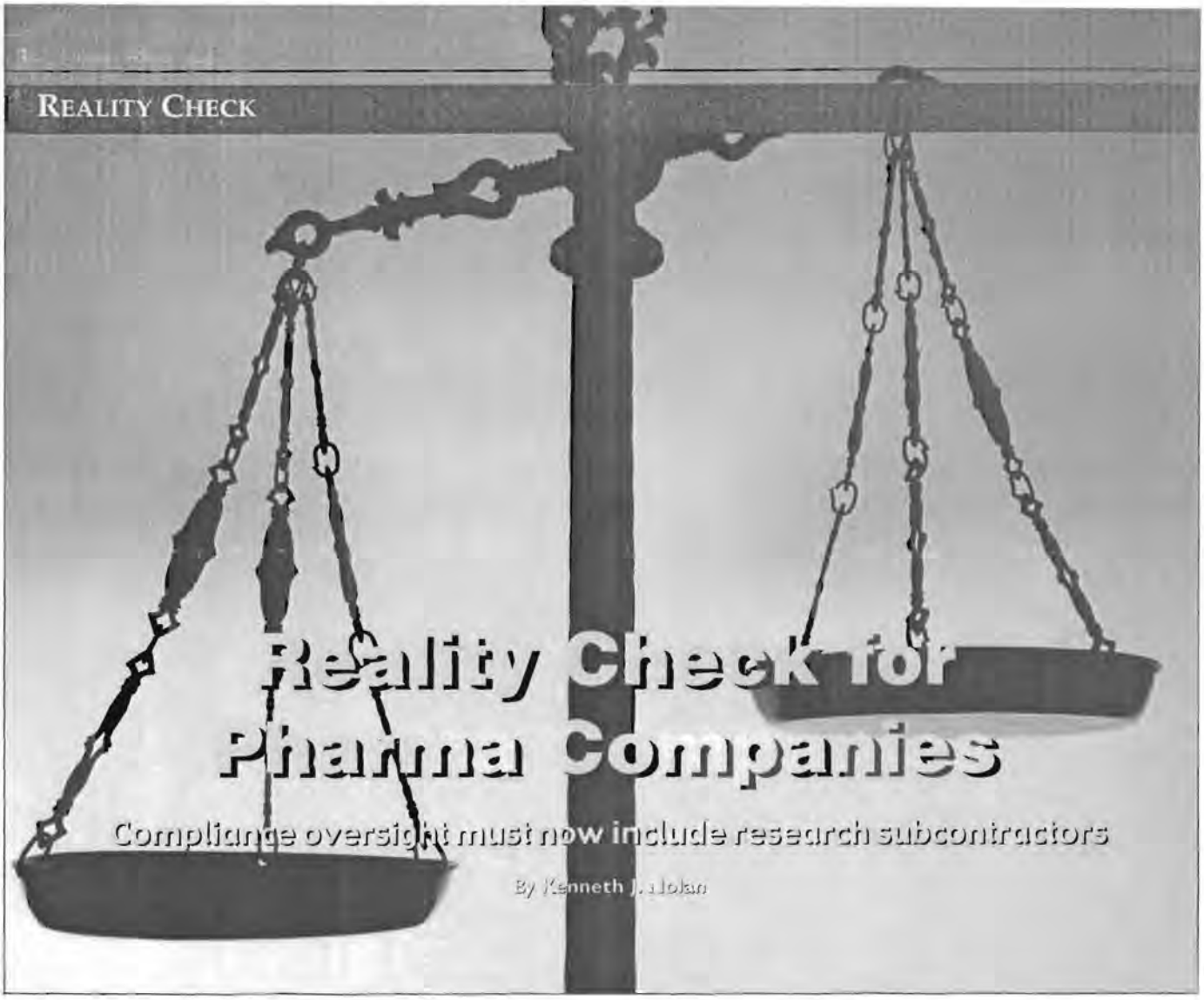

Reality Check for Pharma Companies

Compliance oversight must now include research subcontractors

By Kenneth J. Nolan

INDUSTRY INSIDERS KNOW THAT pharmaceutical companies depend on innovative R&D to produce new drug products, which are the key drivers for long-term growth. And of course, the pharmaceutical industry's products face continual generic exposure, so revenue growth requires new product launches. It is no surprise, then, that pharmaceutical companies are ranked among the highest U.S. corporations for R&D expenditures.

Given the emphasis on R&D, it is imperative to understand that every pharmaceutical company that outsources a portion of its drug R&D process (including laboratory and animal testing of a new compound) is risking civil liability under the federal False Claims Act, and that the only way to protect itself in the future is to build a firewall between the CRO or other subcontractor, and the pharmaceutical company. Included within that firewall should be an R&D process that is made a part of a corporate compliance plan, so that early detection of fraud will minimize any financial loss[1].

The public is demanding zero tolerance for double-dealing companies, and Congress is itching to root out fraud and abuse, haul offending executives before committees, and regulate industries that violate ethical standards. Whistleblowers within unscrupulous companies are filing increasing numbers of big-money lawsuits. More and more states will enact whistleblower and false claims laws to encourage and protect employees who report their company's illegal activities.

Pharmaceutical Industry as a Target

In such a business climate, the pharmaceutical industry has become a larger target, its image currently partially tarnished as a result of having more than its share of fraud investigations and multi-million-dollar whistleblower lawsuits. For example, after a corporate executive and a doctor blew the whistle, TAP Pharmaceutical Products, Inc. ("TAP"), the joint venture of Abbott Laboratories and Takeda Chemicals of Japan, agreed to pay $875 million in civil and criminal penalties and plead guilty to a criminal charge of conspiring with doctors to submit false claims to government insurers for Lupron. The case involved an alleged kickback scheme, which included free samples and educational grants. In addition, TAP allegedly maintained an artificially high reported price for Lupron, on which

Kenneth J. Nolan, P.A., is located in Fort Lauderdale, FL. Mr. Nolan has significant experience in qui tam/False Claims Act recoveries. His clients' cases are responsible for the return of over $70 million to the federal treasury, including the first qui tam to successfully recover monies for the federal government due to "off-label" sales.

government payments were calculated. At least six physicians who received free samples of Lupron and billed the government for reimbursement were indicted, along with TAP employees, including three district managers.

For those in the industry who are still not aware, major changes are coming down the pike. Reality check: Since 1999, there has been a growing number of government investigations, civil lawsuits and criminal prosecutions, all concerning the sales, marketing and pricing practices of pharmaceutical companies. Most cases are brought under violations of the federal False Claims Act as well as the federal Food, Drug and Cosmetic Act. Indeed, major drug companies, including Bristol-Myers Squibb, Biovail, and Schering-Plough, just to name a few, face government probes of sales and marketing practices. TAP Pharmaceutical Products, Pfizer, AstraZeneca, Bayer, and GlaxoSmithKline, for example, have relatively recently resolved cases in which their marketing and/or pricing practices were at issue. Other companies have faced and continue to face FDA investigations and fines concerning their manufacturing practices. It was not surprising, then, with increasing government and whistleblower scrutiny concerning sales and marketing practices emerged, the pharmaceutical industry banded together through the Pharmaceutical Research and Manufacturers of America (PhRMA) to adopt a voluntary code on interactions with physicians.[2]

As the new code went into effect for PhRMA's members on July 1, 2002, it marked a first step in the recognition that compliance with the federal Anti-kickback Statute was a major regulatory issue to confront, although the effectiveness of a voluntary code could still be questioned by some.

Almost one year later, the Department of Health and Human Services, Office of Inspector General ("OIG") issued its final "Compliance Program Guidance For Pharmaceutical Manufacturers." "This Guidance explains the value of compliance programs and details specific elements that pharmaceutical manufacturers should consider when developing and implementing an effective compliance program," Inspector General Janet Rehnquist said at the time of its release. "It is designed to help companies prevent health care fraud and abuse by promoting a high level of ethical and lawful corporate conduct."[3] Although directed at pricing and sales and marketing practices, the April, 2003 Guidance should be a wake-up call to pharmaceutical companies to implement a compliance plan and program covering all of its departments, including R&D.

R&D Exposure

But what about the R&D process? There have been several criminal prosecutions of individuals associated with falsification of data in laboratory studies and against physicians participating in clinical trials, but the use of civil laws such as the federal False Claims Act against pharmaceutical companies for marketing and selling drugs based on falsified research would be breaking new ground—at least to date. In the present climate of pharmaceutical companies facing extremely high scrutiny, and the projected reliance on more CROs for research[4], one should expect that such cases will be brought; it is only a matter of time. What's worse, once the case is made public, tag-along class actions will surface based on the same facts and theories.

In 1996, the FDA published its "Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance." In section 5.2, the FDA makes it clear that pharmaceutical companies, as sponsors, are liable for a CRO's[5] actions. It states:

> 5.2.1 A sponsor may transfer any or all of the sponsor's trial-related duties and functions to a CRO, but the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor. The CRO should implement quality assurance and quality control.
>
> 5.2.2 Any trial-related duty and function that is transferred to and assumed by a CRO should be specified in writing.
>
> 5.2.3 Any trial-related duties and functions not specifically transferred to and assumed by a CRO are retained by the sponsor.
>
> 5.2.4 All references to a sponsor in this guidance also apply to a CRO to the extent that a CRO has assumed the trial-related duties and functions of a sponsor.

Pharmaceutical companies and CROs must self-police the integrity of data compiled in the research process. The FDA relies on data that sponsors submit to decide whether a drug should be approved. The FDA's Division of Scientific Investigations ("DSI") conducts inspections of clinical investigators' study sites. Although the DSI compares information that clinical investigators provide to sponsors on case report forms with information in source documents such as medical records and lab results to determine such facts as whether a study was conducted according to the investigational plan and whether all adverse events were recorded, its oversight is hampered by the job itself (finding fraud), and limited resources[6].

Application of the Federal False Claims Act

The OIG and other federal agencies have jurisdiction to investigate healthcare billing fraud, including Medicaid and Medicare payments for drugs that were FDA-approved but based on false information. If a violation is believed to have occurred, the DOJ, through its local U.S. Attorney's office, typically enforces healthcare billing fraud. From a monetary standpoint, the DOJ's most effective offensive weapon in its arsenal is the federal False Claims Act.

The theory of liability for R&D fraud is simple: If the FDA approved a product based on false information, then the product is not necessarily safe and effective. An unsafe or ineffective drug is not reasonable or necessary and therefore would not be covered under any federal healthcare program. If a drug company caused claims to be submitted for such drugs, then it could be held liable under the False Claims Act.

A private person[7] on behalf of, or the U.S. itself, are the proper parties to file a False Claims Act lawsuit. The federal False Claims Act is triggered by conduct by any person who:

1) Knowingly presents, or causes to be presented, to an officer or employee of the U.S. Government or a member of the Armed Forces of the U.S. a false or fraudulent claim for payment or approval;
2) Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the Government.

Thus, a pharmaceutical company can be held liable for drugs paid for by government healthcare programs because it submitted false information, as provided by the CRO, to obtain FDA approval of its drug. As the theory goes, without such false information, the drug would not have been approved, a condition for reimbursement under the Medicare and Medicaid programs. Given this potential liability, risk areas for pharmaceutical companies include:

1) falsification of study results in order to falsify the outcome;
2) falsification of data in order to influence study results;
3) knowing violations of recognized norms of research in order to influence outcomes; and
4) knowing failure to follow study protocol.

It makes sense: falsification in the R&D process presents the potential to affect the safety, therapeutic value, or bioequivalence of the drug. Thus, the drug is of unknown safety and efficacy, and is therefore of no value to the patients. And look out—there is plenty of legal authority indicating that the appropriate measure of the actual loss suffered by consumers and government healthcare programs is the pharmaceutical company's gross sale of the drug, a figure that is trebled under the federal False Claims Act. Thus, the introduction of a drug into the market based on falsified research is a potentially huge liability.

Pharmaceutical companies must take steps to ensure that their relationships with CROs withstand the strict scrutiny that is emerging. Compliance oversight must be directed not just to the end of the stream (sales and marketing), or to the middle (manufacturing processes), but also to the beginning (research before FDA approval).

Like it or not, pharmaceutical companies now have no choice but to adopt a policy of zero tolerance. Those who claim that pharmaceutical companies have a right to rely on third parties are purposely trying to muddy the issue. Legitimate outsourcing (with full oversight) is in no way, shape, or form to be confused with paying for research without checks and balances. And deep down, everyone knows the difference between the two.

Of course, pharmaceutical manufacturers will never be able to protect themselves 100%, but the best way for pharmaceutical companies to minimize or eliminate FDA and False Claims Act liability is to accept nothing at face value and implement a corporate compliance program to ensure appropriate and sound research results[8].

Without making R&D part of a corporate compliance plan as vigilant as those now in place to prohibit unlawful sales and marketing practices, pharmaceutical companies are opening the door for the next round of whistleblowers and government enforcement. The focus will next be directed at research practices, not just at their pricing and sales and marketing practices.

Times have changed. Pharmaceutical company sales and marketing divisions have begun the process. Remaining divisions such as R&D must change with them or hold themselves responsible for the negative consequences of their own making. ■

Notes:

1. In June, 2003, Endovascular Technologies, Inc., a wholly owned subsidiary of Guidant Corporation, agreed to pay $92.4 million for misleading the FDA by covering up malfunctions and problems related to its stent product used to treat aneurisms. The coverup may have led to 12 deaths and many other problems. Although liability was founded on failure to report this information after its device became FDA-approved, the indictment indicates that the manufacturer was on notice that the delivery system of the device was perceived as more difficult to use than a competing product—a difficulty which may have ultimately led to the malfunctions described in the indictment.

2. The text of the "PhRMA code" can be found online at http://www.phrma.org/publications/2002-04-19.391.pdf.

3. The Guidance is available online at http://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf.

4. Indeed, the trend of private physicians conducting clinical trials by mining their patient lists is reversing due to increasing anti-kickback enforcement and conflict of interest considerations, and now more business will be shifted to CROs.

5. This is not to say that the CRO and/or its employees would not be liable—only that the sponsor is liable for the CRO's actions as well.

6. According to the FDA, the Center for Drug Evaluation and Research (CDER) conducts about 300-400 clinical investigator inspections annually. Only about 3% are classified as "official action indicated" (which signifies a finding of serious deviations, such as falsification of data).

7. A private person, commonly an employee, files a sealed lawsuit on behalf of the United States under the qui tam provisions of the False Claims Act. She is generally entitled to 15-30% of all monies recovered from the defendant.

8. Indeed, the best way for CROs to serve pharmaceutical companies well is also to demonstrate a policy and practice of zero tolerance for fraud.