PUBLIC CITIZEN HEALTH RESEARCH GROUP

Health Letter

SIDNEY M. WOLFE, M.D., EDITOR OCTOBER 2001 ◆ VOL. 17, NO. 10

Health Care Reform Coming? Don't Bet the Farm On It

On the federal agenda for this fall is a shakeup of the nation's admittedly sick health care system, specifically Medicare. But what are the chances of anything truly curative coming out of the current mess? As one cynic is supposed to have remarked about the future, "In the short run I am pessimistic; in the long run we are all dead."

The trouble we are in on the health care front is vividly illustrated in a new report from Congress' General Accounting Office (GAO) on the subject of Medigap insurance, a relatively recent federally authorized patchwork of voluntary programs to supplement Medicare, the rudimentary health plan for seniors created early in Lyndon B. Johnson's administration. In the 36 years since Medicare's creation, supplementary health benefits for the elderly have become a major industry with, today, more than 10 million customers and an annual gross income of over $14 billion.

Where does Medigap stand now, at the start of a new century, and what does it do and (more importantly) fail to do? The GAO took a look at the situation and painted a not-very-pretty picture for legislators to contemplate in the months ahead. Whether anything remedial will come out of the next session of Congress depends on a lot of factors including the allegedly compassionate conservativism of "Landslide George," the willingness of legislators to act in the interests of ordinary citizens, and—of course—the influence of lobbies, notably those of the insurance and pharmaceutical industries.

Doesn't look good, eh? Well, read on and consider what will happen in the future if the present, GAO-documented situation is allowed to continue with a predictable—even inevitable—increase in the relative size of the senior segment of the American body politic.

The subhead to GAO's Medigap insurance report is, "Plans are widely available but have limited benefits and may have high costs." People reaching the age of 65 these days find themselves between a rock and a hard place: a basic government-sponsored health benefit (Medicare) that isn't anywhere near adequate for the average elderly person's needs, and a voluntary supplemental program (Medigap) that often costs more than a retired person can pay.

If you don't get sick after Medicare kicks in at age 65 and, in the end, die quickly and quietly, the basic program is fine. But if you start falling victim to the infirmities of advancing age, and run up against a growing need for prescription drugs, basic Medicare benefits are totally inadequate. In a nutshell, Medicare Part A (which all

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beneficiaries get without additional premium cost) pays for "inpatient hospital care, skilled nursing facility services following a hospital stay, hospice care, and certain home health services," according to the GAO report. For $50 a month extra, deducted from your Social Security payment, you can get Part B, "which helps pay for selected physician, outpatient hospital, laboratory, and other services," GAO goes on, "[but] beneficiaries are also responsible for part B deductibles, coinsurance, and copayments."

Something's missing here, however: except for drugs that are administered in the hospital under Part A or drugs which require administration by a health care professional (such as injectables), pharmaceuticals are not covered by Medicare. That, notably, is where Medigap comes in, albeit inadequately in most cases. Of 10 federally authorized Medigap plans, only three offer some kind of outpatient prescription drug benefit, and these have comparatively few takers.

"When Medicare was started in 1965, nobody worried about covering prescription drugs because they were so minor compared with the cost of doctors and hospitals," says *Washington Post* health columnist Abigail Trafford. "Today, drugs are as costly and important as surgery.

"That's why it's time for Medicare to cover outpatient drugs as a basic element in the standard medical benefits package," she continues. "People over 65 represent about 12 percent of the population, but they use one-third of all the prescriptions. Many have supplemental health policies to cover drugs. One-third have to pay for their drugs out-of-pocket."

The idea of including prescription drugs in Part A of Medicare is one that the drug lobby hates as the devil hates holy water. Just as the bean-counters of privately owned health maintenance organizations (HMOs) try to hold down drug costs by substituting generics for brand name medications whenever possible, a federal Centers for Medicare and Medicaid Services (CMS)—the new name for the old Health Care Financing Administration—would certainly clamp price ceilings on drugs dispensed under a reinforced Medicare Part A. And if HMOs are regarded as the proverbial 600-pound gorilla by drug makers, under this sort of Medicare reform CMS would be seen as King Kong himself.

The mushrooming cost of pharmaceuticals is forcing a major crisis on the country

The GAO report focuses not only on the problems and shortcomings of Medigap nationally, but also takes a sharp look at state-by-state variations in the supplemental program. Like so much in America today, the way Medigap is administered makes a mockery of the Pledge of Allegiance's words, "one nation indivisible." An act of Congress in 1990 set up 10 Medigap benefit packages (effective July 1992) that individual states could offer or not, as they saw fit. Three states (Massachusetts, Minnesota and Wisconsin) were grandfathered out of the new arrangement because they already had standardized Medigap plans of their own.

The result, conceived as a way of bringing uniform coverage to the Medicare area, turned out to do just the opposite, the GAO report shows. In 1999, the average annual premium per "covered life" under the standardized plans was $1,185 for the nation as a whole, ranging from $706 in Utah to $1,600 in (where else?) California. Multiply these figures by two and you have the out-of-pocket cost to a senior couple. And these are only average figures that do not truly reflect the high cost of drug benefits because 92 percent of seniors enrolled in Medigap plans in 1999 did not opt for the prescription feature, the GAO report shows.

As the Medigap industry has grown, the number of participating insurers has expanded over the years in almost all states and in almost all the types of plans they offer seniors. Guess which plans are the exceptions: that's right, the ones offering prescription drug

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THE PUBLIC CITIZEN HEALTH RESEARCH GROUP
Health Letter

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

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Unsafe Drugs: Congressional Silence Is Deadly

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

Over the past decade, Congress has abdicated its constitutional responsibility to oversee the performance of the Food and Drug Administration in protecting the public from dangerous drugs. In fact, not one subcommittee with jurisdiction over the FDA has held a single oversight hearing on FDA's handling of 13 drugs that were pulled from the market for safety reasons since 1992: the infamous diet pills Pondimin and Redux; the antibiotics Omniflox and Raxar; the anti-hypertensive Posicor; the antihistamines Seldane and Hismanal; the painkiller Duract; the diabetes treatment Rezulin; the heartburn reliever Propulsid; the irritable bowel pill Lotronex; the anesthetic Raplon; and, most recently, the cholesterol-lowering medication Baycol.

Although these withdrawals inspired spirited debate in the press and medical literature on FDA's drug safety standards, Congress has been sitting idly by, determined not to question whether the FDA could have prevented the immense human suffering inflicted by these dangerous products.

The weight reduction drugs Pondimin and Redux alone make the point. Removed from the market in 1997, Pondimin and Redux generated the most massive wrongful conduct litigation against a pharmaceutical manufacturer in American history. As a result, American Home Products (AHP) Corp. has taken an unprecedented total charge of $12.25 billion to pay claims arising from scores of deaths and hundreds of thousands of personal injuries.

Meanwhile, all four juries that have returned verdicts in these diet drug cases have granted huge awards to victims after reviewing internal AHP documents and hearing testimony from company representatives. However, much of the evidence raises as many questions about FDA's conduct as it does about AHP's.

For several years Pondimin's labeling acknowledged only four cases of pulmonary hypertension, a devastating lung disorder with more than a 50 percent mortality rate. Yet the company knew by mid-1994 of 41 cases; by mid-1996 it knew of 62 cases. Was the FDA aware of this drastic underreporting? If not, why not? If it did know, why didn't the FDA demand truthful labeling, as federal law requires? Despite Congress' oversight duty, no subcommittee has bothered to investigate the diet drug disaster.

It wasn't always this way. For decades, few, if any, agencies found themselves more subject to congressional scrutiny than the FDA. In fact, massive pharmaceutical litigation, such as that involving the catastrophically defective Dalkon Shield IUD, was often built on congressional revelations. In 1973, for example, a House subcommittee chaired by Rep. L. H. Fountain (D-NC) held hearings on the dangers of the Dalkon Shield. Years later, the manufacturer, A. H. Robins, was forced to establish a $2.475 billion trust fund to compensate tens of thousands of Shield victims.

From the mid-1960s through the 1980s, Congress was an integral link in assuring drug safety. Meticulously reconstructing FDA's review processes by probing countless case histories of inadequate or misdirected regulation, examining thousands of documents, and interviewing agency personnel and others, congressional investigators repeatedly revealed significant weaknesses in FDA's drug review processes.

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benefits.

More and more it is becoming obvious that the mushrooming cost of pharmaceuticals is forcing a major crisis on the country. *Washington Post* columnist Trafford acknowledges that some new drugs are justifiably expensive, citing one that costs in the thousands of dollars per dose, but this medication is rarely administered—to "only 163 patients in the United States last year," she points out.

Such drugs are typically used in a hospital setting and thus are largely covered by basic Medicare. Far more seniors suffer from chronic conditions that do not require hospitalization and thus do not come under the basic Medicare umbrella: hypertension, arthritis, diabetes and other age-related disorders. Trafford cites a reader's message about her elderly mother with Alzheimer's disease who "spends about $1,000 a month out-of-pocket for all her different prescription drugs."

The GAO document does not go into the numerous instances of sharp practice, deceit and even criminality within the medical industry that have come to light in the *Health Letter* and elsewhere (that would not be politic in a report to a closely divided Congress), but the underlying truth is in there somewhere. Whether the legislators to whom the report is addressed will pull up their socks and do something about what may be America's No. 1 need—health care for all—is a question for the future to answer.

And as the man quoted at the opening of this article said, "In the short run I am pessimistic; in the long run we are all dead."

The anti-arthritis drug Oraflex is an example. In approving it for sale in 1982, the FDA was unaware of six reports in its own files of serious liver and/or kidney disease in patients in whom the manufacturer, Eli Lilly, had tested it. Three months after the FDA approved the marketing of Oraflex, reports linking it to liver and kidney failure forced Lilly to withdraw it.

Sometimes it has even been congressional investigators who have alerted the FDA to significant violations of the drug safety laws. In the 1980s, this happened with Oraflex and later, when the late Ted Weiss (D-NY) took over the subcommittee led by Fountain, with Merital, an antidepressant. In both cases, Congress informed the FDA that Lilly and Hoechst AG had not made required timely reports to the FDA of numerous deaths and serious adverse reactions. Subsequently, the government successfully criminally prosecuted both companies.

But over the past decade, Congress has dropped drug safety from its radar screen. As this has been a bipartisan dereliction of duty, it is far from clear that resumption of Democratic control of the Senate will usher in an era of renewed congressional attention to the safety of new drugs. Drug safety oversight began to decline in the 1980s, while the Democrats controlled the House, and had all but disappeared entirely by the early 1990s, well before the Republicans took control of both the House and Senate.

Over the decade ending last December 31, the pharmaceutical industry's investments in politicians totaled nearly $49 million. The share going to Republicans has increased by nearly 50 percent, rising from 52 percent during the 1991-1992 election cycle, when Democrats still ran the House, to 77 percent during the last election cycle, several years into Republican control of both sides of the Capitol.

Yet the $49 million does not begin to approach what the industry spends to lobby federal policymakers. From January 1997 through June 2000, pharmaceutical companies spent a staggering $322 million lobbying Congress and the President. In the 1999-2000 election cycle alone, the drug industry spent over $177 million on lobbying, by far more than any other industry—in fact, substantially more than the oil and gas, tobacco, auto, and food processing and manufacturing industries combined. So it can hardly come as a surprise that Congress has supplanted oversight with incessant nagging of the FDA to hurry the approval of new drugs. This is exactly what the drug industry wanted—and paid for.

Beginning in 1992, Congress authorized the FDA to take drug company subsidies, called user fees, to hire approximately 600 additional persons to review marketing applications. Since then, nearly all so-called Congressional "oversight" of drug regulation has been designed to justify even swifter drug approvals.

It is far from clear that resumption of Democratic control of the Senate will usher in an era of renewed congressional attention to the safety of new drugs

In 1997, Congress capped this industry-inspired effort by enacting "modernization" legislation lowering the barriers to approval of new drugs, partly with "fast track" procedures. "No area of FDA responsibility has been more closely scrutinized by Congress" than the "speed" with which new drugs are approved, Deputy FDA Commissioner Michael A. Friedman told a House hearing in 1997. "We heard the messages," he testified. That was an understatement. From 1996-2000 the FDA approved a record 184 new drugs while substantially reducing the time taken to review the evidence of safety and effectiveness in their marketing applications. In 1999, then-FDA Commissioner Jane E. Henney appeared before Congress, not to report on what the agency had done to protect the public in compliance with the drug safety laws, but to boast how the agency "enhances U.S. competitiveness in global markets, provides a level playing field for industry, and strengthens the domestic economy as a whole by inviting increased foreign investment . . ."

Understandably, this speed-up has increased the burdens on FDA's already indefensibly understaffed office responsible for monitoring the safety of marketed drugs. The FDA only has 10 professionals trained as physicians or epidemiologists to assess the safety of all of the thousands of medicines now being sold, including increasing numbers of often hastily cleared drugs marketed in recent years. The FDA's Senior Associate Commissioner, Linda Suydam, protested in 1999 that the agency is "increasingly hard-put to monitor adverse events reports, which for drugs alone have tripled in the last 8-9 years."

Congress has caved to the demands of the pharmaceutical industry by prohibiting the FDA from spending user fees for monitoring drug safety or any purpose other than reviewing marketing applications. Thus the FDA finds itself clamped in a vice made on Capitol Hill. While pressuring the FDA to approve new drugs in record numbers, Congress simultaneously denies its safety monitors the resources required to meet the increased burdens these very new drugs impose.

The task of meeting congressionally imposed performance goals has created, in the words of Janet Woodcock, FDA's drug office director, a "sweatshop environment that's causing high staffing turnover." Congress' willful neglect of drug safety oversight would be disturbing enough if approvals of new drugs were proceeding at a normal pace. But the pace is frantic in a "sweatshop" scrambling to meet stringent time goals in the face of escalating

workloads. This is an environment that breeds neglect of safety concerns.

Indeed, based on information that has trickled into the public domain, a number of medicines, in addition to Pondimin and Redux, cry out for Congress' informed and sustained attention. For example, in March 2000, the FDA requested Parke-Davis, a unit of Warner-Lambert, to remove Rezulin from the market because of its deadly liver toxicity. Congress has ducked any inquiry into FDA's delay in taking this step when at least nine other safer diabetes drugs of presumably comparable effectiveness were available for use. The FDA approved Rezulin on a "fast track" basis in 1997 over the opposition of medical officer John L. Gueriguian, who objected to its adverse effects on the liver and heart. His review was purged from FDA files. Why? By whom?

As evidence of Rezulin's exceptional toxicity to the liver mounted, some FDA medical professionals strongly opposed continued marketing of the drug. Moreover, the agency freely acknowledged that periodic liver monitoring eventually recommended for patients on Rezulin could not protect them from serious and even fatal liver failure. Why did FDA senior managers ignore all this?

In the midst of revelations, particularly by Pulitzer Prize-winning investigative reporter David Willman of the *Los Angeles Times*, of severe internal agency strife over management's handling of this hazardous drug, what was Congress' response? While warning FDA Commissioner Henney in a letter in March 2000 not to retaliate against a medical reviewer who had vociferously advocated immediate market withdrawal of Rezulin, a powerful House Committee chairman hastened to emphasize that "I take no position on the merits of the Rezulin controversy," thereby ensuring no blemish on Congress' record of studied avoidance of drug safety matters. However, when it came to FDA's apparent hesitation to approve a new colorectal cancer therapy, that same chairman just one month later felt no compunction about questioning the FDA "on the merits" as he pressed the agency to justify "why" this drug "was not approved . . ."

Massive pharmaceutical litigation, such as that involving the catastrophically defective Dalkon Shield IUD, was often built on congressional revelations

Like Rezulin, the nonsteroidal anti-inflammatory drug (NSAID) Duract was withdrawn from the market by the Wyeth-Ayerst Laboratories unit of AHP due to its liver toxicity. In 1995, an FDA medical officer had concluded that Duract causes liver damage more than do other NSAIDs. Yet the FDA approved Duract two years later, although 19 other NSAIDs were already on the market. Why? Congress didn't want to know.

In March of this year, Organon removed its surgical anesthesia drug Raplon from the market after it was implicated in numerous reports, including five deaths, of bronchospasm, a condition in which lung air passage muscles go into spasm and force the airways shut. In August 1999, an FDA physician noted that an alarmingly high 10.9 percent of adult and geriatric patients administered Raplon from a newly reported data set of clinical trials experienced bronchospasm and cautioned that the frequency of this side effect "may be greater than originally suspected." Yet, just two days later, the FDA approved the drug with labeling listing bronchospasm as occurring in a mere 3.2 percent of clinical trial patients, less than one-third the rate suggested by these studies. Why did the FDA rush to approve Raplon in the face of disturbing new revelations about its safety, to say nothing of letting Organon downplay the drug's risks to physicians? No congressional panel has called the FDA to account for its regulation of Raplon.

The antihistamine Seldane was known to cause potentially lethal heart rhythm abnormalities years before it exited the market in 1998. Hoechst Marion Roussel, the drug's manufacturer, also eventually produced Allegra, a breakdown product of Seldane considered responsible for the drug's antihistamine effects which apparently does not cause such disturbances. Why did the FDA delay seeking a ban on Seldane until it had approved Allegra, since the market already contained at least one other one-a-day non-sedating antihistamine without this nasty feature? Needless to say, Congress never confronted the FDA with this or any other question about its regulation of Seldane.

For decades the FDA was commonly heralded as the world's premier drug safety regulatory authority. But no more is this true. Even a widely respected commentator like Richard Horton, editor of the prestigious British medical journal, *The Lancet*, has decried how the FDA "has become the servant of industry." His call for "an independent congressional audit of the FDA's drug approval processes," if recent history is any guide, is likely to fall on deaf ears.

Certain drugs that remain on sale have also raised troubling safety issues, as shown by their regulatory history. Congress has also turned a blind eye to these issues. One such drug is Pharmacia & Upjohn's sleeping pill Halcion. In the early 1990s, the media reported that summaries of Halcion clinical studies sent to the FDA prior to approval understated Halcion's adverse behavioral effects, as reflected in raw data submitted to the FDA two decades earlier. The FDA's counterparts in several countries, including the United Kingdom, banned Halcion. But the FDA decided to permit the drug to stay on the market.

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Product Recalls

August 18—September 10, 2001

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

DRUGS & DIETARY SUPPLEMENTS

The recalls noted here reflect actions taken by a firm to remove a product from the market. Recalls may be conducted on a firm's own initiative, by FDA request, or by FDA order under statutory authority. A Class I recall is a situation in which there is a 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*.

Class I Recalls

Name of Drug or Supplement; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
MSM Eye and Nasal Drops, 1 fl. oz., OTC eye and nasal drop containing methylsulfonylmethane; Microbial contamination (Pseudomonas mendocina/Klebsiella pneumoniae)	All lots and codes; 44,000 bottles distributed nationwide, and in Puerto Rico and American Samoa; Allure Cosmetic, Inc., Hayward, California. Recalled by All That's Natural II, Inc., Gardena, California
MSM Eye Drops, 1 fl. oz., OTC eye and nasal drop containing methylsulfonylmethane, packaged under the brand name "UB Ultra Botanicals MSM Eye Drops," manufactured for: Ultra Botanicals, Inc., Los Angeles, California; Microbial contamination (Pseudomonas mendocina/Klebsiella pneumoniae)	All lots and codes; 18,026 bottles distributed nationwide; Recalled by Allure Cosmetic Inc., Hayward, California and Ultra Botanicals, Inc., Los Angeles, California

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UNSAFE DRUGS, *from page 5*

In 1992, in a stunning admission to *The New York Times*, Dr. Alan Lisook, then a senior FDA investigative official, conceded that the agency has no good way of determining when clinical study summaries submitted by pharmaceutical manufacturers misrepresent underlying patient safety data. It is difficult to overstate the significance of such an admission. It strikes at the very heart of FDA's ability to assure that the clinical trial summaries upon which it bases its approvals completely and accurately reflect the experiences of study patients receiving new drugs.

In 1996, a chairman of a House oversight subcommittee with jurisdiction over the FDA publicly chastised the FDA for delays in submitting an agency task force report on Halcion. But neither he nor anyone else on Capitol Hill has held a hearing on this revelation or, for that matter, on any issue raised by the international controversy surrounding Halcion.

There is no telling how many additional matters of great urgency could be unearthed and revealed about the safety of withdrawn as well as marketed drugs by congressional investigators unfettered by confidentiality barriers to government and industry files and armed with subpoena power to hear from the many conscientious FDA employees who would help such an investigation. Yet, whether motivated by an aversion to alienating its benefactors in the pharmaceutical industry or by a determination not to risk even the slightest possibility of public backlash against the hurry-up approval agenda it has imposed on the FDA, Congress has assiduously avoided even the pretense of overseeing drug safety regulation.

Although the pharmaceutical industry and the legislators beholden to it will bitterly resist informed, unshackled investigations of drug safety regulation, it is long overdue for both Republican and Democratic leaders of the House and Senate to call for investigations of the pressure filled drug approval "sweatshop" Congress itself was instrumental in creating. To delay any longer is to further endanger public health and safety with a continuing flow of drugs which should not have been approved and are banned only after leaving a path of unnecessary death and human suffering in their path.

Name of Drug or Supplement; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Alupent (metaproterenol sulfate) Inhalation Solution, 0.4% (10mg/vial) and 0.6% (15mg/vial), packaged in 25 X 2.5 ml Unit-Dose Vials, under the Boegringer Ingelheim label, and **Metaproterenol Sulfate Inhalation Solution**, 0.6% (15mg/vial) generic brand, packaged in 25 X 2.5 ml Unit-Dose Vials, under the Roxane Laboratories label; Class II; Lack of assurance of sterility	Lot numbers and EXP dates: Alupent 0.4%: 057144 7/02, 780508 5/02, 780507 4/02, 780506 3/02, 780505 2/02, 780503 12/01, 780502 10/01, Alupent 0.6%: 690552 11/02, 690551 8/02, 699554 10/01, Metaproterenol Sulfate 0.6%: 992862 10/01; 662,650 vials distributed nationwide; Roxane Laboratories, Inc., Columbus, Ohio. This firm is part of the Boehringer Ingelheim Corporation
Antacid (liquid—regular and maximum strength) packaged in 1-gal. jugs and 12-fl. oz. bottles, each 5-ml. tsp. contains 200-mg. or 400-mg. aluminum hydroxide, 200-mg. or 400-mg. magnesium hydroxide, and 20-mg. or 40-mg. simethicone. Packaged and distributed in 12-fl. oz. bottles under the following labels and sizes: York Antacid Liquid with Simethicone Antacid—Anti-Gas Original Flavor, 1-gal. container, Lot 0006052; ShurFine Fast Acting Antacid Anti-Gas Original, 12-fl. oz. bottles, Lot 0003018; Dollar General Regular Strength Fast Acting Antacid Liquid Antigas/Antacid Original, 12-fl. oz. bottles, Lot 0006052; Smart Choice Liquid Antacid Plus Simethicone, 12-fl. oz. bottles, Lot 0006052; Class II; Total aerobic microbial count failures and lack of preservative effectiveness testing	Lot numbers and EXP dates: 0003018 and 0003048 EXP 3/02, 0006052 and 0006092 EXP 6/02; Approximately 3,553 cases of 12 oz. bottles and 267 cases of gallon jugs were distributed in Oklahoma, Mississippi, Missouri, Maryland, California, Oregon, Arkansas, North Dakota, New York and Ohio; York Pharmaceuticals, Inc., Kansas City, Kansas
Clonidine HCl, in bottles labeled as containing 1, 5, or 25 grams per bottle; Class II; Current good manufacturing practice deviation—production records do not correspond to amounts of product distributed	Lot UC99021002, packaged 02/99, CAS: 4205-90-7 and Lot UC99021002A, CAS #4205-91-8; 176 bottles distributed nationwide; Hawkins Chemical Inc., Minneapolis, Minnesota
Cortizone 10 Plus (1% hydrocortisone) Cream, 1 and 2 ounce tubes; Class III; Contamination: product is cross-contaminated with the firm's Ben-Gay product (methyl salicylate, menthol, and camphor)	Lot numbers 2400453, 2400452 and 2400470 EXP 7/02; 441,336 tubes distributed nationwide; Pfizer, Inc., Parsippany, New Jersey. Recalled by Warner Lambert Consumer Health Care/Pfizer, Inc., Morris Plains, New Jersey
Dynabac Tablets, delayed release (Dirithromycin) 250 mg, 10 and 60 count; Class III; Related substance test failure at stability (12 month)	Eight different lots; 189,892 bottles distributed nationwide; Eli Lilly and Company, Indianapolis, Indiana
Fluocinolone Acetonide Ointment, 0.025%, in 15 gram and 60 gram tubes, distributed under the E. Fougera & Co. Label; Class II; Lack of homogeneity leading to super-potency	Lot G018 EXP 1/03; 47,731 tubes distributed nationwide; Altana Inc., Hicksville, New York
Lithobid (Lithium Carbonate) Slow-Release Tablets, bottles of 100 tablets, 300 mg. tablets; Class III; Dissolution failure	Lot 90574, EXP 7/01; 14,480 units distributed nationwide; Solvay Pharmaceuticals, Inc., Baudette, Minnesota
Lorazepam Tablets, 0.5mg, packaged as 30 tablets per 'bingo' card, 140 cards per case; Class III; Container defect—the plastic material used to repackage the individual tablets is de-laminating	Lot 18291 EXP 5/31/03; 10,588 cards distributed nationwide; Geneva Pharmaceuticals, Broomfield, Colorado. Recalled by Heartland Repack Services, Toledo, Ohio
Overtime Stimulant Tablets, 200 mg caffeine, sold in 100 and 500 count bottles; Class III; Stability, there is no data to support labeled expiration date	Lot numbers 6085 EXP 7/01, 10362 EXP 2/03; 125 bottles distributed in Indiana; Nittany Pharmaceuticals, Inc., Milroy, Pennsylvania
Perphenazine Tablets, 2mg, 4mg, 8mg, and 16mg strengths, packaged in 100 and 500 bottles; Class III; Tablet discoloration	Numerous lot numbers; 50,000,000 tablets distributed nationwide; Zenith Goldline Pharmaceuticals, Northvale, New Jersey

DRUGS & DIETARY SUPPLEMENTS *cont.*

Name of Drug or Supplement; Class of Recall; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Tegretol Tablets (carbamazepine), 200 mg; Class II; Dissolution failure	Lot 232E9126, bottles of 1,000 tablets; 3,238 bottles distributed nationwide; Novartis Pharmaceutical Corp., Suffern, New York
Vanceril 42 mcg (beclomethasone dipropionate) Inhalation Aerosol, 16.8g -200 metered actuations per canister; Class II; Potency—Lack of assurance that canisters/product can meet specifications (high or low)	Lot numbers 1-AMA-202, 1-AMA-203, 1-AMA-204 and 1-AMA-205 EXP 2/03; 322,644 canisters distributed nationwide; Schering Corp. Kenilworth, New Jersey
Vioxx 50 mg Tablets (Rofecoxib Tablets), solid oral dosage form, bottles of 100; Class III; Mislabeling—product fails to declare container is a bulk package not intended for dispensing and not child resistant	Lot numbers and EXP dates: J9310, J9311, J9312, J9313, J9314 11/01; K2013, K2014 8/01; K2015, K2016, K2021, K2022, K2036 3/02; K2026, K2031, K2033, K2034 5/02; K2037, K2708, K2709, L3164, L3165, L3166, L3174 11/02; L3175, L3176, L3179, L3180, L3181 1/03; L3182 2/03; 622,427 units distributed nationwide; Merck Sharp & Dohme Quimica de PR (Arecibo Pharmaceutical Operation), Arecibo, Puerto Rico
White with Blue Specks Caffeine Tablets, 150 mg., 100 count and 500 count bottles. The label states manufactured for: Pittsburgh Pill Emporium, Pittsburgh, PA or Casey's Distributors, Williamsport, PA. The Casey labeled product is only for the 100 count size; Class III; Stability—there is no data to support labeled expiration date	Lot #6076 EXP 2/02; 142 bottles distributed in Pennsylvania; Nittany Pharmaceuticals, Inc., Milroy, Pennsylvania
Yellow Rockets Tablets, 200 mg Caffeine, in 100, 250, and 500 count bottles; Class III; Stability—there is no data to support labeled expiration date	Lot 10293 EXP 2/03; 1,083 bottles distributed in Iowa; Nittany Pharmaceuticals, Inc., Milroy, Pennsylvania

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*
Insulin Pump (Animas R1000); Class II; Infusion pumps may have defective vents causing unintentional dose of insulin	Numerous codes; 239 units distributed nationwide; Animas Corporation, Frazer, Pennsylvania
Insulin Infusion Pump; Class II; Claim of waterproofing was not cleared	H-TRONplus V100; 30,000 patients using the pump nationwide; Disetronic Medical Systems, St. Paul, Minnesota
Pride Jazzy Scooter; Class II; Tire exploded	Model numbers: 1100, 1104, 1120, 1170, PHC1; 61,510 units distributed nationwide, and in England, Brazil, China, Belgium, Italy, Murcia, and Australia; Pride Mobility Products Corp., Exeter, Pennsylvania
Revo Scooter; Class II; Scooter drive system may engage while parking brake is inactive	Models: SC60RRED, SC60RBLU, SC60RYEL; 1,152 units distributed nationwide and in Canada; Shanghai Global Fabtech Plastic Products, Shanghai, China

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*
Children's Cargo Pants; Toggle on the pockets of the pants can break off, posing a choking hazard	"Koala Baby" or "Little Legends" in navy, khaki, or stone color with an elastic waistband and drawcord; 7,000 sold at Kids "R" Us, Babies "R" Us, and Toys "R" Us stores nationwide from June through July 2001; Kids "R" Us and Babies "R" Us, divisions of Toys "R" Us Inc., Paramus, New Jersey
Dollhouse Furniture Sets; Yellow paint on the furniture contains lead, which can present a risk of lead poisoning	Bathroom furniture—packaging for the set reads "Little Tree," "Distributed by Target Corporation," and "MADE IN CHINA"; 10,000 sold at Target Stores nationwide from August 2000 through June 2001; XL Machine Ltd., Eden Prairie, Minnesota (866) 746-8097 www.target.com
Infant Carriers/Slings; Welds of the metal rings that support the carriers/slings can break, posing a fall hazard to young children	Sold in a variety of colors, prints, and sizes. A large white label sewn in the slings reads in part, "MAYA WRAP" and "HECHO EN GUATEMALA"; 5,000 sold nationwide from January through July 2001; Maya Wrap, Omaha, Nebraska (800) 501-9979
Oil Lamps; Glass can shatter when lit, posing a fire and laceration hazard	Rectangular and square designs; 16,000 sold at Discovery Channel stores and The Nature Company stores nationwide from September 1999 through July 2001; The Discovery Channel Store, Inc., Berkeley, California (800) 752-1937 www.shopping.discovery.com
Propane Camping Lanterns; Insufficient connection between the lantern and the propane cylinder can allow gas to escape and ignite unexpectedly, posing a potential fire and injury hazard	Ozark Trail and Wenzel models; 290,000 sold nationwide at Wal-Mart from January 1999 through August 2001; Wenzel Co., St. Louis, Missouri (800) 325-8368 www.wenzelco.com
Recumbent Bicycle Suspension Forks; Link pins in the forks can fall out, causing the rider to lose control of the bicycle	FX and RX models serial number starts with "F" and is followed by five digits or starts with "B" followed by one character and six digits; 1,400 sold nationwide from December 1999 through August 2001; BikeE Corp., Corvallis, Oregon (800) 231-3136 www.bikee.com/recall
Skateboard Helmets; Helmets failed required impact testing. Riders wearing these helmets are not adequately protected from falls and could suffer head injuries or death	Black, blue and white with the name "World Industries" printed on the chin strap, the back of the helmet, and the inside padding. Yellow and blue cartoon characters appear on the sides; 10,000 sold nationwide from October 2000 through May 2001; World Industries Inc., Huntington Beach, California (888) 338-4562
Strollers; Lock mechanisms, found on both sides of the stroller, can break and cause the stroller to suddenly collapse	LiteSport model 36122; 115,000 strollers sold nationwide from December 1997 through December 1999; Kolcraft Enterprises, Inc., Chicago, Illinois (800) 922-2130
Toys; Toys can break causing small balls to be released, posing a choking hazard	Two PC Tambourine Set, Bathtime Water Wheel, Funny Loco Wind-Up, Pull Back Duck in Boat; 110,000 sold at dollar stores nationwide from September 1999 through May 2001; STK International, Los Angeles, California (800) 536-7855

OUTRAGE, *from page 12*
lected by the American Association of Poison Control Centers (AAPCC) which shows that there was a sharp increase from 1997 through 1999 in the number of adverse event reports for these highly pharmacologically active and dangerous drugs masquerading as "dietary supplements."

FDA Analysis of FDA Adverse Event Reports

The recently updated review of FDA's Center for Food Safety and Applied Nutrition's (CFSAN) Special Nutritionals Adverse Event Monitoring System (SN/AEMS), including data collected from January 1993 until February 2001, shows that ephedrine alkaloid dietary supplements are associated with more reports of deaths, myocardial infarctions, cardiac arrhythmias, hypertension, stroke and seizure events than all other dietary supplements combined. According to the FDA analysis, during this interval there were:

- 3,308 adverse events for all dietary supplements, 1,398 of these (42 percent) for the ephedrine alkaloids (EA);
- 137 reports of death, 81 deaths (59 percent) associated with EA;
- 38 reports of myocardial infarction/ heart attack, 32 reports (84 percent) associated with EA;
- 98 reports of cardiac arrhythmias, 62 (63 percent) associated with EA;
- 144 reports of hypertension, 91 (63 percent) associated with EA;
- 85 reports of stroke, 69 (81 percent) associated with EA; and
- 121 reports of seizure, 70 (58 percent) associated with EA.

Two earlier FDA-commissioned reviews of a much smaller number of adverse events reported to the FDA involving the use of ephedrine alkaloids (did not include data from 2000 and 2001) confirmed the cardiac toxicity of these chemicals. The first study found that 47 percent of cases involved the cardiovascular system (17 cases of hypertension, 13 with palpitations or fast heartbeat, 10 strokes). There were also 7 reports of seizures. The second study, by our co-petitioner Dr. Ray Woosley of the University of Arizona, found that of the 104 reports in which causation by ephedrine alkaloids was very likely, there were 10 cases of sudden death, 9 cardiac arrhythmias, another 23 possible arrhythmic events, 3 heart attacks, 10 cases of chest pain and 15 severe strokes.

FDA Analysis of AAPCC Data

The second source of data about ephedrine alkaloids is a recent FDA analysis of data collected by the American Association of Poison Control Centers (AAPCC), which clearly shows that the number of serious adverse events associated with ephedrine alkaloid dietary supplements is on the rise. The total number of adverse events related to EA increased from 211 in 1997 to 407 in 1999, an increase of 196 reports, almost a doubling from the number of reports in 1997.

Between 1997 and 1999, AAPCC reports of central nervous system adverse events with ephedrine alkaloid dietary supplements increased 19 fold from 11 to 211. Cardiovascular adverse events increased 2.4 fold from 85 to 204, while gastrointestinal adverse events doubled from 70 to 140.

Underreporting Flaws Result in Fewer Adverse Events

The seriousness of the underreporting to the FDA database is demonstrated by the fact that there were a total of 1,398 adverse event reports with ephedrine alkaloid dietary supplements in the FDA database during an eight year period (1993-early 2001), but there were 876 ephedrine alkaloid dietary supplement adverse event reports to the AAPPC database in just three years. Furthermore, the Texas Department of Health reported approximately 500 adverse events in the period between December 1993 and September 1995. The fact that in under two years a single state could collect over a third as many ephedra adverse event reports as SN/AEMS has gathered between January 1993 and February 2001 speaks to the pitiful inadequacy of the current FDA system. Furthermore, dietary supplement labeling does not include instructions on how to contact either the FDA or the AAPCC which increases the likelihood of underreporting of adverse events. When both of these limited monitoring systems indicate that a product is causing hundreds of adverse events, thousands of consumers are likely being affected.

Cardiovascular Complications of Ephedrine Alkaloids Use

Randy Sasich, M.D., the son of our colleague Larry Sasich, Pharm D., MPH, was in an internal medicine residency at Barnes-Jewish, the main teaching hospital of Washington University in St. Louis. Within just a seven-month period, he took care of two patients admitted to the coronary care unit because an ephedrine alkaloid dietary supplement (Metabolife) had induced life-threatening cardiac arrhythmias. He is aware of a third patient, also discussed below, who used Metabolife and experienced an arrhythmia but was not hospitalized:

Case 1—April 1999. This patient, a female in her late 50s, presented at the emergency room with a dangerously rapid rate of contractions of one of the large chambers of the heart, or ventricles (ventricular tachycardia or V-tach), after using an ephedrine alkaloid dietary supplement for weight control. She was admitted to the coronary care unit for observation. She was subsequently discharged.

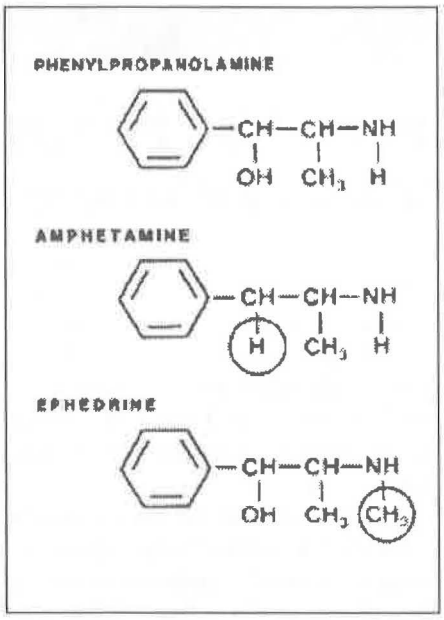
Case 2—April 1999. This patient, a female in her late 30s, suffered a heart attack (acute anterior myocardial infarct) and cardiac arrest while using an ephedrine alkaloid dietary supplement for weight control. She was a smoker but had no evidence of previous atherosclerotic disease of any significance. She suffered brain damage due to a lack of circulation.

Case 3—October 1999. A female nurse, age unknown, experienced a rapid heart rate while using an ephedrine alkaloid dietary supplement. The rapid rate was documented by her colleagues using an electrocardiogram (ECG or EKG). She was observed until her rapid rate resolved.

These three cases of cardiac injury from ephedrine alkaloid dietary supplements in one hospital in only seven months are further indication that ephedrine alkaloid toxicity is a much more common problem than the FDA and AAPCC data indicate.

The AAPCC data show 416 ephedrine alkaloid dietary supplement related cardiovascular adverse events reported between 1997 and 1999. According to the SN/AEMS data, the most common manifestations of injury were hypertension, stroke, arrhythmia, chest pain, and palpitations.

The chart on this page shows the close chemical structures of PPA, ephedrine and amphetamine. Notice that PPA is identical to ephedrine except for the absence of a methyl (CH_3) group. In fact, the body metabolizes a small portion of ephedrine to PPA which is also called norephedrine (nor meaning no methyl group).



Central Nervous System Complications of Ephedrine Alkaloid Use

The AAPCC data report at least 364 neurologic adverse events associated with the use of ephedrine alkaloids in the period between 1997 and 1999. Compared to *all* other dietary supplements combined, ephedrine alkaloid dietary supplements were responsible for the majority of reports of seizures, personality disorders, sleep disturbances, and headaches in the FDA database (SN/AEMS). The literature also describes cases of agitation, hallucination, seizures, psychoses, and mania. As with the arrhythmia reports described above, all psychiatric manifestations resolved after the offending agent was removed.

Some women reported continued use of ephedra-containing products despite adverse effects due to withdrawal symptoms such as fatigue and weight gain. Furthermore, 7 out of 36 users described frank ephedrine dependence. The sale of ephedrine alkaloid dietary supplements for the indications of weight loss and energy boosting almost guarantees a pattern of abuse. Since many consumers of dietary supplements consider them to be natural, and hence safe, a certain element of informed consent is lost when users are not properly educated about the likelihood of developing chemical dependence. This possibility is of particular concern in light of the increased risk of cardiovascular and central nervous system injury described above.

Conclusions

The wide range of adverse events associated with the consumption of ephedrine alkaloids demonstrates a significant and unreasonable risk of illness and injury. Especially because these risks are not balanced by any long-term benefits, it is imperative that you act quickly and decisively to prevent future death and injury. This problem is exacerbated by the underreporting of ephedrine alkaloid dietary supplement use to physicians by patients, and by health care professionals to national data collection authorities. The April 2001 report of the Department of Health and Human Services Inspector General revealed that voluntary data collection methods currently available to the FDA are woefully inadequate, and fail to account for 99 percent of all adverse events associated with dietary supplements. The problem of underreporting is multifaceted and is beyond the scope of this petition. Even with the limited data available via the SN/AEMS, AAPCC, and the medical literature, it is clear that ephedrine alkaloid dietary supplements present an unreasonable risk of illness *and* injury to American consumers. It is your responsibility to act upon our recommendation to remove ephedrine alkaloid dietary supplements from the market. Failure to do so will surely result in increased death and injury due to an unsafe product that has no proven benefit to consumers.

We expect a rapid response to this urgent petition. From the perspective of defending the public health, you must be willing to take on this drug (ephedra)-pushing part of the dietary supplement industry.

* * * *

Consumers can report adverse experiences with prescription drugs, nonprescription drugs, medical devices, and dietary supplements to the Food and Drug Administration's Office of Emergency Operations by telephone at 301-443-1240 or over the Internet at *www.fda.gov/medwatch/report/consumer/consumer.htm.*

Do Not Use Ephedra

This Is a Dangerous Substance and Should Be Taken off the Market

The following are excerpts from a letter sent in September to Health and Human Services (HHS) Secretary Tommy Thompson by Dr. Sidney Wolfe, Health Letter *Editor*

The Public Citizen Health Research Group, representing 135,000 members, petitions the Food and Drug Administration (FDA) to ban the production and sale of dietary supplements containing ephedrine alkaloids. These dietary supplements include, but are not limited to, those containing ephedra, ephedra extract, and ma-huang. The grounds for FDA action are that these products present "a significant or unreasonable risk of illness or injury under conditions of use suggested or recommended in the labeling" or, if the label is not specific, "under ordinary conditions of use." Therefore, under 21 USC 331(a) and 342 (f) HHS must declare these products adulterated and issue an immediate ban on their sale and production.

You are known to be extremely concerned about food safety and these dangerous "food supplements" pose a clear threat to the safety of the food supply in this country for those who use them. Among the frequent targets of these ephedrine-containing products are young people for whom they are being promoted as athletic performance enhancing. Due to the gravity of the situation, the Canadian equivalent of the Department of Health and Human Services, Health Canada, recently issued a public advisory in June 2001 "warning consumers not to use products containing the herb Ephedra." Health Canada based its decision to release the advisory, in part, on the United States' FDA adverse event reports. We urge you to immediately issue a similar advisory warning Americans not to use ephedra-containing dietary supplement products while you review our petition for the ban requested above.

We have obtained an internal FDA analysis of recent adverse event reports to FDA's own database that demonstrates that the ephedrine alkaloids are the most lethal and otherwise dangerous dietary supplements. We also obtained an FDA analysis of data col-

continued on page 10