Recent Developments in Pharmaceutical Product Liability Litigation

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I. Update on "New" Pharmaceutical Mass Torts

A. Vioxx

VIOXX (Rofecoxib) is a prescription drug used to reduce inflammation and ease mild to moderate pain for such conditions as arthritis, painful menstrual cycles, or pain after dental or surgical procedures. The FDA approved Vioxx in 1999 for the reduction of pain and inflammation caused by osteoarthritis, as well as for acute pain in adults and for the treatment of menstrual pain. It was the second of a new kind of NSAID (Cox-2 inhibitors) approved by FDA. Subsequently, FDA approved Vioxx to treat the signs and symptoms of rheumatoid arthritis in adults and children.

In June 2000, Merck & Co., Inc. (the manufacturer of Vioxx) submitted to FDA a safety study called VIGOR (Vioxx Gastrointestinal Outcomes Research) that found an increased risk of serious cardiovascular events, including heart attacks and strokes, in patients taking Vioxx compared to patients taking naproxen. Although FDA required labeling changes to reflect the findings from the VIGOR study, the results of the study were confounded by the possible beneficial effects of naproxen and Merck did little to clarify the potential dangers of Vioxx.

On September 30, 2004 Merck, announced a voluntary worldwide withdrawal of Vioxx. The Company's decision, was based on, APPROVe (Adenomatous Polyp Prevention on VIOXX) trial. The study was designed to evaluate the efficacy of VIOXX 25mg in preventing recurrence of colorectal polyps in patients with a history of colorectal adenomas. In this study, there was an 400% increased in the incidence of cardiovascular (CV) events, such as heart attack and stroke, beginning after 18 months of treatment in the patients taking VIOXX compared to those taking placebo.

Recent articles in the New England Journal of Medicine note that Cox-2 Inhibitors "have been aggressively marketed directly to consumers in the United States and have rapidly dominated the prescription-drug market for NSAIDs, accounting for worldwide sales of roughly $10 billion" and one commentator concluded: "Sadly, it is clear to me that Merck's commercial interest in rofecoxib sales exceeded its concern about the drug's potential cardiovascular toxicity. Had the company not valued sales over safety, a suitable trial could have been initiated rapidly at a fraction of the cost of Merck's direct-to-consumer advertising campaign."

B. Zyprexa

ZYPREXA (olanzapine) is an anti psychotic drug manufactured by Eli Lilly and Company. Zyprexa has been prescribed for the treatment of schizophrenia and bipolar disorder and also used for depression and a myriad of other mental illnesses and conditions. Since being approved for sale in the United States by the FDA in 1996, Zyprexa has been prescribed to more than 12 million people worldwide. Zyprexa is a class of anti psychotic drugs that also includes Clozaril, Risperdal, Seroquel, Geodon, and Abilify.

In September 2003, as a result of hundreds of adverse reactions and reported complaints of hyperglycemia (abnormal increase of blood sugar levels) diabetes, ketoacidosis, pancreatitis and other related conditions in patients taking Zyprexa, the FDA ordered Eli Lilly to change the Zyprexa label to warn of such complications. In February 2004 The American Diabetes Association published a Consensus Statement in its journal, Diabetes Care. In that statement, the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity, stated that "the data consistently show an increased risk for diabetes in patients treated with ... olanzapine [aka Zyprexa]

..." This finding was based on input from drug companies, including Eli Lilly, and after consultation with various experts and reviewing the medical literature.

C. Hormone Therapy

Hormone Replacement Therapy ("HRT") medications have been for many years prescribed by doctors, to ease symptoms and effects of menopause. Many women with intact uterus who chose to take HRT medication to ease symptoms of menopause used the two tablet therapy of PREMARIN (conjugated estrogens tablets) and PROVERA (medroxyprogesterone acetate tablets) till the single tablet therapy of PREMPROTM (conjugated estrogens / medroxyprogesterone acetate tablets) was developed.

It is believed that many of the manufacturers of HRT promoted and encouraged long term use of their products when there were serious questions about their promotional claims for which there were no adequate clinical study. The Federal government stepped in and funded a series of studies to determine the safety and the effectiveness of these products. One of these studies was conducted by the Women's Health Initiative (WHI) a program established by the National Institute of Health to research quality of life issues in women. A report released in 2002 by the WHI showed that, women taking the combination estrogen plus progesterone HRT medication developed breast cancer more often then those taking placebo (inactive) pills. The breast cancer in the combination estrogen plus progesterone HRT group tended to be more invasive and more advanced. The types of breast cancer women developed ranged from Lobular to Ductal Invasive Carcinoma, which was both estrogen and progesterone positive. In reaction to the 2002 report the FDA required that the manufacturers of PREMPRO and similar estrogen plus progesterone product to introduce new labeling warning of the risks.

D. Neurontin

Neurontin may be linked to suicide and suicide attempt. Neurontin was approved for sale in the mid 1990s as a treatment for epileptic seizures. However it is believed that approximately 80 percent of all Neurontin prescriptions were filled for unapproved medical conditions; it is not illegal for a doctor to prescribe a drug for unapproved conditions, however it is illegal for a drug company to market a medication for unapproved uses.

In July 2003, NBC's Dateline broadcasted an investigation which accused Parke Davis of deliberately falsifying medical information about Neurontin so doctors would prescribe the drug to treat "off label" conditions. State and Federal prosecutors have launched investigations into the allegedly illegal marketing of Neurontin. In its year long investigation, Dateline interviewed a former Parke Davis scientist who alleges company officials encouraged him to persuade physicians to prescribe Neurontin for a number of disorders, including attention deficit disorder and bipolar disease, even though there was minimal preliminary data indicating that Neurontin could help patients with those diseases. In May 2003, The US attorney's office in Boston said in court documents that the drug company Parke Davis, now Pfizer, gave illegal kickbacks to doctors, including trips to Puerto Rico and tickets to the 1996 Summer Olympics, to prescribe what has become the nation's best selling anticonvulsant, Neurontin.

II. Legal Issues

A. Failure to Warn/Learned Intermediary, Overpromotion, DTC Advertising, Publication Bias, and the "Whole Label" issue.

Pharmaceutical manufacturers sued for failure to warn about risks associated with their prescription drug products have complete defenses which frequently hinge upon the knowledge, training and practice of the plaintiff's treating physician. The physician's medical chart and testimony can literally make or break both the plaintiff's case and the manufacturer's defenses. Often the plaintiff has also sued the physician for medical malpractice in prescribing the drug, and the physician will not want the pharmaceutical company to help the plaintiff prove a medical malpractice case.

Manufacturer Defenses: Depending on the facts, manufacturers' counsel typically focus their defense of the plaintiff's failure to warn claim on three main liability defenses: 1) the learned intermediary doctrine; 2) the treating physician' s own prior knowledge of the drug's risks; and 3) lack of product identification. A brief review of these defenses shows why it is worth the effort to enlist the physician's cooperation to the extent possible. The learned intermediary defense, unique to unavoidably dangerous products such as prescription drugs, requires a judge or jury to determine whether the drug manufacturer's warnings adequately conveyed to the medical community the risk of prescribing or administering the drug. Generally speaking, if the judge or jury determines that the warnings are adequate, the manufacturer is not held liable for the patient's injuries or damages which result from the drug's unavoidably dangerous propensities. See McCombs v. Synthes, 266 Ga.App. 304 (2004); (Rest. 2d of Torts, § 402A, comment k.).

A finding that the warnings were adequate under the circumstances of a particular case will

usually require the trier of fact to sift through large amounts of extremely technical and often confusing medical expert testimony. The physician's testimony that he understood the warnings to apply to the patient's medical condition and that he had sufficient information from the existing warnings to balance the risks and benefits of the drug for his patient, is persuasive evidence that the warning was adequate. By the same token, since the efficacy of a particular warning can be eroded by overpromotion of the drug by the manufacturer's sales force, (See Stevens v. Parke, Davis & Co. 9 Cal 3d 51 (1973)) the treating physician's testimony that the defendant manufacturer did not overpromote the product can be critical if an overpromotion claim is raised.

Another defense available to the manufacturer is that of the treating physician's own personal knowledge about the drug's propensities. If the manufacturer can demonstrate that the plaintiff's physician was in fact aware from various sources about a drug or medical device's potential risks, yet chose not to warn the patient about them, the manufacturer should prevail, even if there is a dispute among the parties' experts as to whether the manufacturer's warnings were adequate. (See, e.g., Plenger v. Alza Corp., 11 Cal.App.3d 349, 362, 13 Cal.Rptr.2d 811 (1992)). Courts may view this as either a lack of a duty to warn of a risk already known to the physician, or as a lack of proximate cause of the plaintiff's injuries as a result of the manufacturer's allegedly inadequate warnings. But the result is the same: plaintiff cannot prove a prima facie case against the manufacturer for failure to warn. The success of this defense usually requires the physician to affirmatively state by declaration, deposition or trial testimony that despite his knowledge of a potential risk, he made an informed medical decision not to inform the patient about it.

The following are some recent cases relevant to the failure to warn/learned intermediary dichotomy. Vitanza v. The Upjohn Co., No. 16343, 2001 WL 866885 (Conn. Aug. 7, 2001)

(pharmaceutical company is not required to provide warnings on individual promotional sample packages distributed to physicians by its sales representatives); Brown v. Glaxo, Inc., 790 So.2d 35 (Ct. App. La. 2000) (misleading oral communications by pharmaceuticals sales representatives may supersede an otherwise adequate written warning to a physician); but see In re: Rezulin Products Liability Litigation, 133 F. Supp.2d 272 (S.D.N.Y. 2001) (sales representatives have no duty to warn patients of foreseeable risks of prescription drugs). Perez v. Wyeth Labs., 734 A.2d 1245 (N.J. 1999) (Norplant litigation, learned intermediary doctrine undermined by direct to consumer advertising); but see In re: Norplant Contraceptive Products Litigation, 165 F.3d 374 (5th Cir. 1999). Bryant v. Hoffman-La Roche, Inc., 585 S.E.2d 723 (Ga. App. 2003) (learned intermediary is an affirmative defense; to be applied, the benefits must outweigh the known risks on the date the product is distributed and the risks must be unavoidable in the sense that there was no feasible alternative design which on balance accomplished the same purpose with a lesser risk -- this case also deals with preemption to some extent); Parke, Davis & Co. v. Mayes, 183 S.E.2d 410 (Ga.App. 1971) (allows for possibility of an exception to learned intermediary rule citing California's Love overpromotion case).

B. Statute of Limitations - A Plaintiff's Duty to Discover

See Eberhardt v. Merck & Company Inc., 106 Fed. Appx. 277; 2004 U.S. App. LEXIS 16129 (5th Cir. Aug. 5 2004) and Bridges v. Metabolife Int'l Inc., Case No. 04-20110 (5th Cir. Jan. 11, 2005); King vs. Sitzingers, Inc., 160 Ga. App. 318 (1981).

C. Preemption - Why is FDA Attacking Consumers?

Since 2001, when President George W. Bush appointed former pharmaceutical defense attorney Daniel E. Troy to be Chief Counsel at the U.S. Food and Drug Administration, the FDA has

intervened in at least five private lawsuits, involving both drugs and medical devices, to advocate the preemption of State product liability claims. FDA has openly shifted its position on express preemption of medical device claims and has argued in favor of the implied preemption of prescription pharmaceutical claims for the first time in the agency's history. Mr. Troy, who left FDA under pressure after the 2004 election, openly solicited drug and medical device companies to come to the FDA for help in defeating private product liability lawsuits. It is unclear what policy his replacement, Gerald Masoudi from Kirkpatrick and Lockhart, will adopt.

With respect to prescription pharmaceuticals, there is no express preemption provision in the FDCA. When the "Kefauver-Harris" amendments to the FDCA were enacted in 1962 (which, for the first time, required that new drugs be reviewed and expressly approved by the FDA before they could be marketed in the United States), Section 202 of the amendments provided that "nothing in the amendments ... shall be construed as invalidating any provision of State law ... unless there is a direct and positive conflict between such amendments and such provisions of State law." Thus, FDA's review and approval of new drugs was never intended to impliedly preempt state product liability laws, consistent with countless state court opinions which hold that regulatory compliance is the "minimum" that can be expected from drug companies.

In its 1979 drug labeling Federal Register notice, FDA argued that "drug labeling does not always contain the most current information and opinion available to physicians about a drug because advances in medical knowledge inevitably precede formal submission of proposed new labeling by the manufacturer and approval by FDA", that "[c]ommunication of significant medical information should be encouraged, not restricted", and that "the addition to labeling and advertising of additional warnings ... is not prohibited by [FDA's] regulations.". In fact, FDA cited with approval

a state court case which held that a company may have a common law duty to revise its warnings earlier than obtaining FDA approval.

As recently as 2000, in Bernhardt v Pfizer, Inc., when the plaintiff requested that the court order Pfizer to send out a warning letter, the FDA intervened at the invitation of the court and argued that it had "primary jurisdiction:" a doctrine which permits the court in its discretion to "refer a matter within its original jurisdiction to the appropriate administrative agency if doing so will promot[e] proper relationships between the courts and administrative agencies charged with particular regulatory duties." Even in that case, however, FDA was a long way from forcing state litigants out of court altogether and arguing preemption of all state law tort claims.

Under Chief Counsel Troy, FDA shifted its position in 2002. In the In re Paxil Litigation, against the SmithKline Beechum Corporation ("SKB"), plaintiffs claimed that the adverse effect warnings for Paxil were inadequate and an injunction was sought to prohibit the company from advertising Paxil as "not habit forming." After the court entered a temporary restraining order against SKB, FDA filed a brief arguing that, because the agency allegedly had reviewed and approved of the Paxil label, all of the plaintiffs' claims (including the personal injury claims) should be dismissed. The court vacated its TRO, but declined to adopt FDA's preemption arguments. So, in a shift from Bernhardt and prior cases, FDA began to argue that the court should not only defer to FDA under the primary jurisdiction doctrine on the labeling issue, but that the court must dismiss the entire case including the injury claims.

And, finally, in 2002, FDA totally shifted directions in the Motus v. Pfizer case before the Ninth Circuit Court of Appeals. There, FDA totally abandoned the pretense of conflict preemption and simply argued, without evidentiary support and without ever having made an administrative

determination, that any additional warning which the plaintiffs might argue were necessary would not be approved by FDA and including them would violate FDA regulations. In other words, what FDA argued was that FDA's regulations preempt the entire field of drug labeling - precisely what the agency had said, in 1979, it would not do and what the 1962 Amendments prohibit. In its 2004 decision, the Ninth Circuit never got to the preemption issue and upheld dismissal of the Motus case on other grounds.

Since the Motus decision, however, at least two federal courts in Texas have dismissed Zoloft cases based in part on FDA's amicus brief in the Motus case -- Dusek v. Pfizer and Needleman v. Pfizer, which is now on appeal to the 5th Circuit. In other litigations, defendants have raised the same conflict preemption arguments but, so far, without success.

CONCLUSION – A SAFER FDA FOR ALL?

Product liability lawsuits have traditionally been viewed as a means of indirectly regulating manufacturers, including companies that manufacture and sell prescription medicines. Now that some of these companies have been found neglecting the health and welfare of patients, the drug industry is desperate for federal statutes that would protect their world-wide trillion dollar business without having to change their business habits. These companies argue that their businesses are already so well regulated by the Food and Drug Administration that the only way plaintiffs can win is by tricking jurors. The documents, however, prove those arguments may well be wrong. Increasingly, consumers and health care professionals are discovering that the regulation of the drug industry by the FDA is just not enough. There is a growing consensus that the FDA needs greater powers to protect the safety of patients.

Listed below are some (but by no means all) of the most common current recommendations

for how to make the FDA stronger and medicines safer. None of these recommendations, if enacted, would slow the time it takes to bring new drugs to patients and might even speed drug approvals. Congress and FDA should work together to make sure the FDA can do it's job, before taking away the power of juries to punish drug company negligence and misconduct:

1. FDA needs the statutory authority to compel drug companies to conduct further clinical studies after the drug is approved. As it stands right now, the laws enforced by the FDA do not give it the power to require drug companies to conduct further studies after a drug is approved. FDA has smudged this black line a bit by requiring some companies to agree to conduct certain additional studies as a condition for receiving the FDA's approval to sell their new drugs. This certainly shows that the FDA believes such studies are important. However, as recently as March 2004, about 65% of these post-approval studies remained incomplete. Moreover, FDA frequently states that some drug risks cannot be uncovered until the drug is being used by the general public. Yet the FDA lacks the power to make companies prove or disprove these newly discovered risks.

2. FDA should require long term outcomes studies for all drugs that will be taken long term. In 2004, the FDA drafted guidelines which suggest to drug companies that if their drug is to be taken long term, the company conduct a long term study (after the drug is on the market) to see if the drug is as safe and effective long term as it seems to be in the short term studies done to get the FDA's approval. Shouldn't the FDA simply require companies to do these studies whenever a drug is likely to be taken long term? However, since these are Apost-approval@ studies, chances are good that the FDA will let them fall through the cracks. That's why:

3. FDA needs an independent and adequately-funded safety office. Right now, the office at the FDA that reviews new safety information, such as studies and reports of new risks, is controlled

by the office that approves new drugs. As FDA's Dr. David Graham has pointed out, there is a conflict of interest in those officials at the FDA who allowed a new drug onto the market and don't want to be blamed if it turns out they were wrong. The FDA needs a new, independent office of drug safety that will make sure the post-approval studies are completed and evaluates all the risks.

4. FDA needs the authority to suspend marketing of drugs that appear to be dangerous. If the FDA decides that a dangerous drug should be taken off the market, the agency has three options: it can ask the drug manufacturer to stop selling, it can sue the drug manufacturer, or it can ask the Secretary of Health and Human Services to declare an imminent health hazard and ban the drug. All three are pretty desperate options. The FDA needs an intermediate option: marketing suspension. With a suspension, the FDA can halt sales pending an investigation and complete review of the scientific information about the drug product. Combined with the power to compel additional studies, FDA would have powerful tools to figure out which medicines are worth the risk and which are not before another few million patients use the medicine in question.

5. FDA needs the authority to compare new drugs to others already on the market. Sure, many new drugs are effective if you compare them to doing nothing at all, but if you compare them to older (often cheaper) and generally safer drugs, some won't pass muster. Right now, the FDA can only compare drugs to nothing, a placebo. The agency needs the authority to compare new drugs to older, safer drugs to decide whether the new drug really offers anything at all. New, after all, does not always mean better.

6. FDA needs to enforce labeling and promotion violations and stop selective publication of clinical trial results. Many drug companies have gotten warning letters from the FDA in which the agency has stated that certain promotional materials are false or misleading. Those materials are

usually just the tip of the iceberg when the promotional activities of the entire company are examined. Yet FDA has rarely, *if ever*, done more than send a warning letter. There's a simple answer to this problem: civil money penalties. Hopefully the FDA will learn to effectively stop the misleading advertisements, peer-to-peer selling, and corruption of medical science by imposing serious fines and other penalties. Studies also show that labels don't effectively convey risk information to prescribing health care professionals. FDA needs to make sure that drug companies have a financial incentive to spread risk information, as well as tout the benefits of their products. Perhaps these efforts will also help curb the gross over-use of some over-hyped pharmaceuticals.