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Health Letter

SIDNEY M. WOLFE, M.D., EDITOR AUGUST 2000 ◆ VOL. 16, NO. 8

The Pharmaceutical Industry—To Whom Is It Accountable?

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The pharmaceutical industry is under mounting scrutiny because of rapidly increasing expenditures for drugs in the United States. Drug expenditures are now the fastest growing component of health care costs, increasing at the rate of about 15 percent per year. They account for about 8 percent of health care spending, and at their current rate of increase, they will soon surpass spending for physicians' services and, for many health maintenance organizations (HMOs), the costs of hospitalization. The increase is due both to a greater use of drugs and to higher prices for individual drugs. Patients feel drug costs keenly, because they pay much of them out of pocket. Many private insurers tightly limit drug coverage, and Medicare does not cover outpatient drugs at all.

The President and members of Congress on both sides of the aisle are considering adding some sort of drug benefit to Medicare. Discussions of this issue have drawn attention not only to the acceleration in drug expenditures, but also to the apparent capriciousness of drug pricing and other practices of the pharmaceutical industry. Americans regularly pay up to twice as much as Europeans and Canadians for the same drug. Prices also vary widely within the United States, where—perversely—they are highest for those in greatest need and least able to pay. Medicare recipients with no supplementary insurance pay on average twice as much for the 10 most commonly prescribed drugs as do favored customers, such as large HMOs and the Veterans Affairs System. For example, a month's supply of Zocor (simvastatin) was reported last year to be priced at $103.87 for Medicare recipients, as compared with $42.95 for favored customers. Chronically ill, older Americans may thus be hit with annual drug costs of many thousands of dollars—sums they simply cannot pay. There are frequent stories of older Americans who play out their prescriptions for as long as possible by taking reduced doses, or who share drugs with their spouses, or who simply do without, choosing food and heat over drugs.

The media have recently highlighted another inequity in drug access—the inability of people in the underdeveloped world to obtain the drugs they desperately need. Some underdeveloped countries, overwhelmed by the human immunodeficiency virus (HIV) epidemic and unable to afford brand name antiretroviral agents, have sought exceptions to patent protections, so that they can manufacture or import generic drugs. The pharmaceutical industry, with the support of the U.S. government, has fought these efforts. The industry has

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also been notably uninterested in developing drugs to treat tropical diseases that afflict millions of people with low purchasing power. A recent story in the *New York Times* described the reluctance of manufacturers to maintain production of drugs to treat trypanosomiasis in Africa. According to a spokesman for one of the drug companies, "The industry has never been philanthropic. It has always produced products with an aim to getting a return on investment."

How do the drug companies respond to these criticisms? First, they point out that the American pharmaceutical industry has, over the past two decades, produced remarkably effective drugs—drugs that not only extend life and improve its quality, but also save money by holding chronic diseases at bay and averting hospitalizations. High prices, according to this view, simply reflect high value. As for the fact that Americans pay more for the same drugs than people in other countries, the industry maintains that it needs to make up for the depressed prices in countries that impose price controls. Similarly, it is argued that differential pricing within the United States is justified by the need to offset the steep discounts demanded by high-volume purchasers of drugs. Supporters say that someone needs to pay prices high enough to attract the investment necessary to sustain the industry's extraordinary research and development costs. They frequently remind critics that for every drug brought to market, there are innumerable false starts—drugs that never make it. Prices reflect the development costs of not just a particular drug, but all the potential drugs that enter the pipeline.

In sum, the industry contends that it leads the world in innovative drug development because it functions in a free market where returns can be commensurate with the very great risks. Yes, drug coverage should be extended to everyone, but not at the cost of price controls or other government interference that would stifle innovation. (That is why the industry opposes a Medicare drug benefit unless it is administered through the private sector.)

The case for the pharmaceutical industry sounds reasonable, but is it valid? Some of it undoubtedly is. There is no question that the past 20 years have seen the introduction of many new drugs that have changed the face of medicine and improved the lives of millions. (Whether they have resulted in net savings from averted hospitalizations is far less clear.) But much of the case for the pharmaceutical industry is exaggerated or misleading, and some of it is simply false. Let's look at the argument more closely.

How risky is the pharmaceutical business? For a small company pinning everything on a few products, it may be immensely risky. But that is not the case for the large drug companies that dominate the market. True, their research and development costs are high, as compared with those of other industries. The top 10 drug companies are reported to spend on average about 20 percent of their revenues on research and development. (Many critics charge that marketing and promotional costs are misleadingly included in this figure.) But the pharmaceutical giants have so many drugs in the pipeline at any given time that they can count on being able to bring a certain number of drugs to market regularly.

It is instructive to compare the research and development costs of the large drug companies with their profits. The top 10 drug companies are reported to have profits averaging about 30 percent of revenues—a stunning margin. Over the past few years, the pharmaceutical industry as a whole has been by far the most profitable industry in the United States. According to a recent issue of *Fortune*, in 1999 the pharmaceutical industry realized on average an 18.6 percent return on revenues. Commercial banking was second, at 15.8 percent, and other industries ranged from 0.5 to 12.1 percent. An industry whose profits outstrip not only those of every other industry in the United States, but often its own research and development costs, simply cannot be considered very risky.

What about the picture of the drug industry as an exemplar of the free market? That image is very far from the truth. On the contrary, the pharmaceutical industry enjoys extraordinary government protections and subsidies. Much of the early basic research that may lead to drug development is funded by the National Institutes of Health. It is usually only later, when the research shows practical promise, that the drug companies become involved. The industry also enjoys great tax advantages. Not only are its research and development costs deductible, but so are its massive marketing expenses. The average tax rate of major U.S. industries from 1993 to 1996 was 27.3 percent of revenues. During the same period the pharmaceutical industry was reportedly taxed at a rate of only 16.2 percent. Most important, the drug companies enjoy 17-year government-granted monopolies on their new drugs—that is, patent protection. Once a drug is patented, no one else may sell it, and the drug company is free to charge whatever the traffic will bear.

Is it correct that the U.S. pharmaceutical industry is highly innovative? Only partly. Some recently launched drugs do indeed fill important, previously unmet medical needs. But it is hard to escape the conclusion that many other new drugs add little to the therapeutic armamentarium except expense and confusion. Consider the welter of very similar drugs to lower cholesterol levels. Developing genuinely innovative drugs is difficult and chancy. It is easier to make "me-too" drugs or minor variants of established products. To be profitable, the variation need only be sufficient to secure a new patent, and the rest is marketing. Critics believe drug companies are doing far too much of that sort of thing. They also charge that many industry-sponsored clinical trials are designed more to find small advantages that can be highlighted in promotional campaigns than to find clinically meaningful effects.

The industry has certainly been ingenious in finding ways to extend patents on its best-selling drugs. For example, a recent *Wall Street Journal* article describes a complicated business deal between Merck and Schering-Plough for the marketing of two new drug combinations, one to lower serum lipid levels and the other to relieve allergies. Each combination will pair one company's "blockbuster" drug, whose patent as a single product will soon expire, with a drug with supplementary action owned by the other company. The combination drugs will have new patents, and their profits will be shared by both compa-

nies. This may be good business, but the medical soundness of fixed drug combinations as opposed to flexible combinations of separate drugs is debatable.

The marketing budgets of the drug industry are enormous—much larger than the research and development costs—although exact figures are difficult to come by, in part because marketing and administrative expenses are often folded together and in part because some of the research and development budget is for marketing research. According to its annual report, Pfizer spent 39.2 percent of its revenues on marketing and administration in 1999; Pharmacia & Upjohn is reported to have spent about the same. The industry depicts these huge expenditures as serving an educational function. It contends that doctors and the public learn about new and useful drugs in this way. Unfortunately, many doctors do indeed rely on drug company representatives and promotional materials to learn about new and useful drugs, and much of the public learns from direct-to-consumer advertising. But to rely on the drug companies for unbiased evaluations of their products makes about as much sense as relying on beer companies to teach us about alcoholism. The conflict of interest is obvious. The fact is that marketing is meant to sell drugs, and the less important the drug, the more marketing it takes to sell it. Important new drugs do not need much promotion. Me-too drugs do.

How about the claim that the American pharmaceutical industry is the world's engine for drug innovation? The United States accounts for 36 percent of global pharmaceutical research and development. Europe accounts for 37 percent, and Japan for 19 percent. The U.S. fraction is certainly large, but not greatly disproportionate to the country's population. Innovative products come from the pharmaceutical industries of many countries, including those that regulate drug prices, and most large companies have global markets.

The pharmaceutical industry deserves recognition for the many truly extraordinary drugs it has developed. Furthermore, it is hard to imagine any other system for developing new drugs and bringing them to market. This is clearly a job for the private sector. But, in my view, an industry so important to the public health and so heavily subsidized and protected by the government has social responsibilities that should not be so totally overshadowed by its drive for profits. There needs to be a better balance between the interests of the shareholders and those of the public.

This is not the place to propose detailed reforms that might right the balance. My purpose here is primarily to describe the problems. But I would like to suggest a few steps that could be taken.

Congress should modify its enabling legislation to permit the Food and Drug Administration to require some pre-marketing trials to compare new drugs with the best available drugs, not with placebos, and to make its approval contingent on the results of those trials. In some cases, the new drug should be compared with both the best available treatment and a placebo. Requiring manufacturers to demonstrate that a new drug is substantially better than anything available would help to stem the rising tide of me-too drugs. Third party payers might also link coverage to the quality and outcome of trials, as suggested by Ray et al.

The pharmaceutical industry is extraordinarily privileged.

To consider other reforms, I believe we need an independent national advisory panel to study the pharmaceutical industry's practices thoroughly and then make recommendations. There have been such panels in the past, but the magnitude of the problems is greater now and a prominent panel would accordingly have more influence. The panel should consist of distinguished experts with no stake in the pharmaceutical industry. Although its recommendations would not be binding, they would stimulate and inform a public debate that would lead to reforms.

Among the most important questions belonging on the panel's agenda should be whether some form of price controls is desirable, and if so, how it might be implemented. This is an exceedingly difficult question that will require careful study and analysis, but in my opinion, some method of constraining prices will probably be needed. Just as public utilities are not permitted to charge whatever the traffic will bear, neither should drug companies. It is hard take seriously the inevitable industry argument that price controls would stifle innovation and frighten investors when profit margins are so great and so much revenue is spent on marketing.

The panel might also consider whether some small fraction of the industry's revenues should be set aside for social purposes. I believe it should. Such funds might be used to subsidize HIV treatment in sub-Saharan Africa or the purchase of drugs by the needy. The recent decision by five drug companies to cut the price of HIV drugs in Africa was a good but small start. There have been other generous actions by drug companies, notably Merck's 1987 decision to donate millions of doses of ivermectin to treat onchocerciasis and lymphatic filariasis in underdeveloped countries. These are examples that the rest of the industry might do well to emulate in an organized way. Drug companies should also allow exceptions to patent restrictions that currently prevent underdeveloped countries from manufacturing generic drugs for humanitarian purposes or importing drugs from the countries where they can be obtained most cheaply.

The pharmaceutical industry is extraordinarily privileged. It benefits enormously from publicly funded research, government-granted patents, and large tax breaks, and it reaps lavish profits. For these reasons, and because it makes products of vital importance to the public health, it should be accountable not only to its shareholders, but also to society at large.

Hundreds of Thousands of Workers at Risk from Hexavalent Chromium, Study Obtained Through FOIA Shows

Erin Brockovich and Public Citizen to Criticize OSHA Inaction

Public Citizen released a study in July that demonstrates more clearly than any prior research that hexavalent chromium is a potent cause of lung cancer. Lung cancer rates among plant workers exposed to the chemical in their workplaces were almost double what would have been expected among otherwise similar individuals, according to the study, which was obtained through the Freedom of Information Act. The study was funded by the U.S. Environmental Protection Agency (EPA) through a cooperative agreement with Johns Hopkins University School of Hygiene and Public Health.

"The case is closed. Hexavalent chromium is a potent carcinogen. The only remaining question is why it has taken the Occupational Safety and Health Administration (OSHA) so long to adequately regulate it," said Dr. Peter Lurie, deputy director of Public Citizen's Health Research Group.

"The results of this study were first presented publicly five years ago, yet the EPA and Johns Hopkins permitted the results to remain unpublished even as hundreds of workers unnecessarily contracted and died from lung cancer," Lurie said. "This is public health irresponsibility on a grand scale."

In a 1993 petition and a 1997 lawsuit, Public Citizen and the Oil, Chemical and Atomic Workers Union (OCAW, now the Paper, Allied-Industrial, Chemical and Energy Workers International Union, or PACE) argued that OSHA's permissible exposure limit for hexavalent chromium should be lowered from the present 100 micrograms per cubic meter (ug/m^3) to 0.5 ug/m^3.

At the press conference, Public Citizen was joined on the phone by Erin Brockovich, director of research at Masry & Vititoe, whose struggle to compensate residents exposed to groundwater contaminated with hexavalent chromium was featured in the recent movie titled "Erin Brockovich," in which Ms. Brockovich was played by Julia Roberts.

"How long must the suffering continue?" Brockovich said. "I have personally seen the suffering of chromium-exposed people. For OSHA to permit the ongoing poisoning of American workers is a disgrace."

Added Edward Masry, principal partner at Masry & Vititoe, the firm that filed a class action lawsuit seeking compensation for the chromium-exposed residents, "This new study makes OSHA's failure to adequately regulate chromium in the workplace all the more reckless."

...hexavalent chromium is a potent cause of lung cancer

Hexavalent chromium is used in the production of metal alloys such as stainless steel, chrome plating and pigments. Hundreds of thousands of U.S. workers are exposed to hexavalent chromium, particularly those in the pigment and plating industries, and in chromium production plants.

Since Public Citizen and the OCAW filed its petition in 1993, OSHA has made a series of unkept promises about when it would regulate hexavalent chromium, starting with March 1995. The current promise is to issue a proposed regulation by June 2001. The chromium industry has insisted that no regulation take place until the present study was published.

The study, to be published in the August issue of the *American Journal of Industrial Medicine*, included 2,357 men who began working at a chromate production plant in Baltimore, MD, between 1945 and 1974. Unlike previous studies, it was able to adjust for smoking status and had detailed chromium exposure data. It also had seven times as many workers, five times as much follow-up data and twice as many deaths as the previous leading study.

Workers in the study were divided into four groups, or quartiles. Workers in the third-highest exposure quartile had a risk of death from lung cancer 1.6 times higher than would have been expected for otherwise similar individuals; this quartile included the permissible exposure limit for which the OCAW and Public Citizen petitioned in 1993. Workers in the fourth quartile were 2.2 times more likely to die from lung cancer than would have been expected; this quartile included the current OSHA permissible exposure limit. The increased risk of lung cancer persisted even after controlling for other variables such as smoking and race.

"In seven and a half years in office, the Clinton administration has failed to issue a single proposed regulation for an occupational chemical," said Dr. Sidney M. Wolfe, director of Public Citizen's Health Research Group. "This is the poorest record for chemical health standards of any administration since the Occupational Safety and Health Act went into effect in 1971."

Product Recalls

June 8—July 12, 2000

DRUGS & DIETARY SUPPLEMENTS

This chart includes recalls from the Food and Drug Administration (FDA) Enforcement Report for drugs, 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*
Brethaire(r) Inhalation Aerosol (Terbutaline sulfate,) 7.5 mL, Complete Unit. Rx inhaler for relief of bronchospasm; Class II; Aerodynamic particle size failure (stability)	Lot Numbers: 1971259, 2971259 and 4971259, 3971259 EXP 11/99; 72,078 units distributed nationwide; 3M Pharmaceuticals, Northridge, California. Recalled by Novartis Pharmaceuticals Corporation, Suffern, New York
Glyburide Tablets (micronized), 1.5 mg, and 3 mg 100 tablets, Rx as an adjunct to diet to lower blood glucose in patients with non-insulin dependent diabetes mellitus (type II); Class III; Impurity failure (12 month stability testing)	Lot Numbers: 114058B EXP 10/00, 114059B EXP 10/00, 114060B EXP 10/00, 116884A EXP 4/01, 114061D EXP 4/01, 114062D EXP 4/01, 114063D EXP 4/01, 114517B EXP 5/01, and 116893A EXP 12/01; 1,386 units distributed nationwide; Novopharm, Ltd., Toronto, Canada. Recalled by Teva Pharmaceuticals USA, Sellersville, Pennsylvania
Goldline brand Acetaminophen Suppositories, USP, OTC indicated for the temporary relief of fever, ache, pains, and headaches, 120 mg and 650 mg; Class II; Misbranding—Some 650 mg (correctly labeled) suppositories were packaged into cartons labeled as 120 mg.	Lot #AL 606 EXP 9/20/02; 49,392 suppositories distributed in Kentucky; Clay-Park Labs, Inc. (CPL), Bronx, New York
Herbal Dietary Supplements: a) Zhen Qi, Herbal Extract Capsules, 500 mg capsules, in 60-unit bottles; b) Diabetes Angel Pearl Hypoglycemic Capsules, 0.5 grams per capsule, in 60-unit bottles; c) Diabetes Angel Hypoglycemic Capsules, 0.5 grams per capsule, in 60- unit bottles; Class I; Misbranded—All three products contain undeclared prescription ingredient glyburide	All lot codes; Undetermined quantity distributed nationwide and internationally; Tongyi Tang Pharmaceuticals Company, Harbin, China. Recalled by Sino American Health Products, Inc., Torrance, California
Imitrex(r) (sumatriptan succinate) Rx tablets, 25 mg, in 9-tablet units; Class III; Misbranding—Blister text incorrectly declares product strength at 50 mg (outer carton is correctly labeled 25 mg)	Lot Numbers OZP0151 and OZP0152; Approximately 37,710 units distributed nationwide; Glaxo Wellcome, Zebulon, North Carolina
Nasacort AQ (Triamcinolone Acetonide) Nasal Spray, Rx indicated for treatment of nasal symptoms of seasonal and perennial allergic rhinitis; Class III; Stability: (Super-potency) potential for patients to receive a higher dose than labeled of triamcinolone acetonide	120 metered actuations—all lots with EXP DATE 03/00 through 11/01 and 30 metered actuations—all lots with EXP DATE 03/00 through 01/02; 11,870,820 units were distributed nationwide and internationally; Rhone Poulenc Rorer Puerto Rico, Inc., Manati, Puerto Rico. Recalled by Aventis Pharmaceuticals Products, Inc., Collegeville, Pennsylvania

DRUGS & DIETARY SUPPLEMENTS *cont.*

Name of Drug or Supplement; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
a) **UriTAB(tm) Caplets** (Phenazopyridine HCL 95 mg), 30 caplet box, OTC, for urinary pain relief; b) **PremeTAB(tm) Tablets** (Acetaminophen 500 mg, Pamabrom 25mg, Pyrilamine Maleate 15 mg) 15 tablet units, OTC, for use in premenstrual discomfort; c) **PrevenTAC(tm) Caplets** (Aspirin 81 mg), 30 caplets, OTC, to help in the prevention of heart disease and heart attacks; d) **SomaTAC(tm) Caplets** (Diphenhydramine Hydrochloride 50 mg), 15 caplets, OTC, helps relieve occasional sleeplessness due to stress, anxiety, restlessness, and irritability; Class II; Products are unapproved new drugs	a) Lot #J15460; b) Lot #J15466; c) Lot #J16148; d) Lot #J15548; 856 cases distributed nationwide; Formulex Canada, Inc., Quebec, Canada. Recalled by Olus Laboratories, Farmindale, New York
Vasotec Tablets (Enalapril Maleate), 5 mg in 1,000 and 10,000 tablet bottles, Rx indicated for treatment of hypertension and symptomatic congestive heart failure usually in combination with diuretics and digitalis; Class III; Dissolution (low) failure	Lot Numbers: K0634 EXP 12/01 and K0635 EXP 12/01; 149 units distributed in Florida, Nevada, New Mexico, Texas, Arizona, South Dakota, Illinois; Merck Manufacturing Division, Division of Merck & Company, Inc., Caguas, Puerto Rico

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 Helmets; Helmets fail impact testing. Riders wearing these helmets are not adequately protected from falls, and could suffer severe head injuries or death	Pink with silver glitter, size Small; 9,000 sold at Toys R Us nationwide from October 1999 through April 2000; Cycle Express Inc., New York, New York (877)714-6117
Bicycle Helmets; Helmets fail impact testing. Riders wearing these helmets are not adequately protected from falls, and could suffer severe head injuries or death	L.A. Cruisin' various models; 70,000 sold at Kmart and Rose's stores nationwide from April 1999 through March 2000; Rand International, Farmingdale, New York (800) 338-7677
Bicycle Trailers, used to transport young children; The wheel can separate from these trailers during use, and result in crashes and injuries to children riding inside and also can cause the riders to crash and suffer injuries	Burley-Bravo™; 2,200 sold nationwide from November 1999 through June 2000; Burley Design Cooperative, Eugene, Oregon (800) 311-5294
Children's Rocking Chairs; Rear legs of the chair can separate from the rocker's base causing it to collapse	Chairs are 23" long, 13" wide and 16.5" high; 48,000 sold nationwide at Target stores from November 1999 through March 2000; Jetmax International Ltd., Stamford, Connecticut (800) 880-0714
Hedge Trimmers and Augers; Fuel tank vents on these products can leak, posing a fire hazard	Trimmer models THT-2100, 2120, 2510, 2520, 2540 and Auger model TLA-340; 7,500 hedge trimmers and 1,400 augers sold nationwide from September 1998 through September 1999; Tanaka America, Auburn, Georgia (888) 401-3885
Light Boxes; Light boxes have loose wires and lack adequate grounding, presenting fire, electrocution and shock hazards to consumers	Models LB 100, LB 101, LB 102, LB 110; 30,000 sold nationwide from June 1997 through April 2000; Apollo Presentation Products, Ronkonkoma, New York (800) 352-6853
Pacifiers; Because the latex is aging faster than normal, the nipple can detach from the shield, presenting a choking hazard to babies	Classic Patterns Cherubs & Soft Comfort; 1.8 million sold nationwide before June 2000; Playtex Products Inc., Westport, Connecticut (800) 522-8230

CONSUMER PRODUCTS *cont.*

Name of Product; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Sky Dancers® Flying Dolls; The hard plastic Sky Dancers® launching dolls can fly rapidly in unpredictable directions, and can hit and injure both children and adults	Many styles; 8.9 million sold nationwide from November 1994 through June 2000; Galoob® Toys Inc., San Francisco, California (877) 598-5599 www.galoob.com/skydancer
Shingling Hatchets; Heads on these tools can detach when in use, striking the user or a bystander and causing serious injury	13" long with "ACE" etched on tool head; 22,000 sold at Ace Hardware Stores nationwide from March 1994 through April 2000; Ace Hardware Corp., Oak Brook, Illinois (877) 223-4391
Spinning Ride Toys; Center column can break, causing a child to suddenly fall backward or be hit in the face by the broken column	Music & Lights Kidaround Spinner; 103,000 sold nationwide from July 1999 through May 2000; Today's Kids, Dallas, Texas (800) 916-TOYS
Teething Rings; When bent, these teething rings can fit into an infant's mouth and trigger a gagging reflex which poses a risk of choking and aspiration	Yellow, rabbit-shaped; 475,000 sold nationwide attached to bottles of Baby Anbesol from May 1999 through June 2000; Whitehall-Robins Healthcare, Madison, New Jersey (800) 525-2607 www3.young-america.com
Toy Baby Phone; Phones have a ball-shaped antenna which can detach, presenting a choking hazard to young children	Soft Songs Baby Phone 39100; 34,000 sold nationwide at Wal-mart from January through May 2000; Vtech Industries LLC, Wheeling, Illinois (800) 521-2010
Toy Cars; Tires can detach from wheels of these cars, posing a choking hazard for young children	Nascar Pull 'N Go Hot Wheels cars that were packed inside some Kellogg's cereal boxes; 837,000 sold nationwide from March through June 2000; Kellogg Company, Battle Creek, Michigan (800) 962-0037
Tot Wheels® Entertainer® Infant Walkers; Walkers can collapse unexpectedly during use and injure infants	Entertainer Activity Center; 31,000 sold nationwide from September 1999 through February 2000; Graco Children's Products Inc., Elverson, Pennsylvania (800) 345-4109 www.gracobaby.com
Vinyl Window Blinds; These blinds contain lead exceeding government guidelines, and do not have required labeling warning they contain lead	White miniblinds and wood grain roll-up blinds; 87,000 sold at Ace Hardware and other hardware stores nationwide from August 1999 through May 2000; Ace Hardware Corp., Oak Brook, Illinois (877) 223-4391

Report Estimates Air Lead Levels From Some Candle Wicks At Up to 36 Times EPA Standard

Lead Experts Join Public Citizen's Demand for Banning Candle Wicks Containing Lead

The July 12th issue of the *Journal of the American Medical Association* (JAMA) has just published a Public Citizen study indicating that burning lead-wicked candles can result in air lead levels in homes that are 10.1 to 36 times the U.S. Environmental Protection Agency's (EPA) standard of 1.5 micrograms per cubic meter. At these levels, children inhaling lead from candles on a consistent basis could readily reach blood levels associated with behavioral and neurological problems.

Drs. Howard L. Sobel, Peter Lurie and Sidney M. Wolfe, all of Public Citizen's Health Research Group, examined 285 types of candles from stores in the Baltimore-Washington area. Thirty percent contained metal wicks, and 10 percent of those contained lead. The measured lead content of the wicks was converted into air lead levels using calculus and was compared to the EPA standard.

On February 24, Public Citizen petitioned the Consumer Product Safety Commission (CPSC) to immediately ban and recall the millions of candles with lead wicks. Since then, more than a million candles with lead wicks have been sold in the United States. In 1974, the industry voluntarily agreed to stop using lead in candle wicks after a 1973 Public Citizen petition to ban them, but the industry resumed using lead in the late 1970s.

"This study underscores the CPSC's irresponsibility and the need for immediate regulatory action, not more dilly-dallying and caving in to industry," said Peter Lurie, deputy director of Public Citizen's Health Research Group.

Since Public Citizen filed its recent petition, it has been supported by a number of prominent experts in lead toxicity, who filed the following comments with the CPSC:

• Russell Train, administrator of the EPA during the Nixon administration: "The 1974 voluntary agreement has not proved effective. I strongly urge an immediate ban and recall. The 25 years since 1974 would seem to be ample time for the industry to take effective action."

• Dr. Philip J. Landrigan, director of the Center for Children's Health and the Environment, Mount Sinai School of Medicine, and a senior advisor on children's environmental health to the EPA: "I am writing now to urge [CPSC] to take strong and immediate action to ban all manufacture and import of leaded candle wicks in the United States. There is no defense for the persistence of this product. The industry has proven unable to police itself."

• Dr. Howard Hu, associate professor of occupational health at the Harvard School of Public Health: "I am writing in strong support of Public Citizen's petition...to immediately ban and recall all candles with lead containing wicks....I hope you will act expeditiously on Public Citizen's findings."

• Dr. Barry Castleman, environmental consultant: "I am writing to agree with Public Citizen that there is no justification for the U.S. government permitting ANY fraction of lead to be present in candles....There is simply no reason why the government should sanction the use of lead in any amount."

In addition, in a letter to Public Citizen, Dr. Herbert Needleman, professor of psychiatry and pediatrics at the University of Pittsburgh Medical Center, wrote, "It is now established that small amounts of lead can be brain damaging, and that infants and children have increased sensitivity to this poison. The only sane step is to perma-

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THE PUBLIC CITIZEN HEALTH RESEARCH GROUP
Health Letter

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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.

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Our Web address is **www.citizen.org/hrg**.

The Risks of Tranquility

The following article was printed in *Health Letter's* first year of publication and is rerun here. Unfortunately, these drugs are still around, still dangerous, and still overused.

* * *

For years, Librium, (which preceded Valium), and its sister drugs—Ativan, Centrax, Dalmane, Paxipam, Restoril, Serax, Tranxene and Xanax—have been the most prescribed drugs in the United States. Although many of these are no longer as popular as they once were, Americans continue to consume millions of tablets of these drugs and a newer one called Halcion every day. In 1984, for example, Americans filled 78 million prescriptions for these drugs. The peak use of these addicting benzodiazepine tranquilizers and sleeping pills was in 1975 when 91.4 million prescriptions were filled for these drugs. As the public and the medical profession belatedly learned about the addictive properties and other dangers of these drugs, the sales fell, "bottoming out" in 1982 but now beginning to rise slowly. Too little recognized is that because all these drugs belong to the same closely-knit chemical family, the benzodiazepines, they can be dangerous to your health.

Valium, Xanax And Their Cousins Are Addicting

Some benzodiazepines are promoted as tranquilizers; others (like Dalmane, Restoril and Halcion) as sleep aids. For whatever purpose they are advertised, they can be both psychologically and physically addictive and it is all too easy to get hooked on them. According to the Food and Drug Administration, in fact, 1.5 million Americans have taken one or more of these medications long enough to be in serious danger of addiction.

Just how long is long enough is not entirely clear. What is known, however, is that benzodiazepine addiction sends thousands of people to hospital emergency rooms each year and that it is because they have become hooked on benzodiazepines that at least 4,000 Americans annually enter addiction treatment centers for the first time.

The manufacturers of these drugs stoutly maintain that the chances of addiction are minimal if they are used at the recommended dosages and for no longer than specified by the informational leaflets (known as package inserts) the companies provide to physicians. However, scientific studies suggest otherwise. With the passage of time, there has been growing evidence that benzodiazepine dependency can occur even if the manufacturers' instructions are followed to the letter and that, indeed, some patients get hooked on even low doses of benzodiazepines in as little as three or four weeks.

One might suppose, as some benzodiazepine manufacturers have claimed, that it is chiefly the "abuse-prone"—people who have long-standing emotional or psychological problems who are at greatest risk here. Again, it doesn't seem to work out that way. Anyone who takes a benzodiazepine at the high end of the recommended dose range or anyone who takes it for a month or more at *any* dose can get hooked. That being the case, Health Research Group is strongly in favor of using benzodiazepines very sparingly, if at all. And Health Research Group is not alone.

For example, Drs. Jose Catalan and Dennis H. Gath—both of the Oxford University Department of Psychiatry—ran an interesting experiment. In the experiment half of a group of patients with minor affective (mood) disorders such as anxiety, depression and insomnia, were randomly assigned treatment with benzodiazepines. The rest of the patients with the same complaints were chosen by lot to get brief counseling instead. Although the counseling took no more of the doctors' time or the patients' than the benzodiazepine therapy, the rate of improvement in the two groups—both at one month and at seven months after treatment—was the same.

Similarly, another study looked at what happened when patients going to the offices of a surgeon, an internist or an obstetrician-gynecologist were treated for anxiety with either Valium, one of two other benzodiazepine tranquilizers or a placebo (dummy pill).

Weekly evaluations were made both by the patients themselves and by professional evaluators with neither the patients nor the evaluators knowing at the time who was getting which type of medication. At the end of a month, it turned out that all four treatments—including treatment with the dummy pills—were equally effective.

Said another way, it was not whether or not the patients had taken a benzodiazepine that made them feel better, but the opportunity the study had given them to talk with someone about their anxiety that gave them relief.

Nonetheless, there are some doctors—and good ones—who sometimes

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CANDLE WICKS, *from page 8*

nently ban lead-containing candles from the market."

In the time since the Public Citizen petition was filed, New Zealand has joined Australia in banning lead-containing wicks.

"These countries are leading the way in protecting their children from the well-known dangers of lead," said Dr. Sidney M. Wolfe, director of Public Citizen's Health Research Group. "Voluntary bans do not work. This has been proved once again by the CPSC's failure to take appropriate regulatory action in this case."

On April 21, 1997, President Clinton signed an executive order requiring all federal government agencies to account for the unique biological susceptibilities of infants and children when setting standards and regulations.

"It is the height of hypocrisy for the Clinton administration to, on the one hand, issue high-minded proclamations on child safety, while at the same time allowing lead, a known and preventable hazard to their health, to continue to poison them," Dr. Wolfe said.

VALIUM, *from page 9*
prescribe benzodiazepines to counter muscle spasm, for the relief of anxiety or to help their patients through occasional sleepless nights. If your doctor is one of them and you want to take Valium or some other drug in this family, play it smart by asking the physician to write *No Refill* on the prescription and to order the pharmacist to give you no more than 20 pills.

Both of these requests to your doctor are for your own protection. Twenty pills of a benzodiazepine are typically enough for about seven days of use; too short a period for there to be much risk of addiction. And with the addition of the *No Refill* stipulation, you will not have the opportunity to refill the prescription several times without seeing a doctor should you find yourself beginning to crave how the tablets make you feel.

Most importantly, however, urging your doctor to put limitations on your prescription for benzodiazepines is a signal to him or her that coping with your anxiety is your first priority and that you in no way just want to let the situation ride without re-evaluating it soon and at regular intervals.

In the meantime, you can facilitate the process by doing some evaluating on your own. At the end of the first day and the end of every day you take any of these medicines, review for yourself what you have done—by yourself or by talking with others—to find out what is making you anxious so you can alter the internal or external circumstances that are to blame.

Keep a record of these evaluations. And as soon and as often as possible, in consultation with your doctor, try reducing the amount of benzodiazepine you are taking.

But what if this advice comes too late and you suspect you may already be hooked on Valium or one of its close relatives? How can you tell?

Some of the warning signs of benzodiazepine addiction are:

- Feeling that you can't cope without the pills or that you're not at your best unless you take them every day.

- Needing to take more pills as time goes on to get the same effect and taking higher doses than your doctor prescribed.

- Being unable to quit.

When you are physically dependent on Valium, quitting suddenly can make you downright sick. You feel tense and can't sleep, and you may go on to develop a full-blown withdrawal reaction—shakiness, headache, nausea, vomiting, changes in sensation, and at times, hallucinations or seizures. When you resume taking Valium, the symptom usually go away within 24 hours.

Withdrawal symptoms are a very serious danger sign. If you are physically addicted to benzodiazepines, you should taper off these drugs gradually and under a doctor's care. Do not attempt to quit cold turkey or on your own; it is always dangerous and can be fatal.

Other Hazards of Benzodiazepines

As if it weren't bad enough that benzodiazepines can be addictive, they also can have other adverse effects. Feeling drowsy, for example, is to be expected when taking these drugs and they also often take their toll on memory, learning and attention span. Moreover, some people, instead of being calmed by these medications, become very hostile from using them and fly into attacks of rage.

Particularly important is that benzodiazepines interfere with muscular coordination, so that you should not drive or operate other powerful machinery when under their influence. And speaking of being under the influence, benzodiazepines and alcohol are an especially dangerous mix.

These two "downers" potentiate each other. Thus an overdose of benzodiazepines alone or in combination with alcohol, or, for that matter, barbiturates and certain other drugs (see below) can be fatal.

Worth mentioning, too, is that benzodiazepines can cause profound confusion, particularly in the elderly who may then be falsely diagnosed as senile.

Many doctors recommend that these drugs not be prescribed for people over 65. At the least, older people should take only half the usual dose. And if you have narrow angle glaucoma or serious lung disease—chronic bronchitis, for example—benzodiazepines are not for you, whatever your age.

Other people who should not take these drugs or, at least not without bringing it to the attention of their doctors, are those on a variety of other medications. These medications include: antidepressants, antihistamines, barbiturates, narcotics, psychiatric drugs, anticonvulsants (epilepsy drugs), and non-benzodiazepine tranquilizers.

Tagamet (cimetidine), a best-selling drug for ulcers and Antabuse for the treatment of alcoholism should not be used in combination with any benzodiazepines except Ativan or Serax.

Also avoid the use of benzodiazepines in combination with three drugs widely prescribed for Parkinson's disease. Benzodiazepines can make these three drugs—Larodopa, Levodopa and Sinemet—less effective.

Finally, although this is by no means an exhaustive list of the dangers of these drugs, some cautions for women of childbearing age. If you are (or may be) pregnant, taking benzodiazepines may increase the risk of the child's having birth defects. Besides, use of these drugs near delivery has been linked to the so-called floppy baby syndrome. Infants with this syndrome are weak, suck poorly and may have serious breathing problems. Continuous use of benzodiazepines in late pregnancy can cause infants to suffer from withdrawal symptoms as newborns.

Valium and other benzodiazepines also get into mothers milk. A nursing infant whose mother is taking any of these drugs will be groggy and, over time, may eat poorly and lose weight.

OUTRAGE, *from page 12*

duce the incidence of hip fractures (the most serious consequence of osteoporosis) by 50 percent. The CBS reporter described the results as "almost miraculous." None of the stories cited the actual rates, or absolute risk, of hip fractures in the alendronate treated patients (1 percent) and in the group of women receiving an inactive placebo or dummy drug (2 percent), an absolute difference of one percent. Only one network mentioned the gastrointestinal (GI) adverse effects of alendronate. None of the three stories disclosed that the study investigator being interviewed had received money from alendronate's manufacturer, Merck & Co.

Medical conferences, such as the one that spurred the alendronate hype in 1996, are prime sources of news, and drug companies make an effort to attract journalists. Results of clinical studies are often presented at medical meetings as summaries, or abstracts, before the results are published as full length journal articles that have been peer reviewed. These study summaries do not contain enough detail about how the study was conducted to determine if the results are valid or relevant. In some medical disciplines, only about one-half of the study summaries presented at meetings are ever published as full-length, peer-reviewed journal articles, yet too many health professionals and some in the news media accord study summaries the same weight as full-length articles that have been through the peer and editorial review processes.

The summary of the alendronate clinical trial described above was published as a full-length article in the British medical journal *The Lancet* on December 7, 1996, six months after the TV coverage. This study is known as the Fracture Intervention Trial, and goes by the name FIT.

The results of the FIT trial provided evidence that women who have had at least one vertebral fracture (a type of fracture of bones comprising the spine that may go unnoticed by the woman) and take alendronate for three years can reduce their risk of hip fracture from two percent to one percent, or a relative reduction in risk of 50 percent. Alendronate can cause severe ulceration of the esophagus (the tube connecting the mouth to the stomach).

News coverage of drugs can include inadequate or incomplete information

The FIT trial left unanswered the question of alendronate's effect in reducing the risk of all types of fractures, including hip fractures, in the largest group of postmenopausal women—those who have not experienced a vertebral fracture. When this question was answered with publication of the second part of the FIT trial in the December 23/30, 1998 *Journal of the American Medical Association,* interestingly these results went almost totally unnoticed by the news media.

We covered this study in the February 1999 issue of *Worst Pills, Best Pills News.* Over the four-year duration of this part of the FIT study, alendronate did statistically reduce the risk of women developing one or more new vertebral fractures. In women taking the placebo 3.8 percent developed one or more vertebral fractures, while in those taking alendronate 2.1 percent experienced a vertebral fracture. This is an absolute risk difference of 1.7 percent (3.8 percent minus 2.1 percent). We also calculated the number of women that would need to be treated with alendronate for four years to prevent one vertebral fracture. This number is 58, meaning that 57 women taking the drug would receive no benefit from it and would only be exposed to its risks.

Overall, for all types of fractures including vertebral, hip, and wrist, there was no difference between alendronate and the placebo in protecting women from fractures. When the FIT study researchers grouped the number of fractures according to the women with the highest and lowest bone mineral densities some unexpected results were found for wrist and hip fractures. Ironically, the risk of wrist fracture was increased in women taking alendronate, though not by a statistically significant amount. The drug was of no benefit in preventing hip fractures—the most devastating type of fracture a woman can experience—in women with the highest bone mineral density. In women with the lowest bone mineral densities, there were 11 women taking alendronate who suffered hip fractures, while there were only six fractures in women receiving the placebo. This last finding requires more research before any conclusions can be drawn.

Drug companies exercise tremendous influence over the information they allow to see the light of day, and what you see is the good news, while the negative news goes unreported, unless there is a catastrophe.

What You Can Do

Even if you are on a salt-free diet, take news reports about drug innovations (especially reports of the "breakthrough" kind) with a grain of salt. You cannot rely on media reports of studies about new drugs presented at medical meetings to gauge the therapeutic value of new drugs. Likewise, media reports of full-length medical journal articles may be erroneous because of the reporter's lack of full understanding of the subject matter.

Erroneous and Misleading Reports In Media About Prescription Drugs

A study published in the June 1, 2000 *New England Journal of Medicine* found that news coverage of drugs can include inadequate or incomplete information about risks, benefits, and costs as well as the financial conflicts-of-interest between persons interviewed for stories and the drug companies sponsoring the research.

The researchers analyzed coverage of three drugs: (1) the cholesterol-lowering drug pravastatin (PRAVACHOL); (2) alendronate (FOSAMAX), a heavily hyped drug for osteoporosis; and (3) aspirin for its use to prevent cardiovascular disease. A sample of 180 newspaper stories, 60 for each drug, and 27 television reports that appeared between 1994 and 1998 were examined. These 207 reports came from 36 newspapers and four TV networks. In total, 27 (13 percent) were on TV, 53 (26 percent) in national newspapers like *USA Today* and *The Wall Street Journal* and 127 (61 percent) in other newspapers.

Of the 207 stories, 83 (40 percent) did not report benefits quantitatively. Of the 124 that did, 103 (83 percent) reported relative benefits only, three (2 percent) the absolute benefits only, and 18 (15 percent) both absolute and relative benefits (the importance of reporting both relative and absolute benefit will be covered below). Only 98 (47 percent) of the 207 stories mentioned potential adverse drug reactions and only 63 (30 percent) mentioned costs. Of the 170 stories citing an expert or a scientific study, 85 (50 percent) cited at least one expert or study with a financial tie to a manufacturer of the drug that the study's authors had learned about because the tie had been disclosed in the scientific literature. These ties were disclosed in only 33 (39 percent) of the 85 news-media stories.

The authors of the study gave an example to illustrate their findings. On the evening of May 22, 1996, ABC, NBC, and CBS TV news programs carried stories about alendronate, provoked by a medical conference at which the results of a randomized, controlled trial were presented. The three network stories reported only the relative reduction in risk, saying that the new osteoporosis drug could re-

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