
REMAPPING DEBATE

Asking "Why" and "Why Not"

Ignoring a solution to chronic drug shortages

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May 7, 2014 — Since shortages of critical drugs became a fixture of the American medical landscape a decade ago, pundits have proposed an array of incentives to encourage more production from pharmaceutical companies. But an obvious alternative or supplement — having the government manufacture the drugs — appears not to have made it to anyone’s list.

“Unfortunately, we’re at that stage again where we’re saying, yeah, we got together, we came up with a lot of ideas, the FDA got more authority, the FDA increased its staff, the FDA did this and that. But guess what? It’s not working. What are the next steps?” — Allen Vaida

A factory designed, built and run by Uncle Sam could manufacture drugs in short supply — not least the older, low-profit but still highly effective generic medications that drug makers cannot, or simply will not, produce. And yet, when Remapping Debate raised the possibility, the initial reactions of economists, physicians, industry analysts, and others ranged from stammering, chuckling and long, sometimes awkward, pauses, to bewilderment and shock.

Several people we interviewed struggled to explain their reservations by pointing out that the government has no experience in medicine making. Some flatly rejected the idea because, in their view, it was a long shot to gain political traction. Others said the concept gave them pause because it ran afoul of their beliefs of how a free market system ought to operate.

There were those who said a government entry into the generics business might destabilize the markets and send prices for all drugs soaring. (No evidence of this was forthcoming, and several people who said this later altered their opinion, saying the idea had potential.)

No one we reached out to in a position of authority — including at the FDA, Centers for Disease Control, or the National Institutes of Health — gave any hint that they were considering these questions or giving any thought as to how a federal drug factory could work.

But there were also those who — after first inquiring if we were serious — wholeheartedly endorsed the merits of a state drug-manufacturing capability.

Reversing government “de-industrialization”

The idea that governments would manufacture drugs is not novel. In fact, governments churn out medications for citizens in 80 countries around the globe, including Brazil, India, Denmark, Thailand, and Indonesia, according to the World Health Organization; in many places public and private enterprises coexist without incident.

Stephen S. Morse, a professor of epidemiology at the Mailman School of Public Health at Columbia University, says it’s remarkable that more than a decade into what are indisputably the worst and most widespread drug shortages in American history no one has yet thought to suggest or seriously consider a government option — at the very least, to study the benefits and drawbacks of it.

“It’s an interesting question I find rather puzzling,” says Morse, who directs a program at Columbia that specializes in risk assessment of emerging infectious diseases, including influenza. “Even the most conservative economists, the University of Chicago people and so on, have always believed that the one legitimate role for government — they do not admit to any others — is to take up the slack when there are market failures. And there seems to be a market failure here.”

“And yet,” he adds, “no one thinks to have government take an active role in this case, which is interesting because, if there is a market failure going on, as there clearly is, who *is* supposed to step in — foreign manufacturers?”

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Since the 1980s, the U.S. government has increasingly moved away from manufacturing anything — what some call the “de-industrialization” of government. Not long ago, however, the federal government was an active and effective player in the production of things needed to keep citizens healthy.

For decades after World War II, public agencies and institutes produced vaccines for biological threats, substances “which are harder to make because you have to do a lot of work on clinical trials as well as safety,” Morse says. The Salk Institute-Government Services Division once made specialty, bio-defense vaccines for things like Rift Valley fever, a mosquito-borne illness, and states like Michigan and New York made serums for smallpox, anthrax, and whooping cough, before leaving it to industry in the 1990s.

The notion that government is somehow incapable of making generic medications because it hasn’t done so before is myopic, says Aaron Kesselheim, a professor at the Harvard Medical School and a researcher at its department of health policy and management. The state, he says, is perfectly capable of quickly assembling people with the know-how for making pharmaceuticals.

It's worth remembering, he says, how the government successfully managed the Manhattan Project, which developed the atomic bomb; NASA's Apollo missions, space shuttles and stations, and telescopes; the Defense Advanced Research Projects Agency's development of the silicon chip and the Internet. Today, there's the "Green Electricity Network Integration" project at the Department of Energy, which promises to modernize our electric grid, and the National Nanotechnology Initiative, administered by various governmental agencies such as the Department of Defense, the Small Business Innovation Research Program, and the National Institutes of Health.

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Although the NIH devotes just 11 percent of its budget to internal biomedical research, the accomplishments of staff investigators are extensive: in the 1950s, the first use of chemotherapy to cure a solid tumor; in the '80s, the first drugs for treating AIDS; in the '90s, the first successful gene therapy. Today, NIH scientists are creating a four-dimensional atlas of brain development in simple organisms, tracking the origin and evolution of every neuron, the path of every axon, the creation of every synapse; they're pioneering a new way to repair holes in the human heart — the most common form of congenital heart disease — without the need for open-chest surgery; they're inventing probes that capture images of receptors, cells, and tissues at the molecular level — cutting-edge procedures and technologies not available commercially.

Making basic, older generics would not require the government to reinvent the wheel. "Yes, you would have to have good manufacturing practices," says Morse, the Columbia professor, and although there are some sterile injectables that are harder to make, particularly oncology drugs, "some of these substances are relatively easy to produce and very easily marketed. The demand, in fact, is guaranteed. So, again, if the government is capable of doing this, why shouldn't it step in to fill a void?"

U.S.A. Generics, Inc.

Ten years ago, drug shortages weren't the most pressing public-health concern for Allen Vaida, executive vice president of the Institute for Safe Medication Practices, a nonprofit devoted to preventing medication error. But then, in 2008, his organization began finding in hospital surveys that the use of alternative medications for generics in short supply was increasing the duration of diseases and, in far too many cases, leading to the deaths of patients who received improper dosages or who suffered sudden, unexpected reactions from substitutes.

Vaida remembers thinking at the time that the industry would eventually sort things out. Later, as the number of drugs in shortfall doubled, then tripled, then quintupled, he, like many stakeholders, began attending conferences and seminars to seek answers. Invariably, he recalls, discussions continued to center on market-based solutions.

A not-for-profit, government solution simply “wasn’t on anyone’s radar,” he says. Vaida admits he himself “didn’t give it much thought.”

In 2012, Congress reacted to record surges in shortages by granting the Food and Drug Administration expanded powers to manage the problem, a step many observers, including Vaida, viewed as positive.

Indeed, the FDA prevented nearly four times more potential shortages in 2012 than in 2010 — 154 as compared with 38. (The agency recently told Remapping Debate that it had averted 170 potential shortages in 2013.) But Vaida began to look more critically at those numbers: If federal regulators had to act more and more often to prevent shortages, was that a victory? Likewise, if the total number of active and ongoing shortages did not drop below 300 a day — and it hasn’t, in spite of the FDA’s efforts — where was the evidence that the market on its own could make up the shortfalls?

“Unfortunately, we’re at that stage again where we’re saying, yeah, we got together, we came up with a lot of ideas, the FDA got more authority, the FDA increased its staff, the FDA did this and that. But guess what? It’s not working. What are the next steps?”

Once, a market solution seemed to him the only remedy for this problem. But today, he admits, if manufacturers keep showing “there’s no way they’re going to be able to do it, maybe the solution is the government has to do it on its own.”

The notion that government is somehow incapable of making generic medications because it hasn’t done so before is myopic, says Aaron Kesselheim. The state, he says, is perfectly capable of quickly assembling people with the know-how for making pharmaceuticals.

Vaida’s long journey toward acknowledging the private sector’s shortcomings is far from an anomaly; many experts Remapping Debate interviewed initially rejected the notion that our capitalist economy was unable to deliver reliably all the life-saving medicines we need. When first asked what he thought of the concept, Richard L. Schilsky, chief medical officer for the American Society of Clinical Oncology, didn’t answer directly. “Look,” he said, sighing, “We don’t have a state-run pharmaceutical industry. We don’t have a state-run health care system. We’re a free-market economy.”

Days later, however, he appeared to have given the matter additional thought. “I suppose the government could do what you’re suggesting,” he said. “The government could set up a generic drug manufacturing plant and start churning out these drugs during short supply. They would have to go through the same FDA approval process that any other drug-manufacturing facility would, of course.”

For Congress to authorize this, he noted, lawmakers would have to be convinced that drug shortages are as serious a public threat as shortages of vaccines needed to counter pandemics or biological attacks. In Schilsky’s view, the problem is “a substantial public-health issue... You’re talking about kids with curable malignancies whose lives are on the line simply because the substitute drugs aren’t as effective as standard care.” Then, this thought: The government stockpiles serums for pandemics and biological attacks, so “I suppose that’s another kind of precedent that could be invoked” to buttress an argument in favor of a state-run drug factory.

Jennifer Goldsack, a health-services researcher at the Christiana Care Health system in Newark, Del., says that, had she been queried a decade ago about whether the government should step in to stop the shortages, she might not have been very receptive. But now, especially after recently publishing a study that spotlighted the enormous human and financial costs of cancer-drug shortages in this country, she says: “It seems very rational, doesn’t it? I think if there were a simple, market-based solution we would have found it by now.”

Generic drugs aren’t peanut butter

There are, of course, those who continue to believe that the market will satisfy America’s drug needs, harmonizing a profit motive with the public interest.

Skipping upgrades to factories and cutting overhead by making only as many products as they know they will definitely sell is

“a pretty common business model,” Erin Fox says, “and it probably works great for products like peanut butter. I mean, if there’s a shortage of peanut butter, okay, you can do without it until the factories catch up with demand. But if we don’t have some of these critical medications — well, people die.”

One such person we spoke to is David Gaugh, senior vice president for Sciences and Regulatory Affairs at the Generic Pharmaceutical Association in Washington, D.C. Though sidestepping a question on whether there’s been a market failure in the generic drug market — “It is a business, like any business” — he did answer candidly when asked to characterize the current state of generic drug shortages in America, saying: “It’s of crisis proportions.”

The crisis is upon us, Gaugh suggested, “because roughly 30 percent of the normally available capacity of these companies [is] offline while they are doing quality compliance remediation work. And when you have 30 percent going off all at the same time, that creates a drug shortage — or can create drug shortages.”

How did these facilities reach such a state of disrepair? Gaugh said “there are a lot of reasons,” but only gave one: that there are only “a limited number of companies that have the technology, the wherewithal, and the capacity to produce these types of products.” If that’s true, why should Americans expect these companies to resolve these shortages anytime soon?

Because, Gaugh said, drug makers such as Hospira, Inc. and Ben Venue Laboratories, Inc., the U.S. subsidiary of Germany’s Boehringer Ingelheim Corp., are now “pouring hundreds of millions of dollars into [their] facilities to get them to the level that they need to be from a quality-compliance perspective.”

Boehringer Ingelheim did reportedly spend \$350 million to overhaul the aging Ben Venue plant in Bedford, Ohio — the source of more than 100 essential generic drugs, including the chemotherapy drug Doxil — after a brief suspension of operations in 2011 due to serious quality and sterility problems. In

December, however, that troubled plant was shut down for good. The German conglomerate attributed the closing to projections that the facility would rack up \$700 million in operating losses over five years.

Hospira declined to make executives available for interviews, but issued a statement saying that it was investing in new production capacity. Two other U.S. manufacturers, Baxter International, Inc. and West-Ward Pharmaceuticals Corp., did not respond to written requests and phone messages for interviews.

Even if there is additional private sector investment, would a government entry into the market necessarily be a bad thing? Gaugh didn't address that question directly, responding instead that building a government drug plant would be a "complex" undertaking. "We're talking about billions of injectable vials that are made by these five or six private corporations," he said.

Claire Sheahan, the association's media spokeswoman, interjected: "This isn't the first time in history that people haven't been able to get things. And the government doesn't normally take that path where they go into the business. They find other solutions."

Enrique Seoane-Vazquez, director of the International Center for Pharmaceutical Economics and Policy at the Massachusetts College of Pharmacy and Health Sciences, says if the government enters the drug manufacturing business to guarantee supply, "we are going to have an immediate increase in prices." Why? The government, he explains, will have to spend billions to create extra production capacity and inventories for spikes in demand, costs that will lead it to raise some prices.

"It's even ridiculous to think of this as a market" said David Himmelstein. "The very fact that drugs are patented means that there is no market, right? Drug companies are given a monopoly. They control the market. So, by definition, there is no market. They are not in business to do good; they are in business to make money."

Though acknowledging his opinion is not based on any economic analyses (there are no case studies available), Seoane-Vazquez notes that "in the area of vaccines, when you have the government negotiating prices, we know that over time that number of producers goes down. This is something that could generate future problems, if the companies decide not to manufacture specific products."

But hasn't this already happened? A 2011 economic analysis by the Department of Health and Human Services (HHS) found the generic drug market to be highly consolidated, with three or fewer companies cornering the market for sterile, injectable generics — the sort most in shortage. It cited a study in the *New England Journal of Medicine* that said just three manufacturers supplied 71 percent of America's sterile, injectable cancer drugs and 91 percent of sterile, injectable nutrients and supplements.

As brand-name drugs come off patent, big manufacturers expand the number of products they make but not the facilities that make them, according to a study by the IMS Institute for Healthcare Informatics. It reported that between 2006 and 2010 the generic sterile injectable market had grown by half without a proportionate increase in manufacturing capability.

The way pharmaceutical companies have responded to increasing demand for more and more generic medications is to run their factories full tilt, 24 hours per day, adding as many as 50 medications to a single production line.

For decades now, drug makers have run their businesses this way because building extra capacity and backup systems “is a pretty expensive thing to do,” says Bona Benjamin, coordinator of the drug shortages web resource center at the American Society of Health-System Pharmacists in Maryland.

As a result, companies choose which drugs to manufacture based on projections for demand and, if they have competitors, what others may produce. Oftentimes, they prioritize newer generics with bigger profit margins, even if that increases the likelihood of shortages, according to a report released in February on the drug shortages by the Government Accountability Office. What’s more, the watchdog agency said, older generics are routinely “discontinued in favor of producing newer drugs that are more profitable or that have more demand.”

When older, less profitable generics are made, they’re produced in limited quantities because unsold pharmaceuticals can’t be stockpiled like bricks; they have a short shelf life. As HHS pointed out in its 2011 economic analysis: “There is little cost (except reputational) of producing too little of one drug (rather than another), but a potentially high cost of producing too much of that drug.”

Erin Fox, director of the University of Utah’s Drug Information Service, which has been tracking drug shortages in America since 2001, says pharmaceutical companies have been doing this for years: skipping upgrades to factories, cutting overhead by making only as many products as they know they will definitely sell.

“It’s a pretty common business model,” Fox says, “and it probably works great for products like peanut butter. I mean, if there’s a shortage of peanut butter, okay, you can do without it until the factories catch up with demand. But if we don’t have some of these critical medications — well, people die.”

Looking at all of the costs

As for concerns over a market distortion or a sudden jump in prices if the government started producing generics — those fears are overblown, says David Himmelstein, a professor of public health at the City University of New York and a co-founder of Physicians for a National Health Program.

Actually, Himmelstein says, “it’s even ridiculous to think of this as a market. The very fact that drugs are patented means that there is no market, right? Drug companies are given a monopoly. They control the market. So, by definition, there is no market. They are not in business to do good; they are in business to make money. Milton Friedman said many years ago that the acceptance by corporate officials of a social responsibility other than to make as much money for their shareholders as possible is a dereliction of duty. So the problem isn’t that they’re misbehaving, it’s that they *are* behaving. They are behaving exactly as they’re supposed to.”

The pharmaceutical industry manages to make “enormous profits,” he adds, “so you ought to be able to undercut the prices charged for medicines and still do very well. And if government was not in search of a profit, it seems to me that you could make back the initial investment pretty readily.”

Also, is it fair to compare what it costs private industry to produce a drug on the quick and dirty, as opposed to what it would cost the government to do it right — in other words, to build in excess production capacity so as not to get caught short?

Certainly not, says Morse, the Columbia professor. The proper comparison is what it would cost private enterprise to build and maintain sufficient production capacity versus what it would cost the government to do the same — and there’s no evidence to suggest that companies could do it cheaper than the government, only evidence that the private sector has been unwilling to do it.

Even if it did cost the government more to build a factory that could guarantee supply, “the government doesn’t have to make a profit,” Morse says, so the additional expense can be more easily absorbed. “It’s what allows government to do what no private sector enterprise can survive with, because companies have to make money.”

Despite upsides, still off the radar

Given the chronic problems of the current system, why wouldn’t policy makers at least examine the potential upside of including government production of medications?

In part, says Kesselheim, the Harvard professor, there’s a cultural bias at work. “The U.S. government doesn’t make generic drugs — or historically hasn’t done so,” he told Remapping Debate. “And so people, when they think of solutions, are trying to think of private market solutions because that’s how production and supply of pharmaceutical products has been handled thus far. We just don’t have a template for it.”

Himmelstein, the professor of public health at CUNY, says it’s not seriously considered because “in our current political milieu, the forces of reaction are so strong that it makes it almost hard to imagine that we could make real advances where government would be allowed to do what it almost certainly could do well.”

“The point is there are so many hidden costs that if you could actually account for all of them, and if you could shift those costs into a government-sponsored drug production process, it would not necessarily be a huge incremental expense,” says Richard L. Schilsky. “It would just be money shifted from one ineffective use to a more effective use. That’s a very interesting concept.”

Tellingly, federal agencies with the competency and experience that could be useful in operating a state-run drug facility — the FDA, NIH, HHS and the Centers for Disease Control — all declined to

make officials available for interviews. Even when Remapping Debate asked the FDA in writing why no federal agencies had proposed or even explored a government option for the shortages, the answer from the agency's Center for Drug Evaluation and Research was terse: "A federal government-run manufacturing facility would require additional legislation."

Which path is more expensive?

Constructing a state-run pharmaceutical factory would not be cheap. Ken Inchausti, a U.S. spokesman for Novo Nordisk, a Danish pharmaceutical manufacturer that has production facilities in seven countries and offices in 75, says that based on his experience it wouldn't be outlandish to budget a billion dollars for the construction of a standard drug factory with the capacity to manufacture a wide range of generics.

But the alternative — sticking with the status quo — is likely costing *more*.

A joint study by the University of Michigan and American Society of Health-System Pharmacists found that drug shortages created \$216 million in extra labor costs for hospitals in 2011. (And back then, there were half as many drugs in shortage as there are today.)

Another analysis by Premier, Inc., a hospital group-purchasing organization in Charlotte, N.C., found that hospitals nationwide spent \$230 million more on average each year between 2011 and 2013 because they had to pay more for newer, alternative generics when older generics are not produced. Keep in mind that figure is relatively conservative, since it excludes drugs purchased from off-contract distributors, more expensive purchases of therapeutic alternatives and indirect costs such as added labor.

These surveys don't calculate a slew of other hidden costs: the reduced productivity of workers who spend greater lengths of time than they should away from their jobs because the most effective treatments aren't available; FDA inspections of overseas pharmaceutical plants when emergency imports become necessary; higher shipping costs incurred to make sure the drugs arrive on time from abroad; the time and money it takes investigating the illicit activities of gray marketeers and unregulated drug manufacturers that attempt to pass themselves off merely as "compounding" pharmacies.

Another cost routinely left unconsidered: Drug shortages also interfere with clinical trials that require older, generic drugs as controls or in combination therapy with experimental agents. The cost of these delays and stoppages has yet to be measured financially, but could "easily" run in the tens, even hundreds of millions of dollars every year, says Erin Fox, the drug expert at the University of Utah.

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If a government-driven solution to the drug shortages is to gain traction, it will almost certainly need the support of caregivers and scholars willing to check old doctrines of free-market efficiencies at the door — people such as Stacey B. Lee, a health law scholar and assistant professor at the Johns Hopkins Carey Business School, who recently completed a journal article, “The Drug Shortage Crisis: What Happens When Generic Manufacturers ‘Just Say No,’” to be published later this year.

Her article concludes: “The solution to ending shortages lies in removing the economic and regulatory obstacles that prevent manufacturers from achieving profit margins sufficient to produce certain needed medicines.” Nowhere, however, does it address a government option.

Before writing the article, did Lee consider a government solution? (No.) Had she considered it prior to writing, would it have impacted her conclusion? (Probably.) Does she think it’s an idea whose time has come?

“Just as a practical matter, I can’t even get my head around this type of an approach,” she says, and pauses. “I mean, this is — holy cow, this is like — I don’t know *what* it is.” She thinks some more. “Perhaps you could make some headway by making it analogous to Medicare — but even there it’s not as if the government provides the care for seniors in the form of state providers.”

She sighs. “I don’t have a good answer.” But will she consider the idea the next time she delves into the topic? “Yes,” she says, “that I will do.”

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