it provides is truthful and not misleading?

"If you look at the fact scenario they are posing, it is really quite a limited question," says Rein.

In some respects, says Rein, companies can be "trapped" between their ordinary duty to ensure safe use and the government's off-label restrictions. "A lot of product liability law deals with anticipated misuse," he explains, "and says you have a duty to minimize harm by warning against it or giving instruction on how to avoid harm arising from anticipated expected misuse."

Viewed in that narrow context, he says, Allergan's case would create an exception to the general limitation on a company providing information that would promote off-label use.

According to First Amendment expert Bert Rein, the Allergan case can be viewed very narrowly or very broadly.

However, the case can also be viewed much more broadly, says Rein, "They are questioning the whole premise of off-label restrictions," he points out. "They are saying, 'If a product is lawfully on the market and we have something to say about it that is neither false nor misleading, then we have a First Amendment right to say it'."

According to Rein, there is a premise written into the FDCA that says you define a drug by its intended use. If a company promotes it for other uses, he says, the government's view is that the company has expanded it as a product. Because some of that expansion is not preapproved, he explains, the government says it is in violation of law and it is misbranded.

"This suit, if you read it broadly, is challenging that premise," says Rein. "It goes to the whole core of the Act."

Ongoing off-label investigation

According to Rein, the suit likely relates, at least in part, to an ongoing off-label investigation concerning Botox. In short, he says, the company may hope to use it as a defense in that investigation by maintaining that the government cannot hold it liable for exercising its First Amendment rights.

In March 2008, Allergan announced it received a subpoena from the U.S. Attorney's Office for the Northern District of Georgia requesting the production of documents regarding promotional practices involving Botox for therapeutic indications.

According to Allergan, the subpoena broadly requests documents regarding promotional, educational and other activities relating to Botox. The company said at the time that its understanding is that the inquiry involves questions regarding alleged off-label promotion relating to the use of Botox for the treatment of headaches. While Allergan is currently in phase III clinical studies investigating the use of Botox for the treatment of headaches, this is not an FDA-approved use.

Whether that investigation involves safety instructions or a host of affirmative promotional endeavors is anybody's guess, says Rein. "I think a lot depends on what they are trying to defend against in the off-label investigation," he says.

Allergan's complaint references Acting U.S. Attorney for the District of Massachusetts Michael Loucks' explanation of the the breadth of the government's theory, in relation to the criminal prosecution that produced Pfizer's recent $2.3 billion settlement. "Any indication not on the label is off-label, and selling an approved drug intending that it be used for an off-label use is a violation of the law," Loucks is quoted as saying at DOJ's press conference announcing the settlement with Pfizer on Sept. 2, 2009.

See sidebar this page for an excerpt of Allergan's complaint.

Allergan is represented in its lawsuit by former U.S. Solicitor General Paul Clement, now a partner at King & Spalding in Washington, D.C.

According to Van Hove, no court date has been set. "We are hoping that we can have this case heard, presented, and decided on, within the next six months," she says. ■

Excerpt of Allergan's off-label suit against FDA

Below is an excerpt of Allergan's off-label suit against the FDA:

On its face, the [Food Drug and Cosmetic] Act permits a pharmaceutical manufacturer to speak freely to health care professionals about an off-label use of a prescription drug, provided that (1) the manufacturer does not alter the drug's "labeling" so as to (a) "prescrib[e], recommen[d], or sugges[t]" that drug for the off-label use; (b) render the labeling "false or misleading in any particular"; or (c) deprive the labeling of "adequate directions for use" (if § 352(f)(1) applies at all to prescription drugs); and provided (2) that any "advertisement" for that prescription drug discloses the information required under 21 U.S.C. § 352(n).

By regulation, the FDA has radically expanded the scope of materials deemed "labeling," argues Allergan.

The Regulatory Regime

The FDA, however, has promulgated a series of overlapping and interlocking regulations that combine to render unlawful virtually all manufacturer communication, through any avenue, to any audience, about the lawful off-label use of a prescription drug. These regulations may prohibit a manufacturer from providing information about the safe and effective use of FDA-approved drugs for off-label indications and even prohibit a manufacturer from informing medical professionals who already use a drug off-label how to minimize the risk of rare but serious adverse events. The FDA's regulations violate manufacturers' First Amendment rights while also impairing public health and safety.

By regulation, the FDA has radically expanded the scope of materials deemed "labeling." As

▶ *Cont. next page*

noted, the Act defines "labeling" to encompass "written, printed, or graphic matter" found upon the article itself, its "containers or wrappers," or "accompanying such article." 21 U.S.C. § 321(k), (m). This is a relatively narrow category of manufacturer expression. In 21 C.F.R. § 202.1(l)(2), however, the FDA redefined "labeling" to mean any "[b]rochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints and similar pieces of printed, audio, or visual matter descriptive of a drug and references published (for example, the 'Physicians Desk Reference') for use by medical practitioners, pharmacists, or nurses, containing drug information supplied by the manufacturer, packer, or distributor of the drug and which are disseminated by or on behalf of its manufacturer, packer, or distributor." The FDA has thus redefined "labeling" to encompass any tangible materials distributed by the manufacturer that contain manufacturer supplied drug information, irrespective of whether those materials "accompan[y an] article" of a drug as 21 U.S.C. § 321(m) requires.

Due to the FDA's redefinition of "labeling," it is unlawful for a manufacturer to disseminate tangible materials containing manufacturer-supplied drug information if those materials "sugges[t]" that a drug be used off-label, as it is unlawful to make such a "suggest[ion]" in "labeling" absent FDA approval. See 21 U.S.C. §§ 321(p), 355(a). The FDA has not defined "suggest" to provide any guidance to manufacturers as to what, if any, expression in labeling about an off-label use would be lawful.

Due to the FDA's redefinition of "labeling," it is also unlawful for a manufacturer to disseminate tangible materials containing manufacturer-supplied drug information, if those materials contain any statement that is "false or misleading in any particular." 21 U.S.C. § 352(a).

Although the Government may regulate speech that is actually or inherently false or misleading consistent with the First Amendment, Ibanez v. Florida Dep't of Bus. & Prof'l Regulation, 512 U.S. 136, 142, 146 (1994), the Government has interpreted § 352(a) to prohibit not just speech that is actually false or misleading, but also to reach protected speech that is neither actually nor inherently false or misleading.

The Government interpreted § 352(a) to prohibit the inclusion in labeling of any "scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs" where the FDA has not "had the opportunity to evaluate" those claims — even when bona fide scientific research establishes that the manufacturer's scientific claims are true. *Washington Legal Foundation v. Friedman*, 13 F. Supp. 2d 51, 67 (D.D.C. 1998), vacated as moot on other grounds sub. nom. *Wash. Legal Found. v. Henney*, 202 F.3d 331, 333 (D.C. Cir. 2000). Similarly, in criminal prosecutions, the Government has interpreted § 352(a) to be violated by the mere "suggest[ion] that [a] drug is safe and effective for uses which have not been approved by the FDA" — irrespective of the scientific support for such a suggestion. U.S. Sentencing Memorandum at 8–9, *United States v. Warner-Lambert Co*., No. 04-10150 (D. Mass. 2004).

The FDA's expansive definition of "labeling" and the Government's countertextual reading of § 352(a) substantially impair a manufacturer's ability to communicate truthful and important information to health care professionals to reduce the risk of potentially serious adverse events arising from an off-label use of a prescription drug. For example, a statement acknowledging that many doctors have found a drug useful for an off-label use, and then addressing the appropriate dosage for that use in light of a risk of serious adverse events, would appear to run afoul of the Government's interpretation of § 352(a). ■

The Acting United States Attorney for the District of Massachusetts recently explained the breadth of this theory, in relation to a criminal prosecution that produced a $2.3 billion settlement: "Any indication not on the label is off-label, and selling an approved drug intending that it be used for an off-label use is a violation of the law." Michael Loucks, Justice Dep't Press Conference, Health Care Fraud Settlement with Pfizer (Sept. 2, 2009).

Next week!

Leadership Summit on Global Interactions with Healthcare Providers / Compliance and Oversight Strategies to Mitigate Business Risks

October 20-21, 2009
Arlington, VA
www.cbinet.com/globalcompliance

AGENDA

Day One — Tuesday, October 20, 2009

1:15 pm
Chairman's Welcome and Opening Remarks

Understand the Global Anti-Corruption Landscape and Trends in Enforcement

1:30 pm
Understand the Applicable Laws and Regulations Governing Relationships between Industry and HCPs

2:15 pm
Government Enforcement Panel: Update on Recent Fraud and Corruption Enforcement Cases

3:45 pm
Managing an FCPA Investigation — Doing It Effectively and Within Budget

4:30 pm
Ensure Proper Reporting of Potential Violations on a Global Level

5:15 pm
Integrate Compliance Program Requirements into Business Operations

Day Two — Wednesday, October 21, 2009

8:00 am
Chairman's Review of Day One

8:15 am
Discuss Types of High-Risk HCP Interactions

9:00 am
Managing FCPA Risks in Outsourced Clinical Trials

Strategies for Training, Resource Allocation and Global Communication

10:15 am
Build Robust Policies and Procedures as the Framework for Appropriate Global Interactions with HCPs

11:00 am
Develop Local Expertise for Compliance Outside of the U.S.

1:00 pm
Panel Discussion: Overcome Cultural Differences with HCPs Abroad

Actively Monitor and Audit to Ensure Compliance

2:15 pm
Establish Effective Monitoring and Auditing of Engagements with HCPs Overseas

Also next week!

11ith Annual Guidelines for Dissemination Off-label Information

October 22-23, 2009
Arlington, VA
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FEATURING:

The Eli Lilly Zyprexa Settlement — A Prosecutor's View

Joseph Trautwein, Assistant U.S. Attorney, U.S. Attorney's Office for the Eastern District of Pennsylvania

Extended Prosecutor's Discussion: Understand the Criteria Government Uses when Building a Case

Michael Loucks, Acting U.S. Attorney, U.S. Attorney's Office for the District of Massachusetts

James D. Kole, Chief, Chicago Consumer Fraud Bureau, Office of Illinois Attorney General

Joseph Trautwein, Assistant U.S. Attorney, U.S. Attorney's Office for the Eastern District of Pennsylvania

Just announced!

National Pharma Audioconference: Lessons of Pfizer's $2.3 Billion Off-Label Settlement

Tuesday, December 1, 2009
1:00 pm - 2:45 pm (EST)

To register, visit:
www.pharmaaudioconferences.com

AGENDA

1:00 pm
Understanding the New Off-label Landscape

Matthew Hay, Publisher, *Rx Compliance Report* (moderator)

1:05 pm
Overview of the $2.3 Billion Settlement

Charlene Fullmer, Esq., Assistant US Attorney, U.S. Attorney's Office, Eastern District of Pennsylvania,

1:20 pm
Relator Counsel Perspective on the Bextra Investigation

Erika Kelton, Esq., Partner, Philips & Cohen

1:35 pm
Relator Counsel Perspective on the Future of Off-label Cases

Brian Kenney, Esq., Partner, Kenney Egan McCafferty & Young, Avalon, NJ

1:50 pm
A Defense Counsel's Perspective

Joshua Levy, Esq., Partner, Ropes & Gray

Brien T. O'Connor, Esq., Partner, Ropes & Gray

2:05 pm
An Assessment of the Risk Assessment and Mitigation Process (RAMP) and Emerging Compliance Techniques

Gary F. Giampetruzzi, Esq., Chief of Government Investigations, Pfizer Inc.

Douglas M. Lankler, Esq., Senior Vice President, Associate General Counsel and Chief Compliance Officer, Pfizer, Inc.

2:25 pm **Questions & Answers**

2:45 pm **Adjournment**

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EXCLUSIVELY DEVOTED TO PHARMACEUTICAL SALES AND MARKETING COMPLIANCE

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