

THE WAXMAN REPORT

How Congress Really Works



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CHAPTER 4

The Orphan Drug Act



ONE FALL MORNING IN 1979, BILL CORR, A MEMBER OF MY subcommittee staff, was sitting at his desk when the phone rang. A panicked caller named Muriel Seligman told him that her son Adam suffered from a rare neurological disorder known as Tourette's syndrome, for which no treatment was available in the United States. Adam's doctor had told them that a drug called Pimozide, sold in Canada, helped alleviate the involuntary motor tics, cursing, and guttural noises that are symptoms of Tourette's. So Muriel Seligman, feeling she had no alternative, had asked a friend to fly to Canada to obtain Pimozide for her son. She was frantic because earlier that day customs agents at San Francisco International Airport had intercepted the friend as he returned and seized the medication because it was not approved for use in the United States. As a constituent, she was calling to demand my help. "They took the drug that my son needs," she said. "What are you going to do about it?"

A frequent complaint about Congress is that it does not respond to people's needs. But Mrs. Seligman's phone call demonstrates that this is not always the case. The concern for her son

that prompted a call to her congressman set in motion a chain of events that culminated in legislation that addressed not only Adam's plight but those of millions of other Americans just like him who were silently suffering from rare diseases.

Disturbed by the Seligmans' story, my staff began by looking into the obvious question: If Canada offered a safe and effective treatment for Tourette's syndrome, why wasn't one available in the United States? The answer soon became clear. Tourette's was an ailment that afflicted so few people that it did not hold sufficient profit potential to entice any U.S. pharmaceutical company into the costly process of developing and gaining approval for a treatment. Tourette's fell into the broad category of "orphan diseases" whose victims had little hope of ever finding a treatment or cure because their numbers were so few. The situation was especially tragic, we learned, because scientists who discovered promising new treatments for orphan diseases often could not interest profit-minded drugmakers. These products thus became known as "orphan drugs," and pharmaceutical companies rarely pursued them, even in cases when a foreign drug like Pimozide demonstrated clear potential.

When a member of Congress confronts this sort of dilemma, the first challenge is to gain a sufficient understanding of the problem, and then to figure out what the government can do about it. In an effort to learn more about orphan diseases and how we might help those stricken by them, the Health and the Environment Subcommittee scheduled a preliminary hearing on Capitol Hill in June 1980. We invited Adam Seligman, and several doctors, government officials, and representatives of the few organized rare-disease groups we could find to testify.

What we learned at the hearing was that although the federal government and the private pharmaceutical industry spent hundreds of millions of dollars a year for biomedical research and drug development, our country's system of discov-

ering and developing new drugs contained an important flaw: It did not account for the inherent financial disincentives to producing orphan drugs, and therefore failed to serve millions of people like Adam Seligman who suffered from rare diseases. Since no government policy addressed this shortcoming, creating a mechanism to facilitate the development of these drugs seemed a promising line of pursuit.

Every day that Congress is in session, members are constantly being barraged by problems like this one that demand their urgent attention. The number of these competing claims unfortunately far outstrips the time and resources that Congress can apply to them. One benefit of a hearing like the first one we held on the orphan drug problem is that it can take an abstract policy issue like pharmaceutical development and bring it vividly to life with searing human examples of who it affects and why Congress must act on it.

When his turn came to testify, Adam Seligman took a seat before the members of the subcommittee. At eighteen years old, Adam was slender, dark-haired, and handsome, but the simple act of carrying on a conversation required enormous energy; he was constantly fighting through the frequent outbursts and loud guttural noises that Tourette's inflicts, which made his willingness to testify before Congress all the more courageous.

I began by asking Adam to describe what his life had been like. He recounted the story in stages. At age eight, the first signs that something was not right. The tics that began soon after, developed into muscle spasms, and finally into the horrific "dystonic reactions"—the doctor's term for the sudden jerks that snapped his neck back so violently that he couldn't breathe. The emergency room visits that ensued, and the procession of mystified doctors who could not even give his mother a name for her son's affliction. The years of hopeless-

ness and fear continued until, at age fourteen, the genetic clues finally yielded a diagnosis. His eighty-two-year-old grandfather had been the unlocking key. Long ago, doctors had told the old man that the tremors in his hands and feet were caused by Saint Vitus' Dance. But Adam's new specialist recognized Tourette's. Haldol had eased the tremors, but brought fatigue, depression, blurred vision—made it impossible to function. Adam had had to repeat senior year. Pimozide was a magic elixir. He tore through two years of high school in nine months and, just before the hearing, graduated with extra credit. But the Pimozide was gone now, and the symptoms returning.

"What will you do without Pimozide?" I asked him.

"I don't know," he replied. "When the tics start to get really bad again I will have to go back on Haldol, which I would really not like to do."

Amid the sadness of cases like Adam's were also tales of great heroism and perseverance on behalf of the ill, such as that of Dr. Melvin Van Woert. Like Adam Seligman, Dr. Van Woert's patient suffered from a rare but treatable condition, in this case a neurological disorder called myoclonus, so debilitating that it had forced her into a wheelchair. Though a treatment existed, no pharmaceutical company considered it commercially viable, and so none would agree to bring it to market. For years, Dr. Van Woert, relying on grants from private foundations, had hand-mixed the drug himself with ingredients purchased from a biochemical supply house that ordinarily serviced veterinarians, and had kept his patient out of her wheelchair.

The day's testimony convinced most of us that this was a clear case of a problem that Congress could play a constructive role in solving. Next we needed to figure out the best course of action. Only then could we turn to the greatest challenge of all: figuring out how to build public momentum to fix a medical issue that even many doctors were not aware of.

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THAT FIRST HEARING, IN JUNE 1980, DREW A SPARSE CROWD AND little public notice. Only the *Los Angeles Times* sent a reporter, and only because Adam Seligman was a local resident. But this was enough to deliver an unexpected boost. The next day, a Hollywood writer and producer named Maurice Klugman happened upon the *Times* article and was moved by what he read. Klugman himself was battling a rare form of cancer. A producer of the hit television drama *Quincy M.E.*, which starred his brother, the actor Jack Klugman, as a crusading medical examiner, he decided to write an episode of the show devoted to Tourette's syndrome and the orphan disease problem. At the end of the episode, a message explained to viewers that the story was based on real events and invited them to write in if they wanted to help. In the weeks and months after the show aired, thousands of letters poured into the *Quincy* production studio from viewers eager to help raise public awareness.

In the meantime, I used my chairmanship of the Health and the Environment Subcommittee to press ahead. I was not the only member of Congress concerned about orphan diseases. Elizabeth Holtzman, a Democrat from New York, had previously introduced a bill calling for the government to develop orphan drugs through the National Institutes of Health. Holtzman's rationale was that NIH scientists already conducted biochemical research using drugs; she wanted to expand the agency's responsibilities to include developing them for the market as well. Holtzman retired in 1980, but appealed to a colleague, Ted Weiss, a Manhattan Democrat, to reintroduce her bill after she left. Weiss had done so, but the measure had not gotten far because Congress was reluctant to provide the considerable outlay that a major new government initiative would require and because some members wondered whether the private sector might not do a better job. The fundamental

question that we needed to decide in order to put together effective legislation was whether government or the pharmaceutical industry was better suited to the task of developing orphan drugs.

To learn more about the Holtzman-Weiss approach and the private industry alternative, I organized a second hearing for the spring of 1981. Orphan drugs remained an obscure issue, so we needed to draw more attention to the problem to foster a sense of urgency and pressure Congress to act. The *Quincy* episode devoted to Tourette's syndrome was scheduled to run on March 4, 1981. So we decided to hold the hearing the following week and invited Quincy himself—Jack Klugman—to testify, along with pharmaceutical industry representatives, government officials, and a broad group of people with orphan diseases.

Hollywood celebrities are so prevalent on Capitol Hill these days that they rarely cause much of a stir. But in 1981, the appearance of a bona fide television star like Jack Klugman at a congressional hearing was a major news event. On the appointed day, *The New York Times* ran a front-page story on Klugman and the orphan disease problem. While our first hearing, nine months earlier, had taken place before a nearly empty room, this time we arrived to find it jam-packed with cameras and reporters.

This was, of course, precisely the effect we had intended by inviting Klugman to appear. Orphan diseases had been ignored or overlooked for years. Now, suddenly, they were in the spotlight. Klugman's testimony had a mesmerizing effect, and not just on the news media—in a rare moment of levity, my colleague Jim Scheuer of New York began asking the star witness scientific questions, as if he were a real medical examiner, rather than an actor who portrayed one on television.

But even Klugman's star wattage could not overshadow

the testimony of those stricken by orphan diseases, who spoke next. After Adam Seligman appeared before Congress the previous summer, the news had spread to people with all sorts of rare ailments that a few people in Washington had at last noticed their predicament and wanted to help. The first hearing had featured testimony from just one other victim besides Adam because we had had difficulty finding others; no national group existed then to organize and advocate on behalf of this underserved population. This time, however, the hearing room was filled with victims, many of them children, of some of the rarest and least understood disorders known to medicine—people with terrible skin ailments, crippling cancers, elephantiasis, and conditions that caused webbed fingers and internal organs. They had in common the exotic nature of their maladies.

At the time, Tourette's afflicted only about 100,000 people, not nearly enough to interest drug companies, but still more than many of the other diseases and conditions that were represented that day by victims and their families. They included muscular dystrophy, a congenital disorder that weakens the muscles; cystic fibrosis, a deadly hereditary disorder (40,000); spina bifida, a congenital neurological condition (27,500); Huntington's chorea, a degenerative disease of the mind and nervous system (14,000); ALS, better known as Lou Gehrig's disease (9,000). Then there were the truly obscure ailments. Prader-Willi syndrome, a fatal ailment that causes huge weight gain in children, afflicted about 2,000 a year; Wilson's disease, an abnormal accumulation of copper in the liver and brain, just 1,000; and cystinosis, a genetic disorder that usually causes kidney failure by age ten, struck about 100 children a year.

One by one, victims of these diseases and their family members described lives of helpless isolation, driven by the unending and often futile search for answers about their condition

and medical care to treat it. Most had nowhere to turn. The sights, sounds, and personal stories brought many of us to the point of tears. It was as if someone had pulled back a curtain to reveal an entire segment of society that no one knew was there: Gathered together in a congressional hearing room before the national media were human beings with diseases so disabling or disfiguring that they never came out in public. In my thirty-five years as a congressman, I have never witnessed a more powerful scene.

AT THE SAME TIME THAT WE WERE USING THE HEARING PROCESS to conduct a public inquiry and raise awareness, Bill Corr and others on my subcommittee staff embarked on a major survey of drug companies, federal research agencies, and university scientists to gain a thoroughgoing understanding of how the drug development process worked and why it was not yielding treatments for rare diseases. We wanted to know how many orphan drugs existed, why promising compounds often languished in the laboratory, and which entity—government or industry—was ultimately better equipped to address the problem.

From the outset, we met stiff resistance. Drug company executives didn't want to appear before Congress for fear of looking mean-spirited. Instead, representatives of the industry's trade group, the Pharmaceutical Manufacturers Association (PMA), claimed that, contrary to all outward appearances, drug companies in fact had no problem at all developing treatments for orphan diseases, and would oppose any legislation aimed at making them do more. This is an unfortunate and all too common refrain from trade groups in any industry and a big reason why such organizations often pose the greatest obstacle to good legislation. Because trade groups exist to represent the interests of an entire industry, their main concern is maintain-

ing the happiness of all their members. Even legislation that is supported by a broad array of drug companies, and opposed by only a vocal few, will typically engender opposition from the PMA: Trade groups always push to weaken a bill to the point where none of their members object to it, which is why they are often such a negative force in the legislative process.

Our survey nevertheless laid out the full extent of the problem. Doctors had identified about two thousand rare diseases. We turned up 134 drugs used to treat them, forty-seven of which were approved for use in the United States. Contrary to industry claims, only ten of these forty-seven drugs had been developed and marketed by U.S. pharmaceutical companies in the last decade. Here was clear proof that the current system wasn't working.

The survey also revealed other important reasons why drugmakers did not develop most of the promising orphan compounds that scientists discovered. In addition to serving markets too small to make desirable targets, we found out that many orphan drugs were not patentable or that their patents had expired, and thus offered much smaller profit potential. By law, most drug patents provided the manufacturer an extremely valuable seventeen-year period of exclusive control. The clock started ticking when the patent was awarded. But since orphan drug development was seldom cost-effective and therefore not a priority, patented compounds that might have yielded treatments for orphan diseases often lingered undeveloped until the seventeen-year window had closed. Lacking the potential to produce a temporary windfall, developing the orphan drug became an even harder sell.

Finally, we learned that drugmakers had an understandably difficult time meeting FDA testing requirements. It's impossible to run hundreds or thousands of patient tests on a drug designed to treat a disease that only affects a few dozen people

each year. Consequently, the clinical trials surrounding orphan drugs were often fraught with great uncertainty. The risk that the FDA might not accept the improvised testing that orphan drug development sometimes entailed had an additional chilling effect on pharmaceutical companies.

One purpose of the survey was to shed some light on the question of whether government or industry was better equipped to develop treatments for rare diseases. Holtzman and Weiss had shown that a compelling argument could be made for having the NIH do the job. But our investigation convinced us that this was not the best approach because NIH, as a research institute, had no experience in developing drugs for the commercial market. The true expertise and resources lay in the private sector, so finding a way to interest pharmaceutical companies in pursuing treatments seemed to offer the best chance of success. We wrote the Orphan Drug Act with this in mind, creating a host of new incentives for private industry, and introduced our bill in December 1981.

The secret to crafting legislation that works is not ramming through a partisan bill, but rather designing one that is acceptable to all parties. The pharmaceutical industry had made clear that it did not want a new law. But we intended to pass one anyway. From the outset, our challenge was clear: We had to find a way to persuade private drugmakers, which actively opposed our efforts, to address orphan drugs, and believed that the key to changing their outlook was to design legislation that accounted for the financial and procedural hurdles they faced.

The easy way to gain industry support would have been to lower the FDA approval standards for orphan drugs. Many patient groups, desperate for a cure, would have accepted this as the only feasible way to bring these drugs to market. But weaker safety and effectiveness standards would have further imperiled sick people's health and tempted drugmakers to

abuse the loophole, so while flexibility is the key to any deal, we vowed that safety and efficacy was the one area where we would brook no compromise. Shortcuts were out of the question.

Instead, our bill encompassed three major incentives for pharmaceutical companies, each addressing a specific impediment to orphan drug development that we had uncovered in our survey and hearings. The first component eliminated the patent problem by providing a "market exclusivity provision" guaranteeing the drug's manufacturer a seven-year monopoly—in addition the clock would not start ticking until much later in the regulatory process, after the drug had received FDA approval. The second component eased the regulatory burden by encouraging pharmaceutical companies to consult with the FDA during the clinical testing phase, collaborating on the tricky question of how best to run tests when a disease affects only a small population and thereby removing the element of uncertainty. This was an admittedly unusual approach, since the FDA is a regulatory body charged with rendering impartial judgment—it was a bit like collaborating with the teacher who was about to grade your test. But we thought it was the best way to remove the deterrent. Toward that end, the third component of the bill was a 90 percent tax credit designed to pay most of the cost of clinical trials. To encourage research and innovation, the bill also established an Office of Rare Diseases at NIH.

THE KLUGMAN HEARING HAD A GALVANIZING EFFECT THAT INSTANTLY improved the bill's prospects. No longer were orphan diseases the obscure problem they had been just a year earlier. A third hearing, held in March 1982 to highlight our survey findings, improved them further, since our proposed solution did not entail an expensive new government program and

offered a package of financial incentives and cost reductions that the Pharmaceutical Manufacturers Association, after some discussion, decided was acceptable after all. Ordinarily, a bill would start out in subcommittee, work its way through full committee, and eventually come to the House floor. But the subcommittee and full committee chairmen can, if they so desire, jointly agree to speed up the process by taking up a bill directly in committee, which is what happened to the orphan drug bill. On September 15, John Dingell, the chairman of the House Energy and Commerce Committee, called up the bill. Seeing widespread support, Dingell called for a voice vote, which is the easiest way to move ahead when you have overwhelming consensus and nobody in the opposition demands to have the vote recorded. As it turned out, no opposition materialized, and the measure passed unanimously.

Nevertheless, popular bills can still run into unexpected trouble or delay. Outside factors like news events can suddenly alter the political landscape and derail legislation that once seemed certain to land on the president's desk. Even in ordinary circumstances a bill's author loses a measure of control when legislation is reported out of committee. The next step on the procedural path is the Rules Committee, which determines the amount of time allotted for floor debate, the number of amendments that can be offered, and sometimes even the specific nature of those amendments. Rules votes are invariably party-line affairs, so the tyranny of the majority always threatens to intrude.

One way to avoid all this is to ask the speaker to place the bill on the suspension calendar, a fast-tracking process for legislation that has at least two-thirds support of the House. The suspension calendar literally "suspends" the rules, forbidding any amendments, limiting debate over a bill to forty minutes (twenty for each side) and bringing the measure to a prompt

vote. The Orphan Drug Act of 1982, as our bill was now officially titled, was placed on the suspension calendar and approved on September 28, 1982.

To become law, an identical bill must pass both houses of Congress. Normally, a senator and a congressman introduce similar bills whose differences are reconciled in a House-Senate conference if both chambers approve them. The compromise bill that emerges from conference then must pass each chamber before it can obtain a presidential signature. Sometimes the back-and-forth between the House and Senate gets tricky.

Since no senator had introduced orphan drug legislation, our House bill was sent over to the Senate for consideration, whereupon it was held at the Senate desk, pending the decision of the Senate's majority party. A senator can request that a bill held at the desk be assigned to the relevant committee for action. If no such request is made, the bill stays at the desk until the majority leader calls it up for a vote. Since Republicans controlled the Senate, the bill's fate lay in the hands of Orrin Hatch of Utah, chairman of the Senate Labor and Human Resources Committee, which had jurisdiction over drug legislation.

Hatch signaled his interest in the orphan drug measure—a potentially worrisome development because we needed his support. We were relieved to learn, however, that rather than block the bill, Hatch intended to use it as a vehicle for a series of unrelated initiatives that he and an assortment of colleagues wanted to pass. This is a common legislative tactic when a non-controversial bill has passed one chamber and awaits action in the other, and Hatch used it more frequently than most. But his benign intentions did not yet get us out of the woods. Any changes to the bill, even ones that were not intended to kill it, could nonetheless have unintended consequences that would bring about the same result.

Hatch's main interest turned out to be an amendment estab-

lishing a cancer research and screening program for 200,000 people in and around Utah who were exposed to radiation from nuclear weapons testing in the 1950s, and, in many cases, later developed cancer. Once again, this came as a relief. The program struck me as an eminently worthy idea. But the next amendment stopped us cold. Bob Dole and Russell Long, respectively the chairman and ranking member of the Senate Finance Committee, had prevailed upon Hatch to strike the 90 percent tax credit we had included for clinical trials of orphan drugs—a move intended to protect their bureaucratic turf, since tax policy ordinarily falls under the purview of the Finance Committee, through which the bill had not passed. We considered the tax credit to be the central feature of our bill, the mechanism by which government could finally persuade pharmaceutical makers to develop orphan drugs. In lieu of a tax credit, the Dole-Long amendment authorized a \$50 million grant program, which, to the uninitiated, might seem a meaningless distinction. But Dole and Long understood the crucial difference: A tax credit can simply be written into law and take effect immediately, whereas a grant requires not only an authorization but an appropriation as well—that is, Congress not only had to authorize the money, but hand it over, too, which would entail a whole new legislative battle. Dole and Long knew that, on its own, a \$50 million authorization wasn't good for much, and by swapping it for the tax credit, they would effectively neuter the bill. The Senate's unanimous approval of the Hatch-modified bill on October 1 made that fear a reality.

This meant that to have any chance of saving the bill, we would have to restore the tax credits and then send the updated measure back to the Senate for approval. Adding to the pressure was the impending *adjournment sine die*, the Latin term used in Congress to mean the end of a two-year session. If we could not repair and repass the orphan drug bill by year's

end, the session would expire and we would have to start from the beginning in the next Congress. So began the real negotiations that settled the Orphan Drug Act.

The narrow time frame confronting us necessitated joint House-Senate negotiations. Because so many committees now held a stake in the bill, my House colleagues and I had to contend with representatives from the Senate Finance, Ways and Means, and Labor and Human Resources committees—with Hatch still controlling the bill's fate in the Senate; and the House Ways and Means Committee, which oversees most tax issues. Through most of October, our efforts to restore the tax credit didn't get very far. Meanwhile, the calendar provided a grim daily reminder that time was running out.

There isn't much that a House member can do to force a senator to act on a bill. But Jack Klugman hit upon a novel idea. He and his brother wrote a second episode of *Quincy*, which aired on October 27 and once again reflected events in Congress. This time the story line revolved around an orphan drug bill that was being held up by a heartless senator. In the show's pivotal scene, the senator dismisses the need for orphan drugs, telling Klugman, "Nobody cares about this bill." A righteous Klugman fires back, "Look outside." Peering down from his office window, the senator sees a large crowd chanting and holding signs that read, "We Want the Orphan Drug Act." To shoot the scene, the show's producers hired five hundred people who really did suffer from rare diseases to serve as extras.

Arriving in the middle of these tense negotiations, the *Quincy* episode brought a new wave of public pressure for Congress to act. In the wake of the show, the talks picked up again, and a deal gradually emerged: The cost of clinical trials for orphan drugs would be subsidized by a 50 percent tax credit, a 50 percent tax deduction, and a much smaller \$12 million grant program—the reduced tax credit and grant pro-

gram face-saving measures for our opponents, who agreed to a very good deal for our side. On December 14, the updated bill passed the House; two days later—and this time, without any changes—it passed the Senate, too. As *stne die* arrived and members returned home for the holidays, what was now officially the Waxman-Hatch Orphan Drug Act moved on to the president.

EVEN AS THE HOUSE-SENATE NEGOTIATIONS GAINED MOMENTUM, ominous signs were emanating from the White House. In late fall, Richard Schweiker, Reagan's secretary of health and human services, had called with a warning. "I want this bill, I think it's great," Schweiker told me. "But I've been told by the president to prepare the veto message."

In an unfortunate irony, the White House opposition had nothing to do with the orphan drug component, but rather stemmed from Hatch's cancer testing and screening program for those whose health had suffered from nuclear weapons testing. Reagan feared the program would leave the government culpable for thousands of cancer patients and exact an enormous toll on the federal budget. But since no president could utter anything so heartless in public, the White House claimed to object to the tax credits, whose cost the Congressional Budget Office had estimated at \$15 million. Strange as it seemed to many of us, Reagan's public stance had him willing to ignore the health needs of hundreds of thousands of sick people in order to save the budgetary equivalent of a drop in the ocean. Regardless, organizing an effort to change his mind became our immediate imperative.

Lobbying a president on legislation is not all that different than lobbying congressional colleagues, except that the president is much harder to reach. The goal is still to apply pressure in any way that you can. For this task, our Senate partner, Orrin

Hatch, now became an invaluable ally. Along with being a Republican, Hatch was a forceful advocate who threw himself into the effort to persuade the White House.

The public nature of our campaign for orphan drugs also helped to lend pressure. One useful side effect of the action in Congress was that it led 140 rare-disease groups to band together as the National Organization for Rare Disorders. NORD took out full-page ads in major newspapers, including in California, where Reagan was spending the holidays, urging the president not to be "the Grinch who stole Christmas" by vetoing the bill.

I, too, tried to persuade the president, publicly and privately. To draw maximum attention, Jack Klugman, Adam Seligman, and I held a Christmas Eve press conference in Los Angeles where I delivered remarks designed to cast the issue against the backdrop of the holiday season: "Last week, years of effort to help people with rare diseases culminated with the unanimous passage by both houses of Congress of the Orphan Drug Act. I had hoped for this Los Angeles press conference to be a joyful celebration of the victory for which all the groups represented here today worked very hard. Unfortunately, it is my duty to tell you that the battle may not yet be over. I have been unable to obtain any reassurance from the White House that the president will sign this bill. Incredible as it may seem, there are reliable reports that even as we prepare to mark the Christmas holidays, the White House is preparing to kill this humanitarian legislation. . . . We need to write, call, and send telegrams to the White House. We also need to urge television stations, key news-oriented radio stations, and the press to give full coverage to this vital issue."

Often, the most effective leverage in a situation such as this does not come from political opponents, but from supporters, especially those who have personal relationships with the

president. Every New Year's Eve, the Reagans attended a party thrown by the Annenberg family in Palm Springs. A Republican businessman from my district named Ted Cummings was part of that crowd, so I called him and said, "I'd like you to talk to President Reagan at the New Year's Eve party." Cummings protested that all talk of politics would be strictly off limits at the party. Don't worry, I assured him, this wasn't politics but a situation where people suffering from rare diseases had a chance to get lifesaving medication. Cummings thought it over, but wouldn't commit. "We just don't do that kind of thing," he said.

I never found out what transpired at the Annenbergs' party. Some things are better left as mysteries. But just after New Year's, Schweiker got a call from the White House telling him to prepare a new message: The president would sign the bill; and on January 4, 1983, the Orphan Drug Act became law.

AS SEVERAL PEOPLE REMARKED AT THE TIME, THE DRAMATIC rescue effort had all the hallmarks of a Hollywood ending. Afterward, Jack Klugman and everyone else who played a role in passing the legislation gathered for a huge party.

But the real Hollywood ending unfolded over the next twenty-five years, as the Orphan Drug Act took effect and produced enormous benefits. Some were anticipated. Since 1983, the FDA has approved more than three hundred orphan drugs—up from ten the decade prior—with 1,100 more currently under development. Rare-disease work at NIH has expanded significantly due to the increased visibility and funding. In January 1985, Pimozide became one of the first orphan drugs to gain FDA approval under the new law, and continues to be widely prescribed as a treatment for Tourette's syndrome. Another group that saw early benefit from the law was the

growing number of those with AIDS. One of the first drugs approved to treat the disease, AZT, was developed and marketed as an orphan drug.

The Orphan Drug Act has worked so well that it has served as a model for similar programs in the European Union, Japan, and Australia. Under the leadership of Abbey Meyers, an early activist for Tourette's who was instrumental in helping us pass the law, the National Organization for Rare Disorders has gone on to achieve global renown, and now organizes the latest drug research from all over the world.

Nearly as significant have been the law's unexpected benefits. The pharmaceutical industry, for instance, has come full circle and now lauds the Orphan Drug Act. While our aim had been to encourage the big drugmakers to develop promising compounds, only about 15 percent of the applications for orphan drugs today derive from the major pharmaceutical companies. Instead, many smaller firms have come into being specifically to develop them.

One reason for this, likewise unexpected, is the degree to which the law's exclusivity provision has fostered new drugs. The critical legislative battle was fought over tax credits for clinical trials because we believed that this expense posed the single greatest impediment to developing orphan compounds. As it turned out, however, drug prices began rising steadily in the early 1980s, generating bigger and bigger profits for pharmaceutical companies the higher they climbed. Consequently, many drugs that were once considered financially unviable suddenly held new profit potential, and the need to subsidize clinical trials diminished.

Instead, the law's guarantee of seven years' market exclusivity became the key issue for its success. In 1985 the Orphan Drug Act was amended to include biological as well as chemical drugs, which helped give rise to an entire new industry,

biotechnology drugs. In the 1980s, as biotech products began to emerge, there was uncertainty about how patent laws would apply to them. While today's patent protection for biotech drugs are robust, at the time they were perceived to be so unpredictable that many companies, especially small upstarts, had little confidence in the market protections available to them. The Orphan Drug Act's guarantee of seven years' protection from competition functioned as an effective substitute, sheltering smaller firms as they developed drugs for orphan diseases that often became profitable. (Many orphan diseases lend themselves to biotech treatments.) Some of the most successful biotech drugs, such as synthetic human growth hormone, came into being as orphan drugs.

Even successful legislation needs periodic updating to close loopholes, address unanticipated shortcomings, and keep up with changing circumstances. This can be a major battle in its own right. The protections outlined in the Orphan Drug Act were designed to make drug development economically feasible where otherwise it might not have been. Some manufacturers took advantage of the protections to inflate profits and stave off competition, reaping windfalls far in excess of development costs that consumers and the federal government (through Medicare and Medicaid) end up subsidizing in the form of higher prices. Another dishonest tactic was to claim orphan drug status for a narrowly defined treatment group and then pile up additional orphan designations for different applications of the same drug, a technique known as "salami slicing."

In 1990, we introduced a package of amendments that would have created "shared exclusivity," allowing firms to develop drugs simultaneously and lower prices through competition. We also tried to give the FDA power to reassess orphan drug exclusivity after three years to determine whether mar-

ket protection was still necessary. This would have ensured that the law functioned as intended, helping to create drugs for small rare-disease populations and limiting opportunities to exploit it. The House and Senate passed the bill unanimously. But President George H. W. Bush vetoed it after heavy lobbying from the pharmaceutical industry. The episode serves as a stark reminder of the industry's tremendous power, and why it is important, when crafting legislation, never to give too much away. In all my years as a legislator, I can't recall a single example of a law where, when drug companies were granted excessive government concessions, we ever managed to scale them back later.

The Orphan Drug Act nevertheless remains an example of government at its finest, demonstrating how Congress applies itself to solve overlooked, but deeply important, problems that affect millions of Americans. Muriel Seligman's phone call became the catalyst for new a law that, twenty-five years later, has helped transform not only the lives of families like the Seligmans, but the entire way in which the drug industry approaches the development of new medications for orphan diseases.