PUBLIC CITIZEN HEALTH RESEARCH GROUP

Health Letter

SIDNEY M. WOLFE, M.D., EDITOR

NOVEMBER 2002 ◆ VOL. 18, NO. 11

Unsafe Drugs: Congressional Silence is Deadly

(Part 2)

The following article was written by Dan Sigelman, an attorney who worked with the Public Citizen Health Research Group and then conducted oversight of the Food and Drug Administration's (FDA) regulation of new drugs as counsel to a House subcommittee principally chaired by Rep. Ted Weiss (D-NY). His work led to a series of congressional hearings that raised serious questions about the adequacy of the FDA's policing of the drug industry regarding the safety of a number of prescription drugs. He then joined a law firm which has represented the victims of dangerous drugs in litigation against the pharmaceutical industry. This article is an update of a previous article he wrote on the same subject (see the October 2001 issue of Health Letter*). An edited version of both articles recently appeared in the* American Prospect.

In May of this year, Congress blithely renewed the 10-year-old arrangement under which drug companies pay "user fees" that now directly fund slightly more than one-half of FDA's review of marketing applications and has enabled the FDA to increase its review staff by 77 percent. In exchange, the FDA rewarded the drug industry with a 32 percent increase in drug approvals from 1993-2001 over the previous nine years.

If this Faustian bargain has been a factor in the recent spate of drug withdrawals—13 new drugs have been removed from the market for safety reasons—Congress was not about to find out. Instead, the lawmakers not only allowed but encouraged the drug companies and the FDA to decide in closed-door negotiations how much the industry would have to pony up this time around and just what concessions it would get from its regulators in return. Then Congress tacked the agreement onto an unstoppable bioterrorism bill and, without a hearing, debate or vote in any committee, passed it.

In 1997, the first time that user fees were about to expire, the user-fee program was renewed as part of so-called "modernization" legislation, which lowered the barriers to approval of new drugs, partly with "fast track" procedures. Prior to this legislation, the history of the modern FDA was marked by a series of disasters that prompted Congress to legislate to protect public health and safety. The turn-of-the-century slaughterhouse scandals led to enactment of the pioneering Food and

continued on page 2

CONTENTS

Drug Act in 1906. After 107 people, including many children, died after ingesting the elixir Sulfanilamide, an untested chemical cocktail containing a poisonous chemical analogue of anti-freeze, Congress passed the Food, Drug, and Cosmetic Act of 1938, which started a new system of drug regulation by requiring drugs to be shown safe before marketing. In 1962, revelations of devastating birth defects caused by the sedative tranquilizer thalidomide led Congress to enact the Kefauver-Harris Amendments, which required the FDA to assure that marketed drugs—including those the FDA had approved as safe since 1938—are proven effective as well as safe.

The 1997 "modernization" law marked the first time in 91 years that public health protections had ever been rolled back. It demanded, besides the continuing speed-up of new drug reviews, a changed legal standard: Instead of requiring two clinical trials before approving a new drug for sale, the FDA could accept just one. The new law also allowed manufacturers, if they met certain conditions, to promote drugs for uses the FDA had never approved. There was more as well in this vein and not a single provision designed to enhance the safety of the drug review process.

The price of ever intensifying congressional and industry pressure to accelerate the new drug approvals culminating in passage of the 1997 "modernization" act may well have compromised safety. Recently, the General Accounting Office reported that 5.34 percent of the drugs approved from 1997 to 2000 were pulled from the market for safety reasons, almost 3 1/2 times the withdrawal rate of 1.56 percent of drugs cleared in the immediately preceding period from 1993 to 1996.

For the past decade, and particularly after the 1994 elections, Congress couldn't be bothered to see whether the FDA has been protecting the public from the dangers of new drugs that may have been too hastily approved. Instead, since 1997, congressional "oversight" of FDA drug regulation has been confined to hearings—one in the House in 1998, another in 2001, and a Senate hearing in 1999—called to ensure that the FDA continues to vigorously implement the 1997 "modernization" legislation mandates to speed drug approvals.

Accompanying the speed-up in drug approvals has been a precipitous increase in the percentage of drugs the FDA has approved. The FDA now clears 80 percent of all new drug applications, up from 60 percent just a decade ago. Congress has done nothing to determine whether this has only been achieved by compromising safety standards the FDA once upheld.

Has the FDA increasingly cleared drugs whose safety and effectiveness have been inadequately studied or which are accompanied by incomplete or inaccurate warnings to prescribing physicians? Has the FDA been so consumed by the imperative to continue approving drugs in record time that it has seriously under-regulated drugs which, once marketed, have proven far more toxic than previously appreciated? Congress has yet to ask such questions.

At the National Press Club on December 12, 2000, then-FDA Commissioner Jane Henney conceded that a "downside" of faster approvals may be "an increased number of recalls" because foreign markets no longer provide the FDA, as they have in the past, with early warning signals about the dangers of new medicines while it is deciding whether to approve them. One year later FDA drug director Janet Woodcock conceded that "'U.S. first in the world' means our population is placed at greater risk because we are [initially] going to discover" adverse drug reactions to newly approved drugs here, rather than learning about them when they crop up elsewhere.

For drugs that represent no significant therapeutic advance, this hardly seems a risk worth taking. Yet among the 13 dangerous drugs withdrawn from the U.S. market in the last decade, not one filled an otherwise unmet medical need.

In December 2000, the *Los Angeles Times* published reporter David Willman's extensive and very detailed report on his two year investigation into seven deadly drugs that had been approved and withdrawn since 1993. He documented, among other things, that the FDA repeatedly approved drugs in disregard of their dangers and the concerns of its medical experts and that the time-limit goals imposed by the user-fee program had become deadlines imposing unremitting pressure on agency reviewers to approve drugs, and to do so quickly. He also established that the FDA delayed seeking some withdrawals until long after receiving myriad reports of grievous injury to patients. Willman's outstanding work earned him the Pulitzer Prize for investigative reporting. It should have been a treasure of leads for numerous congressional oversight hearings. It provided—for even the least inquiring mind among House and Senate investigators—a road map of where to look for possible fallout from the speed-up agenda Congress foisted upon the FDA. Yet—you guessed it—Willman's exposé stirred not one congressional committee into action.

As Congress continues debating a Medicare drug benefit, pressure from employers, governors and organized labor, among others, is intensifying for congressional investigations into pharmaceutical industry price gouging and exploitation of loopholes in drug patent laws that keep lower cost generic drugs off the market. With patents expiring on many of their blockbuster drugs, drug companies are increasingly looking to faster and more porous drug clearance policies to refill their multi-billion-dollar coffers of patent protected monopoly profits, even if these offer only minor variations on what's already out there. For pharmaceutical companies whose patents are expiring on blockbuster drugs, there is much to gain from rushing even unnecessary new drugs to market. But what are the ramifications of requiring the FDA complicity in this business strategy? Yet, neither the economic, to say

nothing of the public safety fallout from these policies, has precipitated congressional calls for hearings into FDA's recent drug approval record.

It is a sign of the times that W. J. "Billy" Tauzin (R-LA), Chair of the powerful House Commerce Committee and James C. Greenwood (R-PA), who leads that committee's investigative panel, recently have taken a page from their Enron play book. Instead of doing oversight that could save lives, they have focused on whether the biotechnology company ImClone misled investors about the FDA approval prospects for its anti-cancer drug Erbitux. Is it too much to ask that they exhibit as much concern for the safety of the drug consuming public as they have for Wall Street investors? They have yet to investigate a drug safety issue.

Not until recently did a few murmurs of discontent appear. The setting was a March 6 House subcommittee hearing on reauthorization of the user-fee program. Three members—Democrats Sherrod Brown (Ohio), Bart Stupak (Mich.), and Henry Waxman (Calif.)—raised a variety of questions and concerns regarding recent drug withdrawals and the capacity of the FDA to monitor drug safety. More fundamentally, they voiced uncertainty about the soundness of forcing the FDA to be financially dependent on, cozy with, and promotive of the U.S. pharmaceutical industry. As Rep. Brown, the subcommittee's ranking Democrat, complained, "this committee and this Congress jump when the drug industry says jump....When the drug industry wants us to move quickly to ensure that the FDA doesn't hold their products up from getting to the market, we move with lightening speed to do their bidding."

This development was surely welcome, but it came from a mere sliver of the 535 House and Senate legislators. None of these minority party members is empowered to launch and direct investigations or to call and preside over hearings, and their doubts can never be equated with probing oversight of drug safety based on a solid evidentiary record of FDA's performance.

All hopes for Congress finally to step into the breach have resided with Ted Kennedy, the Senate's liberal stalwart and chairman of the Health, Education, Labor, and Pensions Committee, who in the 1970s and, to a lesser degree, the 1980s, with the able assistance of his longtime investigator, the late Walter Sheridan, publicly explored inadequacies in FDA regulation. Earlier this year, Kennedy had considered holding hearings on drug safety. When renewal of the user-fee program whisked through Congress, those plans got shelved. It remains to be seen if that is where they'll stay.

The user-fee reauthorization that Congress passed in May has been presented as a reform. Even Kennedy celebrated it on the Senate floor as meeting "our obligation to assure the safety" of drugs brought to market quickly. But the accolades are misplaced. True, Congress has finally agreed to increase public funding for the FDA's understaffed divisions, and industry negotiators for the first time agreed to allow a portion of user-fee revenues to be spent on drug safety monitoring and drug advertising review. But what's still *not* allowed is crucial.

The FDA is prohibited from drawing on user-fee funds to monitor the safety of any drug submitted for review before October 2002—so the overwhelming majority of drugs on or entering the market cannot be scrutinized using these funds. In the few cases where user-fee-supported monitoring *is* allowed, it is limited to only two years (three years if the drug presents unusual risk concerns). The FDA is barred from relying on user-fee dollars to monitor adverse effects that were unanticipated at the time of approval. For the first time, the agency may spend user-fee money to check a manufacturer's compliance with a post-marketing safety plan. But if unanticipated safety concerns arise after marketing begins, user-fee revenues may not be used to assess them. The safety of drugs already on the market is hardly thus ensured by this legislation.

And the pre-market safety of new drugs is not even addressed. To the extent that recent drug withdrawals raise questions about FDA's *pre-market* consideration of drug risks or its will to prevent the marketing of distinctly and highly toxic but questionably necessary drugs, the changes mandated by that law are largely beside the point.

In addition, under the bill just passed, companies that don't do the follow-up research they're supposed to when the FDA lets them sell their drugs "pending further study," still won't be fined or otherwise penalized. Instead, the FDA will now have the authority to post their names on its Web site and try to embarrass them into compliance. It's not much.

The need for Congressional attention is, if anything, greater now than ever. Senator Kennedy should now turn his attention to conducting detailed post-mortems on FDA's pre-market review and post-market regulation of drugs that have been withdrawn from the market for safety reasons in recent years. He could also scrutinize the FDA's handling of dangerous drugs that remain on the market. The diet drug Meridia, linked to cardiovascular side effects and death, and the arthritis medication Arava, implicated in serious and sometimes fatal liver reactions, are obvious candidate targets. Public Citizen's Health Research Group has petitioned for immediate market withdrawal of both drugs.

Kennedy should also build a public record for resuscitating needed proposals to enhance FDA's enforcement powers that he and others—most notably Congressmen Henry Waxman and John Dingell (D-MI)—pushed for and ultimately abandoned in the wake of stiff opposition from Big Pharma, OMB, and the Presidential Council on Competitiveness in the waning days of the Bush I Administration. These include giving the FDA authority to levy civil money penalties for violations of the nation's drug laws, to subpoena industry records when necessary to investigate industry

continued on page 4

FDA Caves In to Industry, Fails to Adequately Address Tylenol Overdoses

Most of us remember the 1982 debacle in which Tylenol capsules laced with cyanide were held responsible for seven deaths. These tragic events led to a reimagining of tamper-resistant drug packages. Yet a far greater Tylenol-related tragedy has been unfolding before and since 1982—preventable deaths due to overdoses from acetaminophen (the active ingredient in Tylenol and many other prescription and over-the-counter drugs) and the resultant liver damage. In fact, acetaminophen is the leading cause of toxic drug ingestions in the U.S.

The impact of acetaminophen overdoses on the health care system is daunting: 108,102 calls to Poison Control Centers in 1999; an average of 56,680 Emergency Department visits per year; an average of 26,256 hospitalizations per year; an average of 458 deaths per year. And deaths appear to have doubled between 1995 and 1999, according to one data source. By any measure, this is a major national health problem.

Yet, for decades the Food and Drug Administration (FDA) has watched this tragedy unfold. As long ago as 1977, the FDA's Advisory Review Panel recommended the following warnings for acetaminophen-containing products: "Do not exceed recommended dosage because severe liver damage may occur" and "Do not exceed recommended dosage or take for more than 10 days, because severe liver damage may occur." This wise advice went unheeded.

On September 19 and 20, 2002, a little-heralded war broke out inside the Hilton Hotel in Silver Spring, Maryland. The occasion was two days of hearings on the safety of acetaminophen, aspirin and non-steroidal anti-inflammatory drugs such as ibuprofen. Representatives of all three camps lobbed missiles of self-serving data at one another, each asserting that its drug was safer but professing concern that unwitting consumers might go unwarned about the dangers of their competitors' products.

Deaths appear to have doubled between 1995 and 1999

Public Citizen's Health Research Group was also present to testify (see the testimony at *http://www.citizen.org/publications/release.cfm?ID=7202* or write to us for a copy). In testimony before the FDA's Nonprescription Drugs Advisory Committee, the group bunkered down at the Hilton, Dr. Peter Lurie, deputy director of Public Citizen's Health Research Group noted that the FDA had estimated that at least 57—74 percent of ingestions are intentional. Nonetheless, the FDA had framed the issue as "Unintentional Acetaminophen Hepatotoxicity," an illogical restriction of the debate that summarily excluded most overdoses from discussion. Dr. Lurie described this as "a capitulation to the notion that nothing can be done for those making suicide attempts," adding that, "This ignores the facts that many suicide attempts are impulsive 'cries for help' and most are not fatal but may leave significant residual disability." He cited data from the United Kingdom in which restrictions on the numbers of acetaminophen tablets per pack appear to have reduced acetaminophen-related overdoses, liver transplants and deaths.

Public Citizen put forward several recommendations that went well beyond the circumscribed debate the FDA wished to have. These included:

Greatly Expanded Warnings for Consumers

Current over-the-counter acetaminophen labeling is inadequate, excluding the liver toxicity warning that was recommended 25 years ago by FDA advisers. In addition to including a general warning about liver toxicity, the label should mention the early symptoms of liver toxicity and instruct patients to discontinue the drug and seek medical attention should such symp-

continued on page 5

UNSAFE DRUGS, *from page 3*

wrong doing (a power already claimed by other federal agencies, among them the Department of Agriculture, the Environmental Protection Agency, the Department of Transportation, and the Federal Trade Commission), and to require mandatory drug recalls and to be promptly notified of ones voluntarily undertaken by manufacturers.

The drug withdrawals of recent years raise real doubts about the FDA's ability to uphold safety standards in an environment where global competitiveness and industry profitability are the reigning concerns. Such incidents instill no confidence in the agency's willingness to say no to dangerous drugs of decidedly dubious value. It is Congress that, at the drug industry's behest, put the FDA in this position, and it is Congress that must investigate and undo the damage.

ACETAMINOPHEN, *from page 4*

toms appear. The symptoms of liver toxicity include: unusual tiredness, abdominal pain, or yellow discoloration of the eyes or skin (jaundice). If these symptoms develop while taking acetaminophen or any drug, you should stop the drug and contact your doctor as soon as possible. The label should also warn against the simultaneous use of multiple acetaminophen-containing products.

Pharmacists should be required to distribute FDA-approved written risk information with each new and refill prescription for acetaminophen. This type of information, known as a Medication Guide, is already required for some drugs (see the August 2002 issue of *Worst Pills, Best Pills News*).

A Reduction in the FDA-recommended Maximum Daily Dose

In unintentional adult acetaminophen-associated liver toxicity cases reported to the FDA or published in the medical literature, a total of 282 between January 1, 1998 and July 25, 2001, the median daily dose was 5 grams per day. This amount is not much above the FDA-recommended maximum daily dose for acetaminophen of 4 grams per day. This is a small margin of safety and is even smaller for those with underlying risks such as heavy alcohol use. Restrictions on daily doses should be considered by the FDA for acetaminophen.

Restricting the Number of Milligrams of Acetaminophen in Tablets

There is a relationship between the amount of drug ingested and the incidence of serious overdose and death. Because there is a practical limit on how many pills a suicidal patient can take, it would be logical to limit the maximum tablet strength to 325 milligrams of acetaminophen, the most common strength currently available. Such a restriction is likely to also benefit pediatric patients who ingest acetaminophen-containing products as well as those unknowingly taking multiple acetaminophen-containing products.

Pharmacists should be required to distribute FDA-approved written risk information

Remove Irrational Acetaminophen-containing Combinations from the Market

Much of the problem with acetaminophen overdoses stems from the absurd way in which it is sold. Manufacturers emphasize brand names over generic names in their packaging and unwitting consumers may wind up taking two or even three medications containing the drug. Approximately 25 percent of patients with acetaminophen-associated liver toxicity collected by the FDA had taken more than one acetaminophen-containing product.

Forty-nine percent of over-the-counter acetaminophen sales is in the form of combination products. Most, if not all, of these combinations are irrational. Here are just a partial list of Tylenol (Johnson and Johnson) products, some containing as many as four active ingredients: Tylenol PM, Tylenol Simply Sleep (doesn't even contain acetaminophen), Women's Tylenol, Tylenol Flu, Tylenol Cold, and Tylenol Sore Throat (regular Tylenol in liquid form). Patients (and their parents) should be encouraged to use only the active ingredient they need, not lapse into this shotgun approach to drug therapy.

Standardize Liquid Products for Children

Pediatric acetaminophen formulations confuse both doctors and parents. Cases of liver toxicity reported to the FDA or reported in the medical literature between January 1, 1998 and July 25, 2001 included 25 pediatric cases. In at least four of these, teaspoonfuls of medication were administered, instead of dropperfuls. Acetaminophen suspension contains one-third as much drug per milliliter as acetaminophen drops, ample opportunity for an unintentional overdose. All liquid forms of the drug should be required to have the same concentration, Public Citizen testified.

The great war of words ended, as many wars do, with the battlefield only minimally changed. The Advisory Committee recommended modest changes in acetaminophen labeling (Johnson and Johnson had already agreed to do this prior to the meeting, in order to ward off worse regulation), but stopped well short of the measures that would actually have had an impact (but which would have undermined the companies' sales).

It was left to the *British Medical Journal* to have the final word on the matter in its September 28, 2002 issue. A confidential draft document obtained by the *Journal* showed that FDA officials wanted the United Kingdom experience to be raised before the committee. They also sought a committee discussion of whether the "maximum tablet strength should be decreased," whether "combination products [should] be reformulated without acetaminophen," and whether there was "a need to standardize the various pediatric formulations." The *Journal* reports that these issues were removed from discussion so as not to offend Johnson and Johnson.

Product Recalls

September 5—October 9, 2002

This chart includes recalls from the Food and Drug Administration (FDA) Enforcement Report for drugs, dietary supplements and medical devices, and Consumer Product Safety Commission (CPSC) recalls of consumer products.

DRUGS AND DIETARY SUPPLEMENTS

The recalls noted here reflect actions taken by a firm to remove a product from the market. Recalls may be conducted on a firm's own initiative, by FDA request, or by FDA order under statutory authority. A Class I recall is a situation in which there is a probability that the use of or exposure to the product will cause serious adverse health consequences or death. Class II recalls may cause temporary or medically reversible adverse health consequences. A Class III situation is not likely to cause adverse health effects. If you have any of the drugs noted here, label them *Do Not Use* and put them in a secure place until you can return them to the place of purchase for a full refund. You can also contact the manufacturer. If you want to report an adverse drug reaction to the FDA, call (800) FDA-1088. The FDA web site is *www.fda.gov*.

Name of Drug or Supplement; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Benadryl Allergy/Sinus Headache Caplets co-packaged with a bonus 4 mL bottle of Visine Tears (diphenhydramine hydrochloride 12.5 mg, pseudoephedrine hydrochloride 30 mg, acetaminophen 500 mg), 24 count package; Class II; Mispackaged—promotional packages may actually contain Benadryl Severe Allergy/Sinus Headache Caplets	Lots 01222CD01, 01222CM01, 01322CD01, 01322CM01, 01422CN01, 01522CD01, 01522CN01 EXP 4/03; 2,270 boxes distributed in Arkansas; Pfizer, Inc., Vega Baja, PR. Recalled by Pfizer Consumer Healthcare R&D, Morris Plains, New Jersey
Betamethasone Dipropionate Ointment (augmented) 0.05%, 0.64 mg, 15g (0.53 oz) and 45g (1.59 oz) tubes, Rx only; Class III; Subpotent	Lots L105039 and L004054; 14,376 units distributed nationwide; Alpharma Uspd, Inc., Lincolnton, North Carolina
Correctol Stimulant Laxative Tablets and **Caplets** (bisacodyl), 5 mg; Class III; Labeling—product label does not declare inactive ingredient sodium saccharin	Numerous codes; 40,774 cases distributed in Pennsylvania, Ohio, Georgia, California and Texas; Church & Dwight Co., Inc., Princeton, New Jersey
Correctol Stimulant Laxative Tablets and **Caplets** (bisacodyl) 5 mg; Class III; Disintegration—failures at the one hour test time (stability)	Item Codes 07299-17, 07296-18 and 07300-17; 5,312,274 packages distributed nationwide; Schering-Plough HealthCare Products, Cleveland, Tennessee
Desyrel Tablets (trazodone HCL), 100 mg, 100 count bottles, Rx only; Class III; Lack of content uniformity—subpotent tablets (stability 18 month)	Lots 0M03491 and 0M03491A EXP 11/02 and Lot 0E02305 EXP 05/02; 1,857 bottles distributed nationwide; Mead Johnson & Co., Evansville, Indiana. Recalled by AmeriSource Health Services Corp., Columbus, Ohio
Halls Sugar Free Cough Drops (menthol 5.8 mg) 25 drops per bag, Mountain Menthol and Black Cherry; Class III; Product may contain metal particles	Lot 0722E EXP 2/7/04 and Lot 00832E EXP 3/8/04; 1,242 cases distributed nationwide; Parke Davis & Co. Limited, Manchester M26 2QT, England. Recalled by Adams USA Div. of Warner Lambert, a Subsidiary of Pfizer, Inc., Parsippany, New Jersey

DRUGS AND DIETARY SUPPLEMENTS *cont.*

Name of Drug or Supplement; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Liquid Oxygen, Refrigerated, transfilled into 46 liter cryogenic home vessels, Rx only; Class II; Good Manufacturing Practice (GMP) deviations, including but not limited to, lack of all batch records and use of an improperly calibrated oxygen analyzer	Serial numbers: 02182013, 01253095, 01190133, 01190112, 01190110, 02204388, 01180794, 01180787, 01180187, 01150090, 01150072; 11 units distributed in Michigan; Laurel Home Healthcare, Ann Arbor, Michigan
Listerine Essential Care Gel and **Tartar Control Toothpaste**, 0.9 oz tubes; Class III; Subpotent—active ingredient Methyl salicylate (stability)	All lots packaged as professional samples; 12,649,365 tubes distributed nationwide and in Puerto Rico; Accupac, Inc., Mainland, Pennsylvania. Recalled by Pfizer Consumer Healthcare Group, Morris Plains, New Jersey
Oxygen, Compressed, type D, E and M aluminum cylinders; Class II; Good Manufacturing Practice (GMP) deviations, including but not limited to, failure to test for purity and identity	All lots; 37 cylinders distributed in Pennsylvania; Tri-State Home Care Inc., Pittsburgh, Pennsylvania
Quinine Sulfate Tablets, 260 mg, 100 count bottle, Rx only; Class II; Tablet mixup—a bottle labeled as containing Quinine Sulfate tablets was found to also contain one tablet of Labetalol 100 mg, an antihypertensive	Lot 3001-105631A EXP 4/04; 12,000 bottles distributed nationwide; Ivax Pharmaceutical Caribe, Inc., Cidra, Puerto Rico. Recalled by Ivax Pharmaceuticals, Inc., Miami, Florida
Softsoap Antibacterial Liquid Hand Soap (with hand pump) Rainforest Series (triclosan), 7.5 fl oz (221 mL) bottles; Class III; Cross contamination with another soap product (contains undeclared ingredients: aloe vera, fragrance, glycerin, hydrolyzed silk)	SKU 127800, code dates 2134, 2135, 2136. Mixed product displays SKU 102781 code dates 2158, 2161; 19,293 cases distributed nationwide; Colgate-Palmolive Co., Piscataway, New Jersey

MEDICAL DEVICES

Device recalls are classified in a manner similar to drugs, Class I, II or III, depending on the seriousness of the risk presented by leaving the device on the market. Contact the company for more information. You can also call the FDA's Device Recall and Notification Office at (301) 443-4190. To report a problem with a medical device, call 1-800-FDA-1088. The FDA web site is *http://www.fda.gov*.

Name of Device; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Blood Glucose Test Strips (50 and 100 Count); Class II; Test strips may give false high readings	MediSense ExacTech lots 45874, 45874 and 45852; 6,241 boxes (50 test strips/box) distributed nationwide; Abbott Laboratories, Inc., MediSense Products, Bedford, Massachusetts
Contact Lens; Class III; A 2-Week Focus lens found inside carton of Focus Night and Day lens	Focus Night and Day extended wear lot 2517083; 933/six-pack cartons distributed nationwide and internationally; Ciba Vision Corp., Duluth, Georgia
LifeScan brand OneTouch SureStep Test Strip and **SureStep Pro Test Strip** used in OneTouch SureStep Blood Glucose Meter; Class II; Use of test strips may give inaccurate very low glucose results	All codes; 749,000,000 units distributed nationwide and internationally; Lifescan, Inc., Milpitas, California

CONSUMER PRODUCTS

Contact the Consumer Product Safety Commission (CPSC) for specific instructions or return the item to the place of purchase for a refund. For additional information from the Consumer Product Safety Commission, call their hotline at 1-800-638-2772. The CPSC web site is *www.cpsc.gov*.

Name of Product; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Basketball Hoops; Hoops can have a sharp protruding bolt on the player's side of the pole that can cause serious leg or body lacerations	Portable, vertically mounted; 70,000 sold nationwide from November 2001 through May 2002; Huffy Sports Company, Sussex, Wisconsin (800) 558-5234 www.huffysports.com
Battery Chargers; A manufacturing defect inside the charger can cause overheating of internal connections or external wiring, presenting a fire hazard	CT-2000 models with a serial number in the range of 030260 to 030603 and/or a day code between "Jan 01 2001" and "June 30 2002"; 200 sold nationwide from January 2001 through June 2002; Chargetek Inc., Oxnard, California (888) 453-4135 www.chargetek.com
Bicycle Handlebar Extensions; Ends can crack when tightened and come loose during use, which can cause riders to lose control of the bicycle	Forte Pro Stix; 900 sold nationwide from April through September 2002; Performance Inc., Chapel Hill, North Carolina (800) 553-8324 www.performancebike.com/help/barendrecall.html
Bobble Head Figurines; Paint contains excess levels of lead	Shaped in the likeness of NFL players; 100,000 sold in Chicago area, Northwest Indiana, Central Illinois and Rockford as part of a promotion that ran from August 19 through September 12, 2002; McDonald's Corp., Oak Brook, Illinois, and Bobble Dreams USA, Fountain Valley, California (800) 244-6227 www.mcdonalds.com
Candleholders; Candleholder can unexpectedly shatter	Giant Champagne Glass-Shaped Floating Candleholder SKU#1884160; 9,200 sold at Pier 1 stores nationwide and online from January through May 2002; Pier 1 Imports, Fort Worth, Texas (800) 245-4595 www.pier1.com
Digital Cameras; Short circuit can occur in battery compartment, creating a possible thermal burn hazard	Coolpix 2000-model, serial numbers 3010001 to 3060980 and 3510001 to 3561916; 9,100 sold nationwide from July through August 2002; Nikon Inc., Melville, New York (800) 645-6587 www.nikonusa.com
Digital Cameras; Due to a manufacturing defect, consumers using these cameras can suffer an electrical shock	Model DC5000; 75,000 sold worldwide from June 2000 through August 2002; Eastman Kodak Company, Rochester, New York (888) 793-2977 www.kodak.com
Electric Air Compressors; Capacitors can overheat, catch fire and ignite the plastic cover	Model 191000 and 192000; 3,400 sold through direct mail and nationwide from January through May 2002; Northern Tool & Equipment, Burnsville, Minnesota (800) 222-5381 www.northerntool.com
Electric Fans; Fans have undersized wiring, use a power plug that is not polarized, overheat and have an improperly sized grill, all of which could cause electrocution, electric shock, fire, and finger entrapment hazards	Top Choice models SF16BU(BE), SF16BK, DF16BU(BE), DF18, FL18, and BSD-18066; 26,000 sold in New York from April 2000 through June 2002; Thrifty Paper Co. Inc., Hempstead, New York (888) 281-3281
Electric Lawn Mowers; Component can overheat, posing a possible fire hazard	Model number CMM1000 or CMM1000R with date codes from 9534 through 200230; 140,000 sold nationwide from February 1996 through August 2002; Black & Decker (U.S.) Inc., Towson, Maryland (866) 229-5570 www.blackanddecker.com

continued on page 11

High Blood Pressure In the Physician's Office?

What You Can Do To Make Sure Your Blood Pressure Is Measured Accurately

If not treated, hypertension (high blood pressure) can lead to stroke and kidney, eye, and heart disease. Accurate blood pressure measurement is important, so that patients are not falsely diagnosed as hypertensive and prescribed unnecessary drug treatment which could be costly and have adverse effects. On the other hand, patients who are hypertensive should not be told their blood pressure is normal and miss needed therapy.

Blood pressure readings are sometimes higher only in the physician's office. This is called "white coat" hypertension, because it assumes that the patient is nervous in the physician's office and that is why the blood pressure is elevated. However, there is another possible reason for this phenomenon—faulty blood pressure measurement.

According to a review in the April 19, 1995 issue of the *Journal of the American Medical Association*, both poor technique and faulty equipment can give falsely high blood pressure readings. Listed below are some good and bad blood pressure measurement techniques that a patient could notice while being measured in the physician's office.

For accurate blood pressure measurement:

1. The patient should be sitting in a chair with her or his feet on the floor and back against the chair.
2. The arm used for measurement should be bare and resting on some support.
3. The blood pressure cuff should be at heart level.
4. The blood pressure cuff should encircle the arm *snugly* before the cuff is inflated.
5. The inflatable part of the blood pressure cuff should encircle at least 80 percent of the arm.
6. At least two blood pressure measurements from the same arm should be done during the office visit. The results should be averaged.
7. Unless the blood pressure is extremely high, blood pressure should be measured at a second office visit before a diagnosis of hypertension is made and treatment initiated.

*What are some common errors that will **overestimate** blood pressure and that a patient could notice?*

1. Placing the cuff over thick clothing.
2. Pushing a sleeve up the arm so that it restricts the blood flow to the arm.
3. Inflatable part of the blood pressure cuff does not encircle at least 80 percent of the arm (in which case, a larger cuff should be used).
4. Cuff does not fit snugly around the arm before it is inflated.
5. Back and/or arm not supported.
6. Elbow is too low, so that the cuff is not at heart level.

An error that will ***underestimate*** blood pressure and that a patient could notice is that their elbow is too high, so that the cuff is not at heart level.

By paying attention to how your blood pressure is being measured, you can help to ensure that you only receive the treatment that you need. Many physicians ask patients to monitor their blood pressure at home and record the results before treatment is started as well as after drug, diet, or exercise treatment is initiated. If home monitoring is done, then the same good blood pressure measurement techniques must be followed.

THE PUBLIC CITIZEN HEALTH RESEARCH GROUP
Health Letter

The Health Research Group was co-founded in 1971 by Ralph Nader and Sidney Wolfe in Washington, D.C. to fight for the public's health, and to give consumers more control over decisions that affect their health.

Material in the *Health Letter* may not be re-printed without permission from the Editor. Send letters and requests to HEALTH LETTER, Editor, 1600 20th St., NW, Washington, D.C., 20009.

Annual subscription price is $18.00 (12 issues). Mail subscriptions and address changes to Health Letter, Circulation Department, 1600 20th St., NW, Washington, D.C., 20009.
Our Web site address is **www.citizen.org/hrg**

Alzheimer's Disease: Major Market Here to Stay

The following is an analysis of an article by Milton Liebman appearing in the August 2002 issue of Money, Marketing, and Media, *a journal directed at the marketing departments of pharmaceutical companies.*

"*There aren't many markets with more potential reward than Alzheimer's disease (AD) offers.*" (Italics added)

This chilling, crass, commercial thought begins the article aimed at the pharmaceutical industry but which will, ultimately and unfortunately, impact the public at large. Chilling because not only are there currently no good treatments for AD but the drugs that are approved by the Food and Drug Administration (FDA) can be quite toxic and subject patients to a diminished quality of life without significant improvement in their disease.

As an example, we found that

... once physicians diagnose AD, 99 percent prescribe a drug to "treat" it

Aricept, which the author touts as "the gold standard" of AD drugs, actually appears to be little better than placebo when plotted on the full 70 unit efficacy scale, rather than the tiny 4-5 unit scale that Novartis has used in medical journal articles and the drug label. Using this method of presentation of efficacy data, physicians are easily misled into feeling that these drugs are beneficial. And caretakers, prodded by physicians and feeling they must do something, rarely say "no."

In fact, according to Liebman's article, the results of a Janssen (makers of Reminyl)-funded survey indicate that once physicians diagnose AD, 99 percent prescribe a drug to "treat" it. The article also states that a Novartis (makers of Exelon)-funded survey showed that it takes an average of about 13 months before caretakers get patients to a doctor. The pharmaceutical companies would claim that this is 13 months when decline could be slowed, but the actual benefit from the currently approved drugs is so minute as to be inconsequential.

However, this is 13 months where no drugs are being bought and so, Liebman informs us, that in an effort to get consumers to physicians' offices earlier, Novartis, along with the National Family Caregivers Association (NFCA), has begun offering free "resource kits" containing, among other things, the 10 warning signs of AD. These warning signs were determined, not by a group of specialists in the field, as one might assume, but according to the author, by another Novartis-funded survey.

Novartis uses the Harris Poll to conduct their surveys. Harris accomplishes this using an online list of chronically ill patients, a "Chronic Illness Panel," comprising 15 major disease states and 41 disease categories. Panel members either have a selected medical condition or live with family members who do. Panel members earn "HIpoints" for each new survey they complete which they then redeem for a "variety of great rewards."

Although the author states that, "Current therapy leaves a lot to be desired," this does not deter pharmaceutical industry marketing strategists from looking at the aging baby boomer population and commencing "educational efforts" aimed at both physicians and "consumers." With the current AD annual U.S. market currently worth $767 million and expected to rise, this is a very tempting target indeed. Physicians are encouraged by pharmaceutical companies to prescribe one of the four FDA-approved drugs (all acetylcholinesterase inhibitors). These drugs include Aricept (marketed by Pfizer), Exelon (marketed by Novartis), Reminyl (marketed by Janssen), and Cognex (marketed by First Horizon).

The article emphasizes the educational efforts that the pharmaceutical industry has undertaken to increase drug use, for example:

Obviously, the idea is to convince people to worry and seek treatment

"Pharmaceutical companies in the AD drug market are assisting in the task of presenting AD as a "distinct disease" and "demonstrating that it can be treated." As part of that effort, Liebman says Janssen has a Web site (reminyl.com), Novartis has two Web sites (alzheimersdisease.com and exelon.com), while Pfizer uses both a Web site (aricept.com) and direct-to-consumer advertisements which play on people's fears of "forgetfulness" and "trouble finding words;" "It could be Alzheimer's disease."

Obviously, the idea is to convince people to worry and seek treatment for themselves or relatives, yet it is not a simple matter to diagnose AD. There are a number of possible causes of dementia and memory loss, which need to be explored before deciding on a diagnosis. As this author admits, "One indication of the problem in dealing with AD is the difficulty in diagnosing it." A number

continued on page 11

ALZHEIMER'S DISEASE, *from page 10*

of written tests are used to examine mental function, but there is no laboratory test for AD; the only certain answer comes from a pathological exam of the brain at autopsy.

The author brings up an even more disturbing issue, the "determination within the last year of a condition known as mild cognitive impairment (MCI)" which the American Academy of Neurology (AAN) in cooperation with the Alzheimer's Association have concluded is a precursor of AD. An editorial in the same issue of *Neurology* as the AAN guidelines, however, asks the logical question, "In the absence of an intervention proven to improve cognition or to arrest progression, how does a subject with a diagnosis of MCI benefit?" A different article on MCI expresses concerns about the rush of pharmaceutical companies to create a new disease (and thus a new market) for the acetylcholinesterase inhibitors, especially since the dividing line between normal physiological evolution and disease are difficult to define. They worry that emphasis on an undefined "disease" will give rise to "morbid concern with occasional difficulties of no clinical importance." Yet, Liebman reports that pharmaceutical companies cannot wait and are already testing two AD drugs in people with "MCI."

The author says, "As getting older is the major risk factor for AD, we are all at risk."

We think we are at even greater risk from exposure to toxic drugs and pharmaceutical propaganda that will end up putting healthy people through unnecessary mental and physical suffering for little, if any, benefit.

OUTRAGE, *from page 12*

agency funds to the review process from other areas, including postmarketing safety surveillance. Thus, even as more drugs are approved more quickly, there is no commensurate increase in the agency's ability to monitor their safety.

The GAO report also documents that staff turnover is higher among FDA scientists than among scientists in other government agencies. Our 1998 report documented how physicians were precluded from presenting data adverse to the drugs they were reviewing at FDA Advisory Committee meetings and how they received harassing phone calls from the industry with whom they now have a "partnering" relationship, thanks to PDUFA. Even the Director of the FDA's Center for Drug Evaluation and Research, Dr. Janet Woodcock, concedes that PDUFA has "create[d] a sweatshop environment that's causing high staffing turnover."

Unwise drug approvals by the FDA, in part because of increased workloads due to PDUFA, have led to unnecessary patient deaths and illnesses and poor morale among drug reviewers. Congress should immediately conduct meaningful oversight hearings on each of the drugs that has been withdrawn for safety reasons. Drug makers have benefited from PDUFA, making millions in profits off drugs that should never have been brought to the market. The government must revert to being the sole funder of the FDA, removing private influence from the equation. (See cover story for more information on this issue.)

CONSUMER PRODUCTS *cont.*

Name of Product; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Gas Fireplaces; Design defect in gas control assembly can allow main burner gas to prematurely enter the firebox during lighting, causing glass window to shatter, presenting the risk of burns or cuts	Model 837AN and 837AP; 730 sold nationwide from September 1997 through January 2002; Valor Heating Ltd., Birmingham, United Kingdom (866) 541-0930 www.valorflame.com
Gas Grills; Product's design allows consumers to light grill at air intake tube, instead of at the burner causing gas inside air intake tube to ignite, posing a burn hazard; grills also can collapse	Red Devil; 10,800 sold at Value City and Schottenstein stores nationwide from April 2000 through July 2002; Value City Department Stores Inc./Schottenstein Stores, Columbus, Ohio (888) 278-6370 www.valuecity.com
Lithium Batteries used in electric bicycles; Batteries can overheat and pose a fire hazard	Sold with EV Global folding Mini E-Bike; 2,000 sold nationwide and by internet retailers from February 2001 through July 2002; EV Global Motors Co., North Hills, California (888) 875-4545 www.EVGlobal.com
Sewing Machines; Solder connections in the main power supply can overheat, posing a fire hazard	Designer 1; 11,000 sold nationwide from January 1999 to January 2000; Viking Sewing Machines Inc., Cleveland, Ohio (800) 446-2333

GAO Report Backs Link Between Drug User Fees and Higher Rate of Drug Withdrawals

For years, Public Citizen has decried the Food and Drug Administration's (FDA's) shoddy performance in approving questionable new drugs and then having to yank them from the market, often after dozens of people are killed or injured. In part, we have attributed this to the Prescription Drug User Fee Act (PDUFA), landmark legislation that was adopted by Congress in 1992. Under PDUFA, pharmaceutical companies pay "users' fees" to the FDA, expanding the number of drug reviewers and thereby bringing drugs to market more quickly. In return, the FDA has to complete new drug reviews within prescribed periods of time. (PDUFA assumes that many important therapeutic advances are being denied to U.S. consumers, an assertion for which there is no evidence since most drugs are, at best, minimal advances over already approved products.)

Clearly, this is a situation that invites conflict of interest. Intent on remaining in the good graces of industry, lest the industry pull the plug on the users' fees, the FDA has an incentive to lower the bar for new drug approvals.

Now comes a report from the General Accounting Office (GAO), an investigative branch of Congress, that shows that since the Prescription Drug User Fee Act (PDUFA) was implemented in 1992, a higher percentage of newly approved drugs has been withdrawn than before. In the period 1993-1996, as PDUFA was being fully implemented, the drug withdrawal rate was 1.56 percent, compared to 5.34 percent in the period 1997-2000.

These findings echo criticisms of PDUFA we have made for years. In 1998, Public Citizen conducted a survey of the FDA physicians who review New Drug Applications and found that the reviewing physicians had opposed the approval of 27 drugs approved in the previous three years (see the January 1999 issue of *Health Letter*). One result of PDUFA, said the GAO, has been the diversion of

continued on page 11