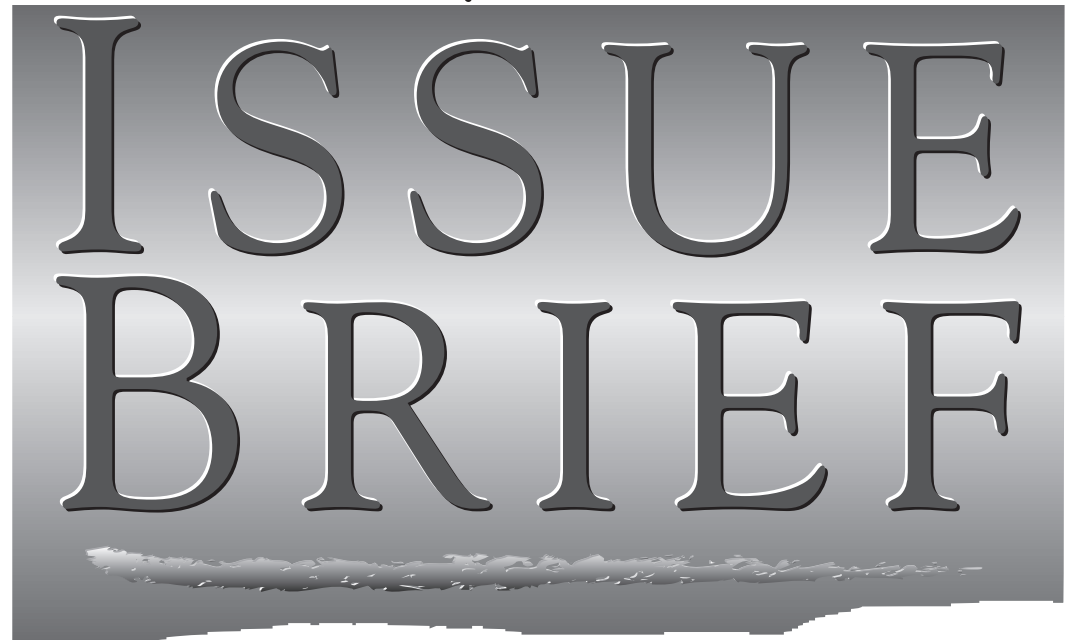


Summary: *Severe acute respiratory syndrome has receded since the epidemic of 2003, but it could one day come back with a vengeance. The world is relying on the pharmaceutical industry to develop a vaccine and effective treatment against SARS and other diseases. Yet drugmakers are being vilified and facing increasing difficulty doing business, hampering their efforts to find a cure for such diseases.*



DRUGMAKERS UNDER SIEGE: *Hampering the Search for Cures for Tomorrow's Epidemics*

by Doug Bandow

For a time, the world faced a deadly new epidemic: severe acute respiratory syndrome or SARS. After suddenly afflicting more than 8,400 people worldwide and killing 774 of them—while virtually shutting down travel to China and Hong Kong—SARS faded away by late 2003.

But it did not disappear. During spring 2004 SARS reemerged in China, although the outbreak was limited. Public health officials especially worry about a renewed outbreak, particularly in winter when respiratory diseases are rife.

If the disease breaks out across China's impoverished rural provinces, it will be hard to stop. The consequence of a deadly illness running wild throughout the

world's most populous nation, many of whose citizens travel abroad and receive visitors from throughout the world, is truly frightening.

While SARS has been nothing like the Spanish flu pandemic of 1918 and 1919 in which at least 20 million and as many as 40 million people died worldwide, that disease only killed 3 percent of those affected. The fatality rate for SARS has been about 10 percent.

Moreover, SARS seemed to mutate, which made it harder to control. Reported Matt Pottinger and Antonio Regalado of *The Wall Street Journal*: "Scientists in Hong Kong and elsewhere suspect two versions may already exist, and constant changes in the virus's genetic makeup could help it find new ways to infect people."

Dr. Anthony S. Fauci, director of the U.S. National Institute of Allergy and Infectious Diseases (NIAID), noted that some diseases are deadly but don't spread easily. And some are highly infectious but don't kill. SARS, however, was both. "It's a really bad combination," observed Fauci.

Imagine quarantined hospitals, closed schools, and travel advisories the world over. Imagine borders shut to visitors from entire countries and regions. Imagine not knowing whether you've caught a cold, the flu, or SARS. Imagine widespread deaths and constant hysteria.

So far it hasn't come to that, thanks to a mix of skill and luck. Precluding a future disaster is going to require a lot more work.

While governments have an important role to play, they are ill suited to develop an effective vaccine and treatment for SARS. Finding a cure requires bold innovation and relentless experimentation, which are characteristics of a competitive, profit-driven market. Drug companies are diligently working toward developing and putting into mass production an effective SARS vaccine and other medicines.

When the SARS virus hit, a dozen labs in the United States, Canada, Germany, Hong Kong, the Netherlands, Vietnam, and elsewhere collaborated to quickly isolate it. Next was the epidemiological task: figuring out how the disease was transmitted. Observed *Newsweek* health editor

Claudia Kalb: "A long road lies ahead. Scientists need to develop precise diagnostic tests, find effective treatments and, ideally, design a preventive vaccine."

Yet at a time when the world just escaped a potential viral epidemic—and faces the prospect of biological terrorism—drugmakers are under siege in America. Demagogic politicians have lumped them with tobacco companies, as if firms that make products that heal are morally equivalent to those that make products that kill.

Numerous states along with the federal government are considering price controls, reductions in patent rights, restrictive drug formularies, imports from price-controlled foreign countries, and advertising controls. Political activists are challenging patents, and state attorneys general have launched a barrage of lawsuits against drugmakers.

Such actions are having a chilling effect on drug research and development. Without a robust pharmaceutical industry, the pipeline of new, life-saving drugs will dry up. If the assault against drug companies persists, the

American pharmaceutical industry could go the way of the European pharmaceutical industry and become a shell of its former self. Were that to happen, who would be around to develop effective remedies for SARS, which so far has proved resistant to drugs?

Innovative treatments for such problems as AIDS, heart disease, and breast cancer demonstrate how we all benefit from profitable drug manufacturers and abundant pharmaceutical research. That should remove any doubts about the importance of having a strong and profitable pharmaceutical industry in order to fight SARS and other deadly diseases.

HEROES, NOT VILLAINS

During the SARS outbreak, pharmaceutical companies took center stage. The initial efforts against the disease focused on finding an existing medicine that worked. Laboratories screened some 2,000 federally approved and experimental drugs.

German researchers thought AG7088, a protease inhibitor undergoing clinical trials for use against the common cold, held promise. Some Hong Kong doctors claimed to have had success using a drug cocktail of the anti-viral ribavirin and steroids. Scientists also hoped for positive results from the protein interferon, a natural biologic that fights

infections. And some protease inhibitors, related to medicines used to fight AIDS, were thought to show promise against SARS.

Despite doubts about many of these treatments—e.g., experts later came to believe that corticosteroids should be used only in severe cases because of serious side effects—Yeoh Eng-kiong, Hong Kong's Secretary of Health, Welfare and Food, observed that not treating the sick wasn't an option: "Under such desperate situations, you try your best." And that meant experimenting. Gurinder Shahi, a doctor in Singapore, explained: "Given how little we know about SARS and the reality that it is killing people, it is justified for us to be daring and innovative in coming up with solutions."

As stated above, daring innovation is most likely to occur where there's a profit-driven and competitive market. For instance, Pfizer worked with NIAID to test 350 compounds developed as part of an earlier project to cure the common cold. NIAID also collaborated with the California biotech company Vical to test an experimental

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vaccine that has protected mice from SARS. Adventis and Merck as well as laboratories around the world are working to develop SARS vaccines.

Most of today's medicines exist only because there is a bevy of sophisticated pharmaceutical companies devoted to finding drugs to heal the sick. Progress has been particularly dramatic in recent years.

For instance, two decades ago not one drug was available to fight AIDS. Today, 74 have been approved and another 83 are in development.

Equally significant has been the impact of pharmaceuticals on the elderly. People not only live longer, they live better. And no small reason is the explosion of new prescription drugs.

More than 800 medicines to combat diseases of aging are now in development. Over 50 of them will target diabetes; more than 40 will address lung and respiratory disorders and the same number for Parkinson's disease. About 30 are directed at rheumatoid arthritis. A score of each are in process for treating Alzheimer's disease and dementia, eye problems, gastrointestinal disorders, and osteoporosis. Other drugs will treat kidney diseases, sleep problems, depression, and much more.

The benefits of such advances are obvious. Columbia University's Frank Lichtenberg figures that fully 40 percent of the increase in average lifespan between 1986 and 2000 is due to new drugs. In many cases medicines directly forestall death.

In fact, *The Washington Post* recently reported on desperately sick and dying people who feverishly search for clinical trials of new drugs that might keep them alive. One doctor repeatedly operated on Minnesota native Todd Hendrickson in order to "keep Mr. Hendrickson alive so he could keep searching for a medical cure." In August 2000 Mr. Hendrickson became the first patient to take the drug Gleevec, three months after its unusually rapid approval by the Food and Drug Administration (FDA).

Gleevec is thought to be just one of a "new generation of cancer fighters," reported Nicholas Wade of *The New York Times*, that "will be the long-awaited payoff for decades of research into the molecular biology of cancer. Unlike chemotherapy and radiation, blunderbuss weapons that attack healthy as well as cancerous cells and can cause severe side effects, the new agents are

designed to kill cancer cells alone. In principle, they should eliminate malignancies more effectively while being far gentler on the patient."

Nor are pharmaceutical companies targeting only cancer. Xigris, which combats sepsis (an infection of the bloodstream), was approved in 2001. Said Dr. Jay Siegel of the FDA: "We're talking about tens of thousands of lives per year potentially saved by this product if used appropriately."

The impacts of other drugs on patients are more subtle, but still important. They bring less pain, greater self-esteem, less nausea, improved well-being, and even lower health care expenditures. Such benefits are shared by families and caregivers as well as the ill.

One important research area is the control of side effects of other drugs. Reports Daniel Rosenberg in *The Wall Street Journal*, "Now, venture capitalists are focusing on the side effect treatment market, funding companies at the cutting edge of such research."

In addition to common side effects such as nausea, there are such things as oral mucosities, which involve sores in the mouth that make eating, drinking, and talking difficult. And neuropathy, a strange feeling in arms and legs, can become debilitating. "Side effects can be very serious, and as painful as the pain of the disease itself. If people are unable to eat or swallow, they find it difficult to continue the treatment," writes Rosenberg.

But all of this progress hasn't come cheap. In 2002 American industry alone devoted \$32 billion to R&D. According to a 2003 study published in *The Journal of Health Economics*, "Between the time research begins to develop a new prescription medicine until it receives approval from the FDA to market the drug in the U.S., a drug company typically spends \$802 million" over 10 to 15 years. That's nearly four times the expense in 1987.

Active in the fight are not just industry giants such as Pfizer. AVI BioPharma, Inc., a Portland, Oregon biotechnology firm, began looking at SARS after having worked on the West Nile virus. And small firms backed by venture capital are focusing on the side effect market because, "In the past, drug companies haven't seen a lot of money in treating side effects that only affect a minority of cancer patients," reports Rosenberg.

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SABOTAGING THE DRUG PIPELINE

But as discussed above, drugmakers are subject to increasing attacks from politicians, the media, activist groups, lawyers, and others. Existing and potential roadblocks such as price controls, lawsuits and drug reimportation are making it more difficult to do business. Not surprisingly, the industry became a target in the 2004 presidential campaign, with Democratic presidential nominee John Kerry calling for reimportation and vice presidential nominee John Edwards criticizing industry advertising.

The explosion of liability lawsuits is a huge problem. Henry Miller of the Hoover Institution points out that the number of vaccine makers has fallen by almost three-fourths since 1967. The basic problem, he notes, is that “compared to therapeutic drugs, vaccines traditionally offer low return on investment but high exposure to legal liability.”

Underlying the widespread political assault is a panoply of distorted and even false claims. Contrary to popular belief, the industry is not uniquely profitable and its returns are commensurate with the cost of raising capital. In a study for the Institute for Policy Innovation, Dr. Merrill Matthews observes that in 2001 Microsoft had a higher return than the most profitable pharmaceutical companies, while a number of drugmakers had single-digit returns or even losses.

Moreover, as Matthews points out, above-average profits “is exactly what you would expect—and want,” given that “the riskier the business the higher the profits must be to induce entrepreneurs to take that risk.” And that is certainly the case where only one in 5,000 or so compounds tested actually makes it to market, and 70 percent of those making it past that hurdle are money losers.

Complaints about rising drug expenditures are common, even though people routinely spend more for a dinner out than on a typical prescription. Moreover, total drug outlays are rising not so much because of price hikes on existing medicines, but mainly because Americans are consuming medicines at a higher rate—buying new products and using more old ones.

Other myths abound. Drug companies actually spend more on R&D than marketing. They devote far more money to finding drugs than does the National Institutes of Health (NIH). The salaries of executives in many other industries are higher than those of the drug industry.

What makes this concerted campaign so perverse is that Washington claims it understands the importance of pharmaceutical research. Dianne Murphy, director of the FDA’s Office of Counterterrorism and Pediatric Drug Development, says of drugmakers working on combating bioterrorism: “We want them to come in and talk to us when the drug is barely a glimmer in a scientist’s eye.”

Yet Washington’s threat to void the patent for Cipro in the midst of the 2001 anthrax scare was a warning to firms that no good deed goes unpunished, and the better the deed (more effectively dealing with a deadlier disease), the greater the likely punishment (losing the hard-won return on a company’s research).

Countries with the lowest prices due to price controls yielded the least productive drug research.

Three years later some patient groups pressed NIH to strip Abbott Laboratories of its patent to the AIDS drug Norvir because NIH made a \$3.5 million grant that helped lead to Norvir’s discovery. NIH refused, with Director Dr. Elias Zerhouni observing that, “The issue of drug pricing has global implications and, thus, is appropriately left for Congress to address legislatively.” Unfortunately, even that stance offers only scant protection for large-scale medical investments.

A EUROPEAN FATE TO BE AVOIDED

The U.S. is essentially the last pharmaceutical free market among leading industrialized states. Price and use controls pervade Europe and other industrialized states, including Canada and Japan. It comes as no surprise that in a 1992 study, E.M. Kolassa of the University of Mississippi School of Pharmacy found that countries with the lowest prices due to price controls yielded the least productive drug research.

Throughout the 1990s, European drug investment only doubled while expenditures in the U.S. quintupled. David Pilling of the *Financial Times* reports that “Only a decade ago, half of all top-selling drugs were European.” Old World companies now account for just three of the globe’s 25 top-selling medicines.

At the same time, Europeans have far less access to prescription drugs, particularly newer, more effective products. Use of cancer drugs, as well as medications for a variety of less-serious conditions, has been artificially limited. Explained *Wall Street Journal* reporter Stephen D. Moore: “Innovative cancer drugs have gotten bogged down even earlier in the system. Herceptin, a new breast-cancer medication from San Francisco-based Genetech

Inc., was approved two years ago by regulators in the U.S., where it benefited from an accelerated review offered to novel cancer therapies. It is still awaiting regulatory approval in most of Europe.”

Nor is that all. Moore adds that “Many European countries also attempt to restrict demand after new medicines reach pharmacy shelves. Drugs can be saddled with tight prescribing rules to limit consumption. Patients across Europe are fighting for improved access to older drugs such as Taxol, the world’s top-selling anticancer drug.”

Moreover, the vast “parallel” trade, or reimportation, that occurs on the European continent has given rise to increased counterfeiting, which has discouraged some people from even taking their medications. A new study from The Center for the New Europe estimates that as many as 14,000 people a year are at risk of death as a result.

Thus, the vast majority of drug innovation derives from the American market. That will end, however, if government arbitrarily seizes—directly, through domestic restrictions, or indirectly, through “reimportation” of American drugs from countries with price controls—the fruit of industry R&D, thereby cutting industry prices and profits. Investment will fall. It will mean less R&D and fewer life-saving products.

STREAMLINING FOR A CURE

Instead of working to slash industry returns, government should cut industry costs. That would be best done by expediting FDA approval of new drugs.

The agency, like most bureaucracies, is conservative: Staffers’ careers are more at risk for allowing an unsafe drug onto the market than for delaying introduction of safe ones. The resulting FDA foot-dragging over the years may have prevented 200,000 lives from being saved.

In response, Congress has provided for an industry-funded user fee, and the FDA has created a fast-track process for some potentially life-saving drugs. But too many pharmaceuticals still are delayed too long. While the FDA approved 44 new drugs in 1996, it only okayed 21 in 2002. In its 2001 annual report, the FDA’s Center for Drug Evaluation and Research warned that drug approval times “have begun to increase because more applications require multiple review cycles to reach approval.” In July

2004 Acting FDA Commissioner Lester M. Crawford warned that more biologics and drugs were failing in Phase 1 trials, further driving up development costs.

Former FDA commissioner Mark McClellan wanted to streamline the regulatory process. That would be a good start, but reforms should be even more far-reaching: the FDA should leave the test of efficacy up to the market; drug approvals in Europe and Japan should be accepted in America; even private groups should be allowed to test pharmaceuticals, just as Underwriters Laboratory assesses electrical and electronic appliances.

As political restrictions on the pharmaceutical industry rise and increasingly complex compounds push up drug development costs, regulatory reform becomes more necessary. Observes Dr. Joseph A. DiMasi of the Tufts Center for the Study of Drug Development, “Faced with cost-containment pressures and high research and development costs, pharmaceutical firms have attempted to make the drug development process quicker, if not less expensive.” By getting out of the way, the federal government could do much to aid them in this effort.

STOP DISABLING THE DRUGMAKERS

Life is uncertain and arbitrary; SARS demonstrated that flying in the wrong plane or sitting next to the wrong person could be a death sentence. And potentially many more people will die if SARS ever breaks out broadly or if an even deadlier infectious disease emerges.

The resources are available to prevent or ameliorate any such outbreak. Writes DiMasi: “A rapid expansion of scientific discoveries and technologic advances has given the pharmaceutical industry unprecedented opportunities to innovate. Combinatorial chemistry, high-throughput screening, and genomics have provided a technologic platform that is highly conducive to growth in innovation. However, given typical lengths for the drug discovery and development processes, most of the fruits of these efforts will likely not be realized for years to come.”

Reaping those long-term benefits to protect people worldwide will require the aid of America’s much-vilified pharmaceutical industry. If critics succeed in disabling the drugmakers, we will all be at risk. It’s time that those who benefit from industry research stop treating drugmakers as the enemy.

Instead of working to slash industry returns, government should cut industry costs.

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