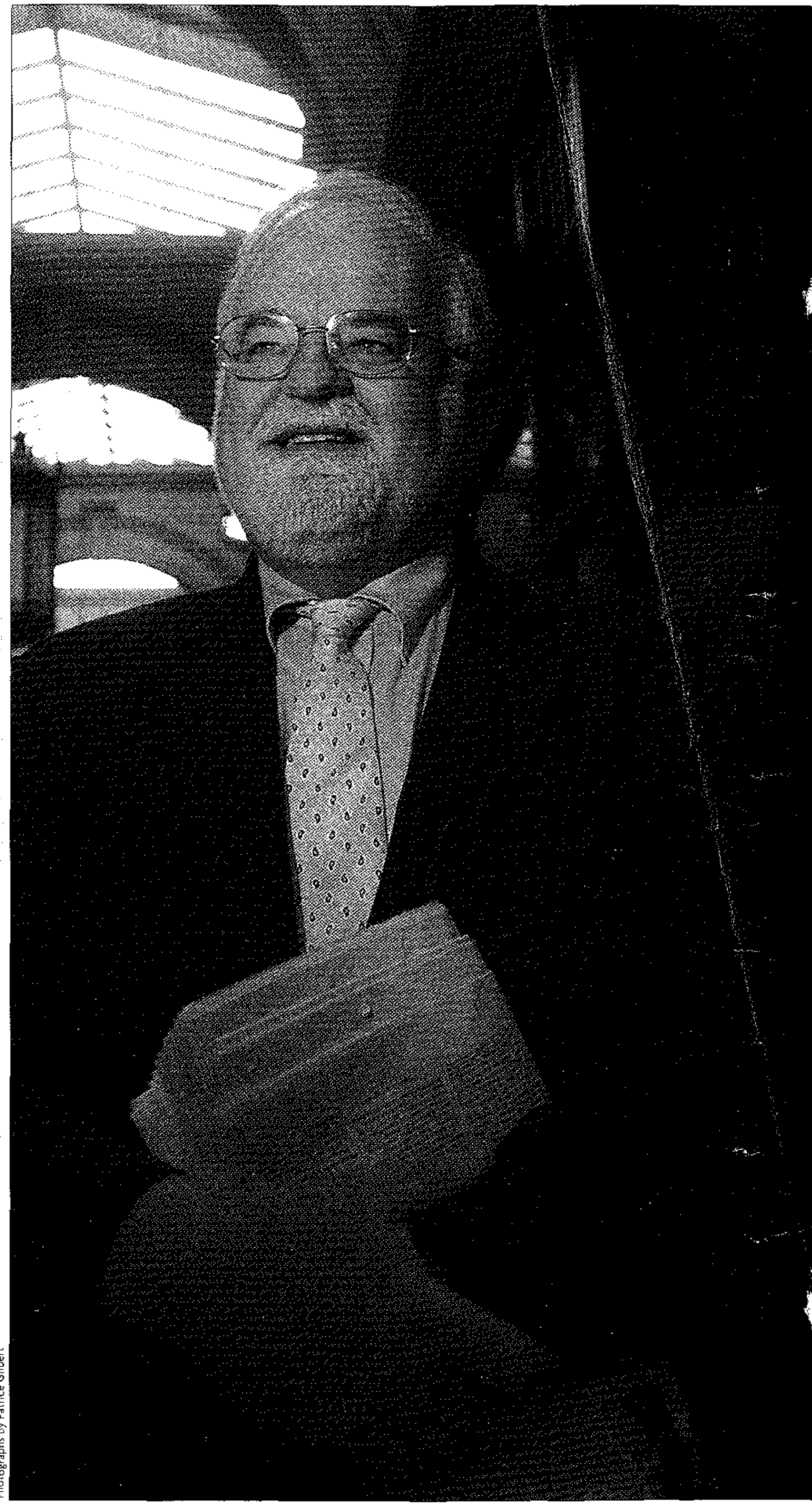
AARP's policy director, at a recent forum on drug prices. "If prescription drug prices continue rising, more retirees will become economically insecure."

Although many Americans have been insulated from the rising prices by prescription drug coverage, at least 65 million have no such coverage, according to the National Center for Policy Analysis. By various counts, anywhere from one-fifth to one-half of seniors are skipping doses or not filling the prescriptions they need because they can't afford them. Some are forgoing food or heat to pay. The Pharmaceutical Research and Manufacturers of America (PRMA) says its member drug companies provided free or reduced drugs to 6.2 million people through patient assistance programs last year, but many patients have found the benefits difficult to access.

In this tough financial environment, some patients have resorted to breaking the law—by smuggling. Although it is against federal law for Americans to buy prescription drugs from Canada or from anywhere overseas—the Bush administration says it is unsafe—more than one million Americans are doing just that, either over the Internet or by hopping buses across the border. Last year Americans bought $1.1 billion of drugs from Canada, according to IMS Health, a pharmaceutical market research firm. Some drug companies have limited their supplies to Canada, to discourage the products from being redirected here. Canadian pharmacies have responded by filling some orders from Europe and Australia, which also have price controls.

For many years, Americans who purchased their drugs from overseas were acting as individuals. But increasingly they are getting help from their elected officials. Cities, counties, and entire states are either buying drugs from overseas or helping their citizens do it for themselves. The rogue governments include the states of Illinois, New Hampshire, North Dakota, Vermont, and Wisconsin; and numerous cities and counties, including Montgomery County, Maryland, home of the Food and Drug Administration (FDA), which opposes drug reimportation.

These local governments are flouting federal law in a way that they haven't done since the bloody aftermath of *Brown v. Board of Education*. In the run-up to the election, some of the law-breaking states were hoping the FDA would crack down, to highlight President Bush's opposition to reimportation. But as of October, the FDA said it was still trying to educate the states. If education doesn't work, "it may come down to a lawsuit," says William Hubbard, senior associate commissioner for policy and planning at the FDA.


Photographs by Patrice Gilbert

Technically, the FDA can choose when and where to enforce the law. But "it's not really legal what the FDA is doing, which is allowing massive public violation of the law," says Bernie Horn, policy director for the Center for Policy Alternatives, which develops model legislation for state governments.

The High Cost of Innovation

When consumers complain about high prescription drug prices, drug companies say they need the profits to plow back into research, so they can develop new drugs to cure our diseases. "The more important drugs are, the more important it is to maintain the incentives to get the drugs that we need," says John Calfee, an American Enterprise Institute economist who also does some consulting for major pharmaceutical companies.

PRMA is more blunt. "We're a lot better off having innovative drugs and having a debate about prices, than we are not having innovative drugs," said Lori Reilly, a PRMA vice president and lawyer, at a recent panel on drug prices.

"If you look at what has happened to the industry in Europe and Canada because of their public policies, they've really driven the industry out. There's not a lot of innovation that goes on in those countries," says Scott Lassman, associate general counsel for PRMA.

Michael Greve, a legal scholar at the American Enterprise Institute, says that overseas price controls stick Americans with the research and development bill. "The rest of the world freerides on America's innovative capacity in this area," he says.

Because so many people are pushing for price controls, drug companies feel they are under fire. They are unsure of how they can continue to produce new drugs. "I do think the industry is beleaguered," says Lassman. "It's [only] as strong as it is because of the policies here. And we hope that we maintain balanced, pro-innovation policies."

Greve worries that within four years drug companies will agree to form what he calls a government cartel, similar to the deal tobacco industries struck with states: drug companies will produce their products at government-set prices in exchange for protection from liability. Drug companies "are buying a death by a thousand cups," he says. "They have to worry about reimportation, [New York attorney general] Eliot Spitzer, . . . Congress. It's just one thing after another. And there's just only so much stuff that any industry can take.

"I can understand if they say, 'Let's be done with it. Let's lock ourselves into a government cartel. We're going to become government producers.'" That, Greve maintains, would be the end of innovation.

Last year the drug industry spent a combined $33.2 billion on research and development, according to PRMA. But industry critics, such as former *New England Journal of Medicine* editor Marcia Angell, insist that a large percentage of those research dollars is spent on so-called me-too drugs (slightly different versions of existing drugs) that drive up costs without delivering significant health benefits, compared to drugs already on the market.

Drug companies argue that it helps patients to have several versions of one drug because patients have different body chemistries. "Ask patients . . . whether having their choice of medicines matters to them," says Reilly.

Rother suggests there is a need for, say, two me-too drugs. "It's very hard to make an argument for seven or eight. These are profit-based decisions. Companies try to go after the big markets where a lot of people are taking the drugs," he says. Drug companies, he adds, are ignoring development of lower profit drugs for diseases that have no other treatment.

The drug industry says it costs more than $800 million to develop a new drug and it can take 15 years to bring it to market. Critics say that number is closer to $100 million.

As it turns out, much of the debate on drug companies' cost structures may be moot. Drug prices are really not based on research costs. Lately, the pharmaceutical industry has been defending its prices based on the concept of "value." As PRMA points out in a 2004 pharmaceutical industry profile: "Prescription drugs save lives, alleviate suffering, and improve the quality of life. They also often reduce the need for more invasive and expensive treatments. A narrow focus on the cost of drugs, without regard to their value and their role in the health system as a whole, would discourage innovation and harm the prospects for health advances."

> "Instead of having drug companies test drugs against placebos, have them test drugs against existing drugs of the same class. That doesn't mean they can't be approved." —John Rother

At least one study shows that prescription drugs do reduce other medical costs. For the general population, every dollar spent switching patients from older drugs to newer, more expensive drugs results in $7 to $8 of savings in other medical costs, according to Frank Lichtenberg, a Columbia University economist.

Vicki Gottlich, an attorney with the Center for Medicare Advocacy, argues that it is precisely because drugs can avert other diseases that it is so important to make them affordable. "That's why most of us wanted a [Medicare] prescription drug benefit," she says.

Some drug industry advocates maintain it would be fair to peg drug prices to the alternatives, such as pain, surgery, chemotherapy, or even death. In a July 22 editorial in the *New England Journal of Medicine*, researcher Deborah Schrag of the Memorial Sloan-Kettering Cancer Center documented the rising cost of chemotherapy for colorectal cancer patients. In 1991, when eight weeks' worth of chemotherapy drugs cost $63 for colorectal cancer patients, patients could expect to survive an average of one year. In 2002, with eight weeks' worth of new chemotherapy drugs costing $12,000, they could expect to survive 21 months. This raised the question for payers, usually insurance companies: is it worth an additional $1,326 a month to extend a human life for nine months?

Now, with the latest cancer drugs, patients can hope to live longer, but it will cost a lot more: $31,000 for an eight-week course. Schrag says such prices underline the need to rethink the way drugs are developed and sold.

Inevitably, such rethinking always returns to the models available in other countries that rely on price controls. Greve says price controls could result in fewer drugs and a sicker populace. "At some point you may reach in the pharmaceutical markets the condition that you've now reached in the vaccine markets: bottlenecks up the wazoo, zero innovation, and [the government] begging the manufacturers [to produce drugs]," Greve says about having price controls.

Our recent experience with the shortage of influenza vaccine provides an illustrative example. In a heavily regulated price control environment, Greve maintains, manufacturers will only agree to produce drugs if the government guarantees demand, profit, and protection from liability.

Comparison Shopping

Consumers might be able to enhance their purchasing power if they could comparison shop, the way they do with most other products. But they can't because the FDA doesn't require drug companies to test their new products against old ones. To get their drugs to market, companies must show only that their drugs work better than a placebo; a new drug can be approved even if it doesn't work as well as the old one. So consumers might be paying more for new, less effective drugs, when they could be paying less for older drugs that have gone off patent.

Rother says requiring head-to-head testing would lower prices. "Instead of having drug companies test drugs against placebos, have them test drugs against existing drugs of the same class," he says. "That doesn't mean they can't be approved. But if that kind of information were in the public realm, it would cut down on the me-too drugs, unless you really had an improvement."

Although most of us assume that newer, more expensive drugs are better than the older ones, recent studies show that is not always the case. In 2002 the National Institutes of Health (NIH) announced that three brand-name heart drugs—including Pfizer's blockbuster Norvasc, then the fourth top-selling drug in the world—proved less effective at preventing heart disease than a far cheaper generic diuretic. Patients who used the more expensive drugs suffered more complications, including strokes and hospitalization for heart failure.

The study, published in the *Journal of the American Medical Association*, also found that more than half of the prescriptions for high blood pressure in 1982 were for diuretics. But over the next 10 years, diuretics' share fell by 50 percent, giving way to newer, more expensive drugs. If diuretics had not lost popularity during that time, prescription drugs for high blood pressure would have cost $3.1 billion less, NIH researchers say.

In his comments to the media when the results were announced, National Heart, Lung, and Blood Institute director Claude Lenfant took pains to point out how FDA drug approval policies had contributed to increased use of more expensive, less effective drugs. "Many of the newer drugs were approved because they reduce blood pressure and the risk of heart disease, compared with a placebo," he said. "But they were not tested against each other. Yet, these more costly medications were often promoted as having advantages over older drugs, which contributed to the rapid escalation of their use."

Older, cheaper treatments for arthritis may be better too. Americans spent about $5.6 billion last year on painkillers called COX-2 inhibitors, even though some research shows that much cheaper, over-the-counter pain relievers like ibuprofen may be just as effective at reducing pain. Doctors favored the COX-2 inhibitors, saying they were less likely to cause ulcers in longtime users. But drug companies weren't allowed to advertise that benefit because they couldn't prove it in clinical trials.

Now it turns out that at least one COX-2 inhibitor presents safety problems far more serious than ulcers: clinical trials show that longtime users of Merck's Vioxx suffer double the risk of heart attack and stroke. Merck withdrew the drug in October, marking the biggest product withdrawal in pharmaceutical history. Pfizer, maker of COX-2 inhibitor Celebrex, the ninth best-selling drugs in the United States, says it is studying whether that drug presents similar problems.

Industry officials say that despite these findings, it would be a mistake to force drug companies to base FDA approval partly on proof that the new drugs are better than the drugs already on the market. "I can't argue that in some cases, when we do head-to-head [trials], we won't find that older drugs do better than a newer drug," says Lassman. If comparative trials become a condition of approval, however, he has "no doubt that's going to cut down on innovation."

> "Drug manufacturers actually have more support from the beneficiary community than they think." —Vicki Gottlich

Sometimes drug companies do conduct comparative tests so their drugs can be approved for an insurance plan's formulary. But these tests are generally skewed from the start, contends Peter Rost, the Pfizer marketing vice president who made headlines this summer when he joined congressional representatives in open criticism of his industry. Speaking for himself and not as a representative of Pfizer, Rost says, "The bias happens in the selection of what trials you do. There is no trial you do with the purpose of showing that a drug doesn't work, or the drug is inferior. You get to pick the competitors. If you want to win, you're going to pick the short and slow."

Marcia Angell, who spent two decades reviewing clinical trials for the *New England Journal of Medicine*, says the trials can be stacked in many different ways. Sometimes new drugs at higher doses are tested against older ones at lower doses. Or sometimes drugs intended for the elderly are tested in younger patients, who are less likely to suffer certain side effects.

Sometimes a company finds out that its drug fared no better than a placebo. But that doesn't always stop it from marketing the drug. Pfizer's Warner-Lambert unit, for instance, marketed the epilepsy drug Neurontin as a cure for bipolar disorder, even though a clinical trial showed that a placebo worked better. It is illegal for a drug maker to promote a drug for unapproved, or off-label, uses, but it isn't illegal for doctors to prescribe it that way. And there is no legal requirement that manufacturers publish negative clinical results. (But there is private pressure. Last fall several medical journals said they would no longer publish study results unless the studies were preregistered in a public database.)

Medicare Modernization Act

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 was supposed to provide a prescription drug benefit for elderly patients. For the most part, it does. At