PUBLIC CITIZEN HEALTH RESEARCH GROUP

Health Letter

SIDNEY M. WOLFE, M.D., EDITOR APRIL 2001 ◆ VOL. 17, NO. 4

Latin America: the Answer to Drug Companies' Problems?

It never seems to end. Once again, U.S. researchers are proposing a study in developing countries in which poor people would receive placebos instead of proven, lifesaving therapies. And this time, the U.S. government, in the form of the Food and Drug Administration (FDA), is playing a leading role.

In April 1997, Public Citizen blew the whistle on a set of 15 research studies involving HIV-positive pregnant women in which some of the women were not given AZT, a drug that had been shown to reduce dramatically the transmission of HIV from mother to infant (*Health Letter* Vol. 14, No. 5). Instead of AZT, thousands of women were given inactive drugs called placebos. Our criticism of those studies on ethical grounds unleashed an international storm that has yet to abate; in fact, the storm has just struck a new front.

The HIV trials resulted in an attempt by the research industry to greatly weaken the World Medical Association's (WMA) Declaration of Helsinki (*Health Letter*, Vol. 15, No. 5). However, at its annual meeting in Edinburgh, Scotland in October 2000, the WMA settled upon the following language: "The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods." The WMA also explicitly rejected the notion that researchers can provide inferior care in poorer countries.

While the researchers in the HIV studies were generally government scientists or academics who were apparently committed to helping residents of the developing world, the new wave of unethical research involves the for-profit pharmaceutical industry whose motives are far less clear. Seizing upon some of the same justifications put forth by the HIV researchers ("they wouldn't have been treated anyway"), drug companies are now invading the Third World with intent to conduct research that would be clearly unethical in the U.S. The number of foreign investigators registered with the FDA grew over five-fold in the decade of the 1990s.

The latest scandal involves a biotech startup company in Doylestown, PA called Discovery Laboratories, which, in collaboration with Johnson & Johnson, manufactures an experimental drug called Surfaxin for the treatment of the often-fatal Respiratory Distress Syndrome (RDS) in premature infants. The drug belongs to a class called surfactants, which are naturally occurring compounds that help the

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Election 2000 Commentators

The following article was written by Health Letter *editor, Dr. Sidney Wolfe and appeared in the publication* Medical Marketing and Media, *a journal directed at the pharmaceutical industry.*

The election of a Republican President, after eight years of a Democrat leading the country, might seem to be good news for the pharmaceutical industry. However, the last several years of the Clinton regime have brought little but praise from the industry, which currently gives the [Food and Drug Administration] FDA the highest marks I have witnessed in the 29+ years I have monitored the pharmaceutical industry and the FDA. There are several reasons for this, including the relative silence and lack of criticism of the industry in the media, especially TV, by the current Commissioner, Dr. Jane Henney and her predecessor, Acting Commissioner Dr. Michael Friedman.

In addition, the 92 new drugs approved in 1996 and 1997 are the largest number ever approved in a two-year period, clearly the result of a lowering of the standards for approval.

Third, the August 1997 relaxing of FDA requirements for TV ads of prescription drugs has created a windfall for the most heavily advertised products whose sales have rocketed up with this massive, frequently misleading TV exposure.

The FDA's performance during the past four or five years is worse than at any time in the past 30 years

Fourth, the passage and signing by President Clinton into law of the 1997 Food and Drug Modernization Act, whose provisions concerning prescription drugs were largely crafted by the pharmaceutical industry, has made the FDA legally more friendly in a variety of ways to the industry.

What has been good news for the pharmaceutical industry, however, is not good news for patients. The FDA's performance during the past four or five years is worse than at any time in the past 30 years, worse than under Presidents Nixon, Ford, Carter, Reagan or Bush the first. Since it is hard to imagine how the FDA's drug safety record can get worse, I am optimistic enough to hope that it will actually improve, prompted in part by the extraordinary spate of drug safety withdrawals in the past several years. The Congress will be no more constructive in its FDA oversight than it has been but there may be some effort to modify the patient-endangering Dietary Supplement Health and Education Act which has crippled the FDA's ability to regulate herbs and food supplements. Negotiated prices or price controls on prescription drugs, at least for Medicare beneficiaries, will be forced onto the table as part of the consideration of a Medicare drug benefit.

LATIN AMERICA, *from page 1*

lungs to inflate. When given to premature infants, mortality is reduced by 34 percent. There are four approved surfactants on the U.S. market, selling at $1,100—$2,400 per course of treatment.

Discovery Laboratories is eager to market its drug in the U.S. because 40 percent of world-wide pharmaceutical sales occur in North America. But the company seeks to include a placebo arm in the study. One reason for this is that it is easier for the company to demonstrate that its product is better than nothing than to show that it is on a par with known effective drugs.

The company must also be well aware that the FDA has a long-standing love affair with inappropriate placebo-controlled trials. Because European regulators are more likely to accept studies in which the new drug is compared to a known effective drug (without a placebo group) as evidence of efficacy, FDA officials have been trying to persuade them to require placebo controls more often.

But, as the FDA readily admits, "Conduct of a placebo-controlled surfactant trial for premature infants with RDS is considered unethical in the USA." Indeed, the company is planning a study in Europe in which its drug is compared to an already approved surfactant, without a placebo group.

This is where the developing world comes in. The company has planned a placebo-controlled trial in Mexico, Bolivia, Peru and Ecuador, ensuring that at least a dozen infants in the placebo arm will die unnecessarily. And these wouldn't be just any Latin American infants; the company and the FDA admit that some hospitals in these countries use surfactants, so the plan is to conduct the experiment in those hospitals that don't—the race to the ethical bottom.

The FDA is currently considering whether to endorse this trial design, an endorsement the company craves if it is to gain access to the lucrative U.S. market. The issue was raised at an internal FDA meeting in late January with the all-too-revealing title: "Use of placebo-controls in life threatening diseases: is the developing world the answer?"

Public Citizen is concerned that this is just the beginning of a new trend in which the poverty of developing countries is used by drug companies and potentially the FDA to justify the provision of substandard medical care to their research subjects. The line in the sand must be drawn now.

Product Recalls

February 12—March 12, 2001

DRUGS & DIETARY SUPPLEMENTS

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

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 reasonable 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*
Advil Suspension (Children's), brand of ibuprofen, grape flavored, 100 mg/5 ml, packaged in 4 ounce plastic bottle, 36 bottles/case; Class III; Some of the product may be subpotent	Lot No. 99231; 8,640 bottles distributed nationwide; Whitehall Robins Healthcare, Richmond, Virginia
Anso Comfort Capsules, Extract of Hainanensis Merr Leaf, 200 mg, 60 capsules per bottle; Class II; Product contains the undeclared prescription drug chlordiazepoxide	Lot 0H0041 EXP 9/03 and Lot 9422 EXP 7/02; At least 6,420 bottles distributed nationwide, and in China and Canada; Numeridian, Inc., Arcadia, California
Aspirin Tablets (adult low strength) enteric coated, 81 mg, 120 unit bottles; Class III; Superpotency	Codes 0032636, 0032637, 0032856, 0032858, 0033126, 0033127, 0033129, 0033203, 0033204, 0033459, 0043676, 0043691 and 0066784; 109,716 bottles distributed nationwide; Time-Cap, Inc., Farmington, New York. Recalled by Leiner Health Products, Inc., Carson, California
Cytomel Liothyronine Sodium Tablets, 25 MCG, bottles of 100; Class II; Subpotency	Lot No. 549D16, EXP 05/01; 23,748 bottles distributed nationwide; Schering Canada, Inc., Pointe-Claire, Quebec H9R 1B4, Canada. Recalled by Jones Pharma, Inc., St. Louis, Missouri
Dilantin Capsules, KAPSEALS (Extended Phenytoin Sodium Capsules) 100mg, 100 and 1000.units bottles; Class III; Dissolution failure	Lot No. 10039F EXP 2/01, Lot No. 00299F EXP 8/01; 44,496 bottles distributed nationwide. 18 bottles sent to South Africa and Thailand; Warner Lambert (Parke-Davis), Fajardo, Puerto Rico. Recalled by PFIZER Inc., New York, New York
Hydrocortisone and Acetic Acid OTIC Solution, 1%/2%, 10 mL bottle; Class III; Degradants out of specification results during stability testing	Lot No. 22900 EXP 05/01, 22725 and 22761 EXP 02/01; 66,581 bottles distributed nationwide; Morton Grove Pharmaceuticals, Inc., Morton Grove, Illinois
Hydrocortisone and Acetic Acid OTIC Solution, 1%/2%, 10 mL bottle; Class II; Subpotency-Hydrocortisone	Lot No. 22864 EXP 05/01; 66,581 bottles distributed nationwide; Morton Grove Pharmaceuticals, Inc., Morton Grove, Illinois
Isosorbide Dinitrate Tablets, 10 mg, bottles of 270 tablets; Class II; Tablet mix-up	Lot No. 12040012 EXP 12/28/01; 3,700 bottles distributed in South Carolina, Virginia, and Kansas; Repacker: Veteran's Administration-Centralized Mail Order Pharmacy, Lancaster, Texas

DRUGS & DIETARY SUPPLEMENTS *cont.*

Name of Drug or Supplement; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Levsinex (Hyoscyamine Sulfate 0.375 mg), 100 (extended release)Timecaps Capsules per bottle; Class III; Product packaged with incorrect insert, providing incorrect description of capsules	Codes: OEO2119 EXP 1/02, OHO3126 EXP 4/02, OHO3170 EXP 5/02; 1,409 bottles distributed nationwide and Puerto Rico; Schwarz Pharma, Inc., Seymour, Indiana. Recalled by RightPak, Inc., Madison, Wisconsin
Medi-Tussin DM Cough Suppressant/Expectorant, (Dextromethorphan HBr, 10 mg/Guaifenesin, 100 mg), in 8 fl. oz. bottles; Class III; Tussin DM product mislabeled as Tussin CF on the bottles	Lots: 9HD0020 mfr. date 8/5/99 EXP 8/02, 9GD0132 mfr. date 7/15/99 EXP 7/02, 0GD0326 mfr. date 8/3/00 EXP 5/03, 9GD0369 mfr. date 8/1/99 EXP 7/02, 9HD0021 mfr. date 8/5,6/99 EXP 8/02, 0GD0379 mfr. date 8/1/00 EXP 5/03; 91,800 units distributed nationwide; Perrigo, Allegan, Michigan
Oxygen, liquid, in Cryogenic Home Units; Class III; Use of improper oxygen analyzer for identity testing	Lot and serial numbers: 120400-7 C065A86, 120400-6 S021185, 120400-7 C034K08, 120400-6 S027185; 4 units distributed in Ohio; Kern Medical Inc. doing business as Dasco Home Medical Equipment Company, Alliance, Ohio
Pancrelipase Capsules; Class II; Dissolution failure	Lot 40629 EXP 12/00; 3,125 bottles distributed nationwide; Mutual Pharmaceutical Company, Inc., Philadelphia, Pennsylvania
PremarinÆ Tablets (conjugated estrogens tablets), 1.25mg in 1,000 count bottles and 2.5mg in 100 count bottles; Class III; Manufacturer's dissolution failure	Lot 00344 EXP 08/03, 01065 EXP 02/04, 00430 EXP 10/03; 6,518 bottles distributed nationwide; Ayerst Laboratories, Div. of Wyeth-Ayerst Pharmaceuticals, Inc., Rouses Point, New York and Wyeth Pharmaceuticals Co., Guayama, Puerto Rico. Recalled by McKesson HBOC, Memphis, Tennessee
Tramadol HCL Tablets, 50 mg, bottles of 240 tablets; Class II; Tablet mix-up: Tartrate 50 mg with tramadol	Lot No. 112000TM94 EXP 11/28/01; 200 bottles distributed in South Carolina, Virginia, and Kansas; Repacker: Veteran's Administration-Centralized Mail Order Pharmacy, Lancaster, Texas

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*
Support Straps: Neoprene Knee Support with Ova Pad, Perforated Knee Splint, 3" Elastic Ankle Wrap, Universal Pelvic Traction Belt, Universal Abdominal Binder 9", Universal Rib Belt 6", Rib Belt, Clavicle Strap II, Clavicle Strap - Self Adjusting, Tennis Elbow Strap, Universal Ambidextrous Wristlet; Class II; Undeclared natural rubber in the products	All codes for products manufactured from 9/30/98 through 12/4/00; 402,742 distributed nationwide and internationally; DeRoyal Industries, Inc., Powell, Tennessee

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 *http://www.cpsc.gov*.

Name of Product: Problem	*Lot #; Quantity and Distribution; Manufacturer*
Bicycle Forks; Forks on these bicycles can break apart, causing riders to lose control and fall	Mongoose S-20 and MGX S-10 (orange) and Roadmaster Ridge Rider (red). Forks are black; 40,000 sold nationwide from June 1998 through June 2000; By Us International Co. Ltd., Taiwan and Brunswick Corporation, Vernon Hills, Illinois (877) 211-3525 www.mongoose.com
Barbie™ Sunglasses; Frames can break, allowing the petroleum distillate and floating glitter to leak out, which could be harmful to children's eyes and skin and fatal if ingested	Pink tinted eyeglasses with floating glitter in the temples and "BarbieTM" and "Mattel(r)" on the left side of the earpiece; 70,000 sold nationwide in Target, Walgreen's and Bradlee's from June 1999 through August 2000; IMT Accessories, New York, New York (800) 868-7870
Bleach; Bottles were mislabeled, containing ammonia. If mixed with bleach or acid, irritating or toxic gases could be produced	UPC Code of 11166 20961, found on the back of the label; 500 bottles sold throughout Pennsylvania, New York, New Jersey, Maryland, and Northern Virginia from January through February 2001; SuperValu Eastern Region, Richmond, Virginia (866) 376-1257
Candles; Candles can burn with a high flame, posing a fire and burn hazard to consumers	Sold in glass containers, a label on the bottom reads, "Nature's Preserves" "Home Fragrance Filled" or "Spring Hydrangea", "Trim wick to 1/4" before each lighting," "The White Barn Candle Co." and/or "Bath & Body Works"; 2.8 million sold nationwide at Bath & Body Works and The White Barn Candle Co. stores from June 1999 through January 2001; Xanadu Candle Co., Guatemala City, Guatemala (800) 395-1001
Commercial Cleaners; Some of the bottles can leak through the cap when turned on their side, allowing contents to come into contact with consumers which can cause irritation and burns to the skin and eyes	Zep Acidic Toilet Bowl Cleaner; Calcium Lime & Rust Stain Remover Grout Cleaner & Whitener; and Driveway, Concrete & Masonry Cleaner; 1.4 million bottles sold nationwide at Home Depot stores from January 1998 through February 2001; National Service Industries Inc. (NSI), Atlanta, Georgia (888) 805-HELP www.zepcommercial.com e-mail to zephelp@zepcommercial.com
Cribs (Recall to repair); Bracket hooks that are used to position the height of the mattress can break, causing the mattress to collapse	"Little Folks" cribs, made in 1998, 1999 and 2000. "Simmons" and the two-digit year of manufacture are written on a label affixed to the crib's headboard; 68,600 sold nationwide from January 1998 through December 2000; Simmons Juvenile Products, New London, Wisconsin (800) 421-2951 www.simmonsjp.com
Cross-training Shoes; Thin metal strip on the outside of the heel can protrude from the shoe and form a sharp edge that can cut consumers	Jordan Trunner LX model number 136040 and Jordan Trunner 2000 model number 136050; 225,000 pairs sold nationwide from May 2000 - February 2001; NIKE USA Inc., Beaverton, Oregon (800) 344-6453 www.nikebiz.com
Educational Games; Metal weights found in the games contain lead, presenting a poisoning hazard to children	Classification Activity Kits and Opposites Take-Home Pack; 13,000 sold to teachers and schools nationwide between January 1992 and January 2001; Lakeshore Learning Materials, Carson, California (800) 421-5354

Name of Product: Problem	Lot #: Quantity and Distribution: Manufacturer
Hairdryers; Hairdryers have undersized wiring, are not equipped with ground fault circuit interrupters, and have loose electrical connections that pose an electrocution and fire hazard	Pebco and Dubl Duck brands Black Jet 1200, Black Jet 1700, and Pebco 1500 models; 22,500 sold at beauty salons and hair care stores nationwide March 1999 through December 2000; Pebco Inc., Congers, New York (888) 391-0900
Happy Meal Toys; Antenna can break off, posing a choking hazard to young children	"Scooter Bug" with "Fisher Price" on the top of the toy; 234,000 distributed with Happy Meals at McDonalds throughout the U.S. and Canada from November 2000 through February 2001; McDonald's Corp., Oakbrook, Illinois www.mcdonalds.com.
Highchairs; Chair's legs can come out, causing the chair to fall to the ground	Model number contains "3170," "36051" or "74001" within it. First six numbers in the serial number indicate the date of manufacture. Recalled chairs were manufactured from January 1, 1995 through December 8, 1997 (010195 through 120897); 860,000 sold nationwide from January 1995 through June 1998; Graco Children's Products Inc., Elverson, Pennsylvania (800) 617-7447 www.gracobaby.com
Kids Meal Toys; Metal pins with plastic caps that attach the paddle wheel to the riverboat toy can come out and pose a choking hazard to young children	Rattling, Paddling Riverboat—red plastic with captain figure; 400,000 distributed nationwide in Burger King Kid's Meals during January and February 2001; Burger King Corp., Miami, Florida, and Alcone Marketing Group, Irvine, California (800) 661-9173 www.burgerking.com
Lighters; Lighters can leak butane when ignited, causing an excessive burst of flame, presenting a risk of fire and burn injuries	10 1/2 inches long, packaged in cardboard display sleeve under brand name "DIY"; 180,000 sold nationwide at Joann Stores, Family Dollar Stores, Bill Dollar Stores, and Hancock Fabrics from December 1998 to December 1999; Double L Inc., Charlotte, North Carolina (800) 253-1399
Nightlights; Electrical connections are loose, made from flammable plastic and the power switch does not work, posing shock and fire hazards	Different colored shades and designs, including some molded in the form of religious figures; 459,000 sold at discount stores nationwide from March 1999 through August 2000; Dura Kleen (USA) Inc., Brooklyn, New York. Call CPSC hot line for more information (800) 638-2772
Outdoor Solar Lights; Beveled lens on the solar light can act as a magnifying glass. Nearby combustible materials can catch on fire	Endura "Contempra" solar light with a beveled lens ring around the middle; 79,000 sold nationwide and through mail order catalogs from February 1998 through December 2000; Brinkmann Corporation, Dallas, Texas (800) 675-5301
Propane Cylinders; Cylinders could be overfilled, which can cause them to release flammable propane gas unexpectedly, posing risk of fires and explosions	20-pound cylinders are white, and at the time of purchase, had a red, white and blue shrink-wrapped sleeve around them with the names "AmeriGas," "Prefilled Propane Xchange" and "PPX(r)" on them; 1,600 sold in Ohio; AmeriGas Propane L.P., Valley Forge, Pennsylvania (888) 428-9779 www.amerigas.com
Toy Brooms; Paint on handles contains high lead levels, presenting a lead poisoning hazard	Ti-dee Helper brooms, 37" long with yellow wooden handle; 2,200 sold from April 2000 through February 2001; EMSCO Inc., Girard, Pennsylvania (800) 458-0839 www.emscogroup.com

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One Drug Company—Schering-Plough—Faces Massive Recalls

The following article includes excerpts of a letter Public Citizen's Health Research Group sent to new Health and Human Services Secretary Tommy Thompson on 3/1/01 regarding huge recalls that had to be done by this company, all of which have been reported in our Product Safety Alerts in previous issues of the Health Letter.

During the past 15 months, 59 million asthma inhalers manufactured by Schering-Plough for treating acute attacks of asthma had to be recalled because of dangerously sloppy manufacturing procedures which resulted in many units failing to contain the active ingredient, albuterol (brand name Proventil). We have obtained a confidential external audit by the AAC Consulting Group of Rockville, Maryland, contracted for by Schering-Plough, conducted at Schering-Plough's manufacturing facility at Kenilworth NJ, where these life-sustaining products were manufactured. This audit took place from February 28, 2000 to April 14, 2000. The auditors were extremely critical of the general attitude of management personnel who described to them "an imbalance between quality and production, leaning considerably toward production". They also found serious specific problems with the quality control of the production of the asthma inhalers such as the fact that "An in-process assay for the active ingredient in Proventil is not performed." Managers told the auditors that "aerosol products are a major money maker for the company". But, the auditors concluded, "significant manufacturing problems have been experienced with this product class, which is indicative of insufficient technical expertise and managerial oversight...."

In addition, we have obtained the summary of a very recent 31-day FDA inspection of the same plant completed January 19th of this year in which FDA inspectors found a persistence of many of the same kinds of problems with the quality of manufacturing uncovered one year ago during the private audit of Schering. The FDA investigators concluded that "The process validation for many products fails to support claims that manufacturing processes were capable of consistently producing products with the same quality, purity and safety."

We urge you to launch an investigation into criminal charges against Schering-Plough based on the possibility that the company knowingly shipped millions of the 59 million units of albuterol-containing asthma drug eventually recalled between the time the company became aware of the seriously flawed manufacturing processes and the time the recall was finally accomplished. We also urge that you investigate the company for continuing to ship other prescription drug products while fully aware of the serious violations of FDA good manufacturing practice (GMP) regulations during their production.

The current quality control problems found in that manufacturing plant during the recent FDA inspection are so serious that there has been a "temporary interruption of some production lines" and it will not be allowed by the FDA to gain approval or start shipping its new allergy drug, Clarinex, a metabolite of the active ingredient in its top-selling Claritin, which it had previously planned to ship very soon. During that inspection, FDA investigators found that "There was no assurance that the manufacturing process, parameters, equipment or protocols...conducted at multiple sites for the production of Clarinex (Desloratidine tablets, 5 mg) are equivalent or capable of producing product of the same quality." No other new Schering-Plough products will be approved until these serious manufacturing problems are resolved.

It is clear that there are an extraordinary variety of serious problems at the Schering-Plough manufacturing plant in Kenilworth, New Jersey which threaten the safety of drugs already shipped out of the facility and bespeak the need for extreme caution in allowing any further products to be shipped from that plant. We expect a prompt response to this request.

CONSUMER PRODUCTS *cont.*

Name of Product; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Toy drums; Mallet sold with the toy drum has spheres on each end that can pose a choking hazard	Little Lessons Music Makers soft drum, shaped like stuffed green crab with multicolored stuffed feet and blue stuffed claws; 5,800 sold nationwide from May 2000 through February 2001; Eden LLC, New York, New York (800) 658-8373
Water Heaters; Heaters can produce dangerous levels of carbon monoxide in the exhaust gas, which can cause serious injuries and death	AquaStar natural gas model number AQ38B NG; 320 sold nationwide from March 1997 to January 2001; Controlled Energy Corporation (CEC), Waitsfield, Vermont (800) 642-3111 http://www.controlledenergy.com

High Drug Prices For Research or Profit?

The following was written by Dr. Sidney Wolfe and appeared in the publication Pharmaceutical Executive.

According to data just released by *Business Week*, U.S. pharmaceutical industry profits for the year 2000 were $23.8 billion and the profit margin of 16.4 percent—net profits before extraordinary items divided by sales—was the highest of any major American industry, roughly two-and-a-half times greater than the 6.3 percent average profit margin for all U.S. industries. Lilly, with a profit margin of 28.15 percent, is the leader, and Bristol-Myers Squibb follows at 22.5 percent. Since the industry is rolling in money, it is hard to sympathize with its whimpers about the extent to which research will suffer when the United States joins the rest of the developed world in controlling prices as an essential part of a Medicare drug benefit.

There are several major arguments against the idea that price controls inevitably lead to a dearth of innovative research for important new treatments. The first is that the industry's profit margin is so high that, even with controls similar to those in Europe, there will still be plenty of money for R&D. If, for example, the profit margin were to fall to a "mere" 10 percent as a result of price controls—a larger decrease than is likely—annual profits would still be $14.5 billion.

Second, halting innovation is anathema to the research-based pharmaceutical industry. According to Charles Versaggi, president of a San Francisco-based marketing and communications firm for the biotech and medical industries, price controls would not plug drug development pipelines. "I don't think it would have any impact at all," he says, pointing out that more than 10 percent of most pharma companies' budgets are invariably devoted to research and development. "[Price control] issues are important, but they will not stop the industry from pursuing new drugs that are needed."

Third, although current industry research efforts are producing some truly innovative products, there is a large quota of me-too drugs that do not represent important therapeutic breakthroughs. Worse, several such products proved to be more dangerous than older ones in the same therapeutic category and were banned after injuring or killing large numbers of people. The painkiller Duract (bromfenac) and the appetite suppressant Redux (dexfenfluramine) are but two recent examples. More emphasis on breakthrough therapies would both improve the quality of pharmaceutical research and decrease the often confusing and dangerous clutter of me-too products.

The [industry's] productions of breakthrough medicines...has actually declined since 1996.

As the industry well knows, postapproval market research often masquerades as clinical research, in which pharma companies pay physicians to encourage them to use and "study" certain drugs. It is likely, if not certain, that some of that counts as part of the R&D expenditures the industry uses to justify its prices.

Fourth, as discussed in a major article in the *Wall Street Journal* last year, for reasons having little to do with adequate research funding, "The [industry's] production of breakthrough medicines...has actually declined since 1996." In that article, titled "Drug Firms, Stymied in the Lab, Become Marketing Machines," reporter Gardiner Harris stated, "Drug makers' solutions to their lab woes—raising prices and aggressively marketing—may make good business sense for individual companies, but they are politically perilous for the industry as a whole."

The major reason for the well financed lobbying campaign against pharmaceutical price controls in the United States is not, as the rapidly eroding story goes, that such long overdue and inevitable controls will harm research because pipelines currently lack many important new products. The real reason is the compelling desire to maintain the bloated profits and profit margins shown in the 2000 data and for most of the last several decades.

In maintaining high prices and in employing marketing machinery rather than developing important new drugs to make money, the industry is obeying the 1962 dictate of Nobel Prize-winning economist Milton Friedman, who said, "Few trends could so thoroughly undermine our free society as the acceptance by corporate officials of a social responsibility other than to make as much money for their stockholders as possible."

Is This Doc Deadly? His Practice Hasn't Been Perfect

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It seemed there was almost nothing that could stop Bucks County family physician Dr. Richard Paolino from practicing medicine. Not a felony conviction in 1988 for defrauding a local bank in a check-kiting scheme aimed at covering up his financial problems.

Not filing for bankruptcy in the late '80s after a failed real-estate deal had him owing his creditors some $4 million—or a second bankruptcy filing last year.

Not a 1991 sexual harassment judgment in favor of four female staffers who said that Paolino had routinely touched their buttocks and waists, had tried to feel their breasts while pinning on corsages he had bought them, had pressed against them, and had made comments like, "I bet you'd be great in bed."

Last summer, the suburban doctor's troubled existence spilled onto the streets of Philadelphia. Several pharmacists in Fishtown began seeing dozens of prescriptions from the Bensalem physician, many for the powerful painkiller OxyContin—typically given to cancer patients but increasingly popular on the street for a heroin like high.

But after the first pharmacist, Ron Hyman, contacted federal drug agents, it still took months for the authorities to move in on the doctor. They have charged that he continued to write prescriptions for months even though his license to practice medicine was suspended last fall by state authorities for failing to keep up his malpractice insurance.

In fact, authorities say that Paolino wrote at least 1,200 prescriptions for OxyContin and the antidepressant Xanax during that time—most, allegedly, to patients who paid cash and were not given physicals, some apparently to dealers who resold them on the streets of Fishtown and Kensington. This time, Paolino's alleged misconduct may have had deadly consequences.

Investigators say that a bottle of pills found in the purse of an 18-year-old Fishtown woman who overdosed on OxyContin had been prescribed by Paolino. Sources said that the doctor's prescriptions were a "significant source" of the drug in the neighborhood and that several people recently arrested were carrying prescriptions from him.

Paolino's long downward spiral raises the question: Should regulators have stepped in sooner to shut him down?

Annual surveys by the good-government group Public Citizen have consistently shown that Pennsylvania ranks near the bottom in its rate of disciplining bad doctors. In 1999, Public Citizen said, Pennsylvania ranked 36th.

Indeed, Paolino's earlier misdeeds, including the criminal conviction and the sexual harassment judgment, led to a slap on the wrist in 1993 from the state agency that regulates doctors: a reprimand and a $500 civil penalty.

Dr. Sidney Wolfe, director of Public Citizen's Health Research Group, said Paolino and doctors who commit similar offenses should be punished much more severely than they are.

"Someone like that should at least get probation, an enforceable probation, if not something more serious," said Wolfe, whose organization recently included Paolino in its book, "20,125 Questionable Doctors."

Paolino, jailed in Bucks County on $8 million bail awaiting a hearing on April 10, has maintained his innocence, telling reporters after his arrest that the reason he had written so many prescriptions was that his specialty was pain management.

"He looks forward to defending himself at trial," said Joseph Diorio, Paolino's business attorney. Paolino has not hired a criminal lawyer.

"I think he's the slime of the earth," countered Theresa Meehan, the Fishtown woman whose granddaughter, Lauren Meehan, 18, died along with her boyfriend's cousin in January after taking OxyContin.

But despite his other woes, investigators and others say there had been few significant complaints about Paolino's medical practice before last summer.

Paolino, 57, was well-known in Bensalem and continued to see some regular patients even after his office began filling up with young people, some glassy-eyed, who were paying cash to obtain prescriptions, drug agents said. Investigators say the mustached, beefy Paolino seemed to have a split personality, coming off as a kind and caring doctor to some, but seemingly nasty and mean-talking to others.

Several who knew him wondered whether his recent downslide was related to the 1997 death after a brief illness of his wife, Elaine, a former Philadelphia teacher who later worked in his practice.

"He was a nice guy," said Joy Silvi, who lived on the same cul-de-sac of stately, $1 million-plus homes amid the farm silos of central Bucks County near Newtown. She said neighbors were surprised in January when moving trucks took away Paolino's possessions—including his cars.

"It just didn't look right," Silvi said. Indeed, attorney Diorio confirmed that a bank had foreclosed on Paolino's home and that the doctor had filed for Chapter 11 bankruptcy last summer, although he said the case was dismissed in January.

It wasn't the first time Paolino had declared bankruptcy. In 1985, as Paolino was unsuccessfully seeking to convert a former school site in Warminster into a 250-unit senior citizen home, he and his wife reportedly owed creditors $4 million.

In addition, prosecutors said Paolino had taken part in a check-kiting scheme that was intended to inflate the value of his bank account as he sought a mortgage for the property and ultimately cost a bank in Bucks County $207,985.

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IS THIS DOCTOR DEADLY?,
from page 9

He was convicted in 1988 of theft by deception and sentenced to from four to 23 months in jail. *The Daily News* was unable to learn last night whether he'd served time.

Three years later, Paolino did not offer a defense against the four former female staffers who won a $254,000 sexual harassment judgment against him.

Public Citizen's Wolfe said state regulators needed to take sexual harassment allegations more seriously, noting that "the record of recidivism is horrendous."

Indeed, a woman who worked just last year at Paolino's office in a nondescript one-story medical park on Hulmeville Road in Bensalem told investigators, according to court papers, that she had quit in part "because of the sexual harassment."

But the documents say she also quit because of another problem: That Paolino was prescribing powerful painkillers, especially OxyContin, to patients—some, she claimed, as young as 15—who were paying from $49 to $66 in cash and not undergoing medical exams.

Last summer, pharmacist Hyman grew concerned when a man walked into his cluttered, 100-year-old pharmacy at Norris and Memphis streets in Fishtown with a prescription from Paolino for four 40-milligram tablets of OxyContin a day, or double the typical daily dosage.

Hyman filled it after calling Paolino's office, but shortly after an 18-year-old female holding a baby walked in with a similar prescription.

"If she was carrying a baby, obviously she wasn't in pain" Hyman recalled. This time he called Paolino directly, and the two had a heated conversation. "He said that if I didn't fill it, he'd find someone else who would."

Hyman then called federal agents, who eventually turned the case over to the state attorney general's office and Bucks County prosecutors. He said he became frustrated as the investigation seemed to drag on for months. At one point he called in Channel 10 news, but the station held the story at the urging of prosecutors seeking to build the case.

According to prosecutors, one patient told an undercover investigator in Paolino's waiting room that, "He is cool and knows what you're here for," while an informant told investigators Paolino handed him a prescription for Vicodin and Xanax as a payment for doing office repairs.

In the meantime, OxyContin, selling for as much as $20 to $40 a pill, was flooding the streets. Investigators believe the drug may have played a role in as many as 20 deaths in the Philadelphia area alone.

In Fishtown, 18-year-old Eddie Bisch, who had been a friend of Lauren Meehan, died in his sleep last month after taking half an OxyContin pill and drinking alcohol.

Two weeks later, police showed up at Paolino's office to arrest him for writing prescriptions without a license. They said they pried open the door to gain access after he refused to let them in.

OUTRAGE, *from page 12*
has moved to milk the *Journal* for cash and to do so by altering the content of the *Journal* itself. The choice of Dr. Drazen, a researcher with extensive ties to the pharmaceutical industry, as the new editor has surely bolstered the *Journal's* attractiveness to drug companies and other advertisers. Long time, highly respected national *Journal* correspondents economist Robert Kuttner and Dr. Thomas Bodenheimer, whose columns documented and sounded warnings about the increasing commercialization of health care, including the dangerous power of the pharmaceutical industry, have been asked to leave. Dr. Drazen told Dr. Bodenheimer, before firing him, that he found the prior editors' policies concerning authors' financial conflict of interests—i.e. links with the pharmaceutical industry—too strict. Dr. Drazen indicated that he wanted to make a "clean break" with such past traditions.

The *Journal's* reputation for scientific and editorial excellence, unbowed by commercial pressure, has grown for two generations under the leadership of editors Dr. Franz Ingelfinger, Dr. Arnold Relman and Drs. Kassirer and Angell. This reputation and the public's interest are now under serious threat as the new regime, apparently willing to make major concessions to the appetite of its cash cow, is moving dangerously backward. We urge you to take steps to reverse this unfortunate and destructive trend.

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To: <TOC-L@society.massmed.org>
Date: 1/11/01 3:37AM
Subject: CASH COW

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CASHCOW—Here a Moo, There a Moo

The following letter was written by Health Letter *Editor, Dr. Sidney Wolfe and Drs. David Himmelstein and Steffi Woolhandler, Associate Professors at Harvard Medical School, to Virginia T. Latham, MD, President, Massachusetts Medical Society which publishes* The New England Journal of Medicine *on 1/24/01 regarding an email they received.*

The week before last, those of us on a *New England Journal of Medicine* email list serve, which normally provides weekly announcements about the contents of the forthcoming issue of the *Journal*, received a surprising message entitled CASHCOW, see box on pg. 11. The message described a get-rich-quick publishing scheme, promising that any participant could "earn $50,000 in the next 90 days by sending e-mail."

The scheme was in no way organized by the *Journal* (it arose from CASHCOW@aol.com), and, not many hours after its dissemination to the list serve by a journal employee, the new editor, Dr. Jeffrey Drazen, apologized for this "administrative error" and promised to prevent a recurrence.

It is ironic, however, that this recent CASHCOW mistake under the *Journal's* new regime is so in tune with a more ominous, purposeful CASHCOW mistake at the *Journal*. During the past several years unprecedented conflict has roiled the relationship between the Massachusetts Medical Society and its flagship publication, *The New England Journal of Medicine*. Indeed, one member described the *Journal* as the Medical Society's "cash cow." The conflict has centered on the Society's desire to cash in on the *Journal's* well-deserved reputation for excellence by sponsoring or "cobranding" profitable subsidiary ventures, such as spin-off publications, of dubious merit. As a result, and in order to resolve the conflict, a distinguished editor, Dr. Jerome Kassirer, was fired. His able successor, Dr. Marcia Angell, was pushed out of the *Journal* after serving as the Interim Editor because of the hostile environment created by the Society. As a letter published in the *Journal* protested: "The Massachusetts Medical Society's decision to fire Kassirer because he refused to squander the *Journal's* reputation for excellence confirms my cynicism about medicine in the modern era: the only thing that matters is the bottom line."

An accident led to the *Journal's* recent email broadcast of the CASHCOW scheme. But it is no accident that the new editorial regime installed by the Medical Society

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