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Dying for Lifesaving Drugs

Will desperate patients destroy the pharmaceutical system that produces tomorrow's treatments?

Kerry Howley | Aug./Sept. Print Edition

Ten years ago, doctors drilled a hole into John Gotschall's skull, inserted two catheters, and pumped a poison into his brain. Using a child's morphine pump, the team of neurosurgeons pushed diphtheria toxin into Gotschall's temporal parietal lobe over a period of four days. Eight weeks later, they did it again, reusing the same cavity and pumping in a slow stream of tissue-killing fluid.

Gotschall was not well. Shortly before he invited a team of surgeons to experiment with his cerebral tissue, the 44-year-old municipal worker had plowed his car into a snow bank on a Baltimore street. When he woke up at the hospital, doctors told him he'd had a seizure at the wheel. An MRI revealed the cause of that seizure: a tumor deeply embedded in his brain tissue. There are different grades of brain tumor, many of them slow-growing. Gotschall had glioblastula multiforma (GBM), brain cancer in its most aggressive and deadly form, and he likely had only months to live.

Gotschall's physicians initially ordered chemotherapy and radiation, the same weapons with which doctors have fought cancers for decades. Neither worked. After he exhausted the standard options, he started searching for nonstandard ones. His neuro-oncologist pointed him to a group of doctors at Johns Hopkins and a drug in development called TransMID. TransMID had survived Phase I testing, in which researchers evaluate a medication's safety and appropriate dosage, and was then in Phase II, in which researchers begin to evaluate efficacy. Gotschall finally caught a break: He qualified for entrance into the trial. Along with 43 other patients, Gotschall would have a chance at a radical new treatment that might add years to his life.

TransMID is a Trojan horse: The drug attacks the tumor under the pretense of a gift. Tumors feed on iron they absorb from surrounding tissue, and the drug delivers deadly, iron-wrapped diphtheria toxin straight to the site of the disease. The method is meant to be more precise than scooping out the cancerous tissue, a technique that can be as clumsy as its cringe-worthy name, *debulking*.

The treatment proved immediately effective in the most dramatic way possible. Gotschall's tumor simply vanished. TransMID's newest poster child, he touted the treatment on *CBS Morning News*. "It is dramatic," Gotschall's neurosurgeon, John Weingart, told CBS. "I mean, there is no question that this is an unbelievable response."

Ten years later, TransMID is still not available to the public. About 18,500 Americans will be diagnosed with GBM this year, and the median patient will survive 14 months. Treatment has not advanced significantly in the last 20 years, so GBM victims will be offered more of the same: chemotherapy, radiation, and when possible, surgery. TransMID entered Phase III tests, meant to confirm efficacy and monitor the drug's side effects, last year. But most currently diagnosed GBM patients probably will

never know about the drug, and most of those who do find out about it will not qualify for trials. If TransMID ever does go to market, these patients will be dead by the time it gets there.

For as long as there are lifesaving drugs in development, there will be dying patients undaunted by the dangers of an unapproved treatment. But within the strictures of the current regulatory regime, very few patients--mainly those who, like Gotschall, meet the criteria for clinical trials--are granted the freedom to risk their lives in the face of certain death. Consider the conditions for admission to the TransMID trial. "The tumor has to have grown 25 percent since the patient's last MRI, but it has to be under five centimeters," explains Patrick Rossi, a physician employed by Celtic Pharma, TransMID's manufacturer. "It can't have grown into the ventricles or the brain stem. The patients have to have failed every other treatment: chemo, radiation, stereotopic radio surgery, any kind of oncology agent, grandma's soup, voodoo, you name it."

To terminally ill patients who do not qualify for such trials, and typically cannot receive drugs until they are deemed effective by the Food and Drug Administration (FDA), this obsession with clinical control can appear deadly and cruel. As TransMID trickles through the FDA pipeline, GBM continues to kill thousands of Americans every year. Most patients who don't meet the criteria for admission to clinical trials will not be granted the right to risk their lives with a developmental treatment.

Since the 1960s, when randomized, double-blind clinical trials became a standard requirement for bringing new drugs to market, clinical researchers have confronted the chaos of disease with the trappings of a regimented, uncompromising order. Drug trials are rooted in centralized authority: trial slots are numbered, subjects handpicked, control groups maintained, patients monitored. Maintaining this level of precision requires not only the cooperation of willing test subjects, but the coercion of the general population. To preserve pristine testing conditions, the federal government curtails our freedom of exchange and our right to take risks. Ailing individuals and drug companies are prohibited from trading in unapproved drugs, and terminal patients forbidden to experiment outside a clinician's watch.

This approach to drug testing is rife with serious ethical problems, but the preconditions for meaningful change are mind-boggling. The current clinical trial regime is cemented in place by legal restrictions that prevent patients from waiving their rights to sue and a regulatory regime that resists even incremental change. Alternatives to the standard placebo-controlled, closed clinical trials exist, but guarantees that such trials will lead to a drug's approval do not. A system meant to facilitate innovation in drug development is itself resistant to change.

With billions of dollars on the line, the clinical trial industry has never been more powerful. But in an age of increasing patient autonomy, the walls surrounding the drug testing system are under assault like never before. An organization called the Abigail Alliance for Better Access to Developmental Drugs is suing the FDA, claiming a constitutional right to trade in lifesaving pharmaceuticals. The group wants to crack open the system, to give patients and their doctors the right to choose between taking experimental, often dangerous drugs and dying untreated.

To the dismay of the medical establishment, bioethicists, and many groups representing cancer patients, a federal appeals court has ruled in the alliance's favor. As the case continues to wend its way through the courts, doctors, researchers, and even patients warn that the suit could bring the drug development process to a screeching, lethal halt.

Resurrection and Insurrection

The FDA runs on $1.5 billion a year, while the global clinical trial industry is worth roughly $10 billion. The Abigail Alliance, based in its founder's home in Fredericksburg, Virginia, subsists on $50,000 a year in donations. Its one full-time employee is Frank Burroughs, father of the late, eponymous Abigail.

Burroughs, now in his sixth year of advocacy, has lost many of his most important co-members. After last year's ruling in the alliance's favor, the FDA argued that the group no longer had legal standing to sue it, since none of the patients who had signed the original affidavits were still members. They were all dead.

The alliance launched its assault on the FDA in 2001, right after 21-year-old Abigail Burroughs died while fighting for access to developmental treatment for head and neck cancer. In 2003, Frank Burroughs and his pro bono lawyers at the Washington Legal Foundation, a public-interest litigation group, filed a federal lawsuit in D.C. They maintain that terminal patients have a constitutional right to lifesaving experimental drugs that have passed the first phase of FDA testing--the phase that establishes the safety and tolerability of a treatment. The right to self-preservation through access to experimental drugs, the alliance argues, is a substantive due process right, implicit in the Fifth Amendment principle that no person may be deprived of life, liberty, or property without due process of law. The Supreme Court has used substantive due process reasoning, which is highly controversial among legal scholars, to recognize unenumerated constitutional rights to abortion, to private sexual activity, and to send children to private schools. The Abigail Alliance argues that it also protects the right of terminally ill patients, acting on a doctor's advice, to obtain potentially lifesaving medication when all other alternatives have been exhausted.

The group's complaint was dismissed, but last year a three-judge panel of the U.S. Court of Appeals for the D.C. Circuit overturned that decision. "A right of control over one's body has deep roots in the common law," Judge Judith Rogers concluded in the majority opinion. "The prerogative asserted by the FDA...impinges upon an individual liberty deeply rooted in our Nation's history and tradition of self-preservation."

The appeals court decision drew little attention, but the media coverage it did attract was almost uniformly negative. "A court makes up a right," snarked the *Washington Post* editorial page. A June 2006 article in *The New Republic* said the court's logic would put us "back in the snake-oil days," and *The Journal of the American Medical Association* lamented "a new era of unapproved drugs."

The FDA sought a rehearing by the D.C. Circuit, and a 10-judge panel heard the arguments of both sides in March. No matter how the court rules, the Abigail Alliance expects its legal battle to end in the Supreme Court.

After Burroughs, the man who spends the most time promoting the Abigail Alliance's cause is a geologist named Steve Walker. In December 2000, Walker and his wife of 20 years--Jennifer McNeillie, also a geologist--were in the process of adopting a child abroad. The two had paid an agency, were looking at pictures, and were preparing to go to Russia to make their final arrangements. Before they got there, Jennifer was diagnosed with Stage 4 colon cancer. At 45, she was told she had a slim chance of making it to 50.

McNeillie's bleak prognosis coincided with a flurry of promising research in colon cancer treatment. Three new drugs, Erbitux, Eloxatin, and Avastin, were in development, and McNeillie decided that the risks of being a test subject were worth taking. She would wait years, her cancer progressing, for the chance to try one. There were no Eloxatin trials in progress at the time, and Erbitux and Avastin trials were both closed to new enrollment. "The drugs were simply unavailable," says Walker. "We couldn't get into the trials."

In September 2002, a bedridden McNeillie was finally admitted into a small Erbitux trial. "The drug resurrected her," says Walker. "We went skiing in Colorado. We went hiking." Without the drug, cancer cells that lined McNeillie's stomach would appear, expand, leak fluid. McNeillie would blow up like a

balloon every four days and have to go to the hospital, looking six months pregnant, to be drained through a catheter. On Erbitux, her worst side effect was a rash. She went back to work.

Six months after she started taking the drug, doctors spotted a new tumor on her colon. By the rules of the trial--rules set to ensure the FDA would accept the results--McNeillie could no longer participate. No trial meant no drug. When Walker pleaded with McNeillie's physician to keep dispensing the drug, the doctor pleaded back: Giving out more Erbitux could mean giving up his license to practice medicine.

Determined to dig up more Erbitux, Walker spent six weeks shuttling between the drug's manufacturer, ImClone, and the FDA. ImClone responded quickly, offering to set up an entirely new trial just for McNeillie so her treatment would conform to protocol. It took ImClone 10 days to set up the trial. The FDA then delayed for two and a half weeks, mulling approval. "This is to give the same drug the same way by the same doctor," says Walker. "During this time my wife is dying. She is tremendously suffering." At the same time, Walker was trying to get his wife into an Avastin trial. She didn't qualify.

Six weeks after she'd been kicked out of the trial, McNeillie was given a dose of Erbitux. She passed away after six months on the drug, in June 2003. Eight months later, the FDA deemed Erbitux and Avastin safe and effective treatments for colon cancer.

The Abigail Alliance has collected many such stories. There is David Baxter, a high school student suffering from colorectal cancer, denied admission to trials for a promising drug because he was too young to qualify. He died at 17 in 2001. Alita Randazzo, also suffering from colorectal cancer, spent years flying to France to get Eloxatin, which had been approved there but not yet in the U.S. When Eloxatin stopped working, she was told by her doctors that her last hope was Erbitux. Trials for Erbitux had closed. She died in 2002, still fighting for access.

A Hard ACT UP to Follow

Enraged patients have jolted the FDA into action before. In New York in 1987, protestors from the AIDS Coalition to Unleash Power (ACT UP) hanged an effigy of FDA chief Frank Young on Wall Street. Activists complained that AIDS drugs were too slow in being approved and too expensive when they went to market. A year later ACT UP brought 1,000 protesters to the FDA's headquarters, vowing to shut the agency down. The FDA stayed open, and 180 protesters were arrested.

Graced with voluminous media coverage, AIDS activists found their confrontational tactics rewarded. AZT had been rushed through the process before the activists showed up at the FDA's doors, the protease inhibitor Saquinavir was approved three months after it was submitted for approval, and a similar drug, ritonavir, was approved 24 hours after an FDA panel recommended that it be allowed on the market. It was as if they'd slipped the FDA a massive dose of Adderall.

In the early 1990s, under congressional pressure to reform, the FDA introduced "fast track" regulations to speed review of certain drugs and complex "expanded access programs" through which terminally ill patients could potentially receive medication. In 1997 then-President Clinton signed the Food and Drug Modernization Act, part of which allowed individual patients to request access to developmental drugs.

But many of the gains applied exclusively to AIDS patients, and from where Burroughs is standing, even the systematic reforms appear inadequate. Setting up an expanded access program, he argues, is such a bureaucratic nightmare that the program is "essentially inoperative." The process involves a significant amount of paperwork for the patient's doctor, who may not be aware of drugs in development; the pharmaceutical company, which has no real incentive to participate; and the FDA, which is not known for its alacrity in tackling administrative tasks. Drugs aren't eligible for such programs until late in the clinical trial process. Still, such programs do exist and they are occasionally

utilized. Two patients have won the right to try TransMID through such a program.

As the heyday of activism passed and the AIDS movement matured, pressure for radical change began to wane. The Abigail Alliance is no ACT UP, and Walker and Burroughs look with envy upon the group's ability to jam drugs through the FDA bureaucracy. "Originally, we tried to get support from the AIDS community," Burroughs recalls.

"But we didn't. They had won their victory." The 1980s marked the first time dying patients had risen against the FDA, and no movement of similar strength has emerged since.

In its fight against a sclerotic system, the AIDS community had a major advantage: It actually was a community. Organized around civil rights, supported by the political left, noticed by the mainstream media, AIDS patients formed a vocal, recognizable class. "Contrast that with the class of patients who are terminal," says Walker. "There are hundreds of cancers. These people have nothing in common. By the time they're sick, they have no way of connecting to anyone else. They don't have time to go to meetings and lobby the FDA. The only thing they have in common is that the FDA stands in their way. And sometimes they don't even know that."

It's more than a lack of organization that plagues the alliance. Groups representing the victims of deadly diseases are often vocally opposed to its agenda. The American Society of Clinical Oncology submitted an amicus brief in the alliance's pending case-in support of the FDA. In a September 2003 press release, Fran Visco, head of the National Breast Cancer Coalition, announced that a victory for the Abigail Alliance would "undermine scientific research and impede our search for answers that will help everyone." The Leukemia & Lymphoma Society, the National Childhood Cancer Foundation, and the National Patient Advocate Foundation have all voiced their intention to side with the government.

‘Piles of Bodies'

While Burroughs and Walker believe they are tearing down senseless bureaucratic obstacles, their opponents charge that the Abigail Alliance is trying to hijack drug development the world over. Clinical trials have been the primary way the medical establishment obtains information about drug efficacy for the last 50 years. To its detractors, the alliance seems prepared to cripple an ever-evolving body of pharmaceutical research. In the interests of a few patients suffering now, it is willing to cause an untold amount of damage to patients yet to be diagnosed.

Trials conducted in the United States are the most rigorous in the world, consisting of three distinct phases, typically involving thousands of patients. Only 11 percent of drugs that enter clinical trials are ultimately approved, and the numbers are markedly worse for cancer drugs. Anyone who argues for the unencumbered right of patients to take developmental cancer drugs must grapple with the fact that 94 percent of them will not work.

To sift the pharmaceutical gold from this vast bed of chemical silt, drug companies need some type of trial system, and for trials they will need patients. Trials are typically randomized, meaning that some patients will receive the treatment and others will not. If patients could simply obtain the medicines they wanted, they would have little incentive to enter the clinical testing lottery.

"How do you take a rational person and get that person to enroll in a double-blind, randomized clinical trial?" asks Steve Walker. "How do you get people to do that? You give them no other choice. They're not lives worth saving. They're lives worth using. If you can't get into the trial, they can't use your life. They need two piles of bodies."

Mindful of medicine's dependence on test subjects, the alliance isn't asking that all patients get access to

development drugs. It's asking that patients *already* denied admission to trials--patients like Abigail Burroughs and Jennifer McNeillie--be able to buy the drugs they're denied. And even this concession, argue their opponents, would dismantle the clinical trial system.

The amicus brief submitted by the American Society of Clinical Oncology argues that if people who didn't qualify for trials had access to drugs, patients would have an incentive to appear ineligible. Their physicians could easily help them game the system by, say, ordering a round of chemotherapy, which disqualifies patients for many Phase II and Phase III trials.

By that logic, Abigail Burroughs had to be denied treatment to protect the integrity of the clinical trial process. Terminal patients who cannot gain admission to trials still must be prevented from receiving developmental drugs, lest future patients refuse to submit themselves to randomized testing. "They need test subjects," says Walker, "and patients are their only resource." Pull even a single thread, and the whole information-aggregating web unravels.

This conflict has a way of pitting those without any hope of survival against those with some chance at life. Take David Welch, co-founder of the successful software company Telco Exchange. In 2004 doctors found a tumor the size of a lemon in Welch's left frontal and left temporal lobes. The 38-year-old chose to be aggressive, pursuing a treatment so risky that three review boards rejected his request to have the operation performed at their hospitals. The treatment was successful, and Welch, now on his 19th round of chemotherapy to keep the remaining cancerous cells at bay, is unambiguously positive about the operation and his right to risk it.

Welch might seem the typical Abigail Alliance booster, eager to argue for the right to experiment in the face of death, but he is deeply ambivalent. "I medically inherit what has been given to me," he says. "Statistically, I've got a time line of five to six years. The more time I buy, the more time I have for clinical trials to play out. I'm still open to arguments, but I fail to see how we can change the process without breaking it down."

Welch also argues that even if pharmaceutical companies were allowed to sell their drugs prior to approval, they have strong incentive not to do so. Anything that happens to a patient taking a drug in development could later be used to argue against approval, halting manufacture and denying that drug to future patients. And under current FDA regulations, patients cannot waive liability for negligence. Whether they want it or not, patients must have the right to sue, which means they may never be given the chance to take a risk. If the Abigail Alliance wins its case, it will face additional legal battles.

There is a serious argument to be made that the entire clinical trial system is antiquated, that it is time to stop counting piles of bodies and to start using more sophisticated measures of drug efficacy. Biomarkers, substances whose presence in the body indicates a particular disease state, could provide objective evidence on how a drug is working on a particular patient. As such measures improve, the need for placebos may lessen. "Clinical trials are very cumbersome," says Thomas Garvey, a gastroenterologist and former FDA supervisor who has designed thousands of clinical trials. "Although they are not the be all and end all. The science is evolving and getting better."

A March 2005 editorial in *The Wall Street Journal* advocated scrapping placebo trials for cancer patients altogether, giving everyone access to the drugs, and using advanced statistical methods to measure patient progress versus the typical survival rate for a particular cancer. This is the kind of change the Abigail Alliance hopes for, but more incremental changes are already in play.

In an attempt to increase flexibility and reduce approval times, some pharmaceutical companies have begun to conduct what are known as "adaptive" trials. Standard trials are blinded: The findings remain

secret from researchers until each phase of the trial is over, and they are conducted on general populations of patients with similar conditions. Even after a standard trial has ended, it can be difficult to know which patients within a population will respond most positively or suffer the most severe side effects from a particular drug.

Alternatively, adaptive trials allow researchers to analyze and respond to data as it comes in, personalizing treatments and assessing how patients with particular characteristics respond to particular dosages. Researchers can tweak the trial design as they move forward, perhaps dropping a method of treatment that proves unpromising or adding more of one type of patient that seems to be responding well. Trial flexibility may prompt shorter approval times and allow companies to sort good drugs from bad more efficiently. "It's a slightly less restrictive straitjacket," says Walker.

Drug development needs to move in lockstep with the regulatory regime, and the FDA has signaled its openness to new trial design with its "critical path initiative," a program meant to jump-start the process of moving toward more sophisticated clinical trials. Its stated goal is to "bring new scientific discoveries--in fields such as genomics and proteomics, tissue engineering, imaging, and bioinformatics--to bear on product development."

While the agency's potential for change is heartening, the critical path initiative is widely acknowledged to be under-funded and lacking in institutional support. For the foreseeable future, the system will be one that pits David Welch against Abigail Burroughs, information gathering aimed at helping future patients against current patients' desire to live. Dying people will be treated as data points; other dying people desperately want those data.

The View From 40,000 Feet

In February the Food and Drug Law Institute, a D.C. nonprofit that promotes education on law and public policy, held a colloquium on the Abigail Alliance's lawsuit that illustrated just how far outside the medical consensus the alliance and its supporters really are. The colloquium included high-profile lawyers, a specialist in pharmacoeconomics, and Arthur Caplan, one of the world's most prominent bioethicists. The only panelist clearly in favor of the alliance's position was Scott Ballenger, the alliance's lawyer.

Most of the panelists expressed profound discomfort with the Abigail Alliance's rights-based argument and its challenge to the regulatory structure. Caplan argued that terminally ill patients are desperate and therefore may be more in need of the FDA's paternalism than other classes of patients. The panelists spoke of caution, of "giving pause," of balancing risk between patient and society.

After hours of staid presentations and speeches before an audience of 100, Steve Walker approached the mike as an audience member. "You're all approaching this topic from 40,000 feet," he charged, launching into an impassioned retelling of his wife's decline. The panelists looked nervously at their colloquium booklets. The moderator, shifting in her seat, looked torn over whether to cut him off.

Such are the P.R. challenges of the Abigail Alliance. As lawyers, medical professionals, and bureaucrats debate the optimal regulatory structure, Walker and Burroughs want to supplement abstractions with anecdote, to replace talk of test subjects with stories of dead wives and daughters. But when they trade the language of clinical science for that of loss and bereavement, they can come off as too invested to be reasonable and too emotional to merit response. In the heavily risk-averse culture of the FDA bureaucracy, talk of rapid, radical change isn't even countered. It's just ignored.

Even more than the regulatory barriers, this deep-seated fear of disorder works against the alliance's

agenda. "I don't have a right to fly somebody's experimental airplane," reasoned Bruce Chabner, clinical director of the Cancer Center at Massachusetts General Hospital, Boston, in the August issue of the *New England Journal of Medicine*, "so why should I have the right to some drug that a company has dreamed up?" In defending the status quo, Chabner apparently did not pause to consider that cancer drugs, as opposed to airplanes, are unlikely to fall out of the air and kill passersby. Nor are people typically forced to choose between flying an "experimental airplane" and certain death. The right to self-medicate is considered so absurd that incoherence passes for analysis in respected medical journals, while opposition is treated as hysteria.

Things weren't looking much better on March 1, the day the alliance defended its case, for the second time, before the U.S. Court of Appeals for the D.C. Circuit. Scott Ballenger began by stating the alliance's claim: that "terminally ill, mentally competent adult patients have a due process right to informed access to potential lifesaving investigational new drugs determined by the Food and Drug Administration to be sufficiently safe for expanding human trials, where there are no alternative government-approved treatment options."

"That's an awfully specific right," barked Judge David Sentelle, less than a minute into Ballenger's argument. "I may have gotten a thin copy, but I had a hard time finding it in my copy of the Constitution."

The FDA argues this very specific right has been "gerrymandered," its boundaries improbably stretched and manipulated to fit the alliance's very specific demands. In order to disrupt the existing legal framework as little as possible, the alliance has settled upon a narrowly defined right to lifesaving pharmaceuticals. "We have described the contours of the right in terms of the present regulatory regime," says Ballenger, "and we're not trying to destroy it." The alliance concedes to the FDA that it has a compelling state interest in protecting the integrity of the clinical process. It concedes that the FDA has the right to deny dying people drugs that have not yet been subjected to Phase I testing. But it still claims this very narrow right is implicit in the concept of due process.

If terminal cancer patients do have a constitutional right to lifesaving drugs, the limits of that right are hard to discern. What does it mean to be "terminally ill," after all, and where is the line between a lifesaving drug and a life-prolonging one? Could a suicidal cancer patient claim she has a constitutional right to marijuana in order to ease her pain? Does it make any sense to say a fundamental right hinges on the FDA's determination that a drug has passed Phase I testing? And if not, what does that say about the Controlled Substances Act, the Supreme Court's recent rulings on medical marijuana, and the FDA's role as medical gatekeeper?

Although the Abigail Alliance has chosen not to assert a broader right of individual autonomy, the narrow right it claims seems to imply profound change to U.S. law. "Wouldn't the right you're asserting here also apply, then, to the right to therapeutic cloning, or to organ purchase?" Judge Brett Kavanaugh asked a few minutes into Ballenger's oral argument. "Don't we have to take into account the repercussions of what you're asking for here?"

This is a slippery slope, and it alarms supporters of the status quo. Once you argue that the government has no authority to deny Jennifer McNeillie access to cancer drugs, that she has a constitutional right to accept a certain level of risk, it becomes difficult to know where the agency's authority stops and her autonomy begins.

Staying Power

John Gotschall's glioblastoma disappeared for five years after TransMID, the Trojan horse, tricked the

tumor into absorbing it. Meanwhile, the drug lumbered along its tortuous road to approval. GBM is a relatively rare disease, and TransMID has a tiny prospective market. Celtic Pharma's Rossi estimates testing has cost more than $600 million so far. And during the last 14 years, the drug has cycled through no fewer than nine pharmaceutical companies in three countries. Every time TransMID's backers are bought out, as often happens in the industry, Rossi needs to justify the enormous costs of clinical testing to new owners with new priorities. Time and time again, an acquisition or merger has left the drug without funding, at which point Rossi cries, pleads, and eventually brings the dead drug back to life. He casts his relationship to TransMID as something out of *Night of the Living Dead*. "My colleagues call me George Romero," he jokes.

In January of this year, Rossi was busy scouring the globe in search of eligible tumors. The planned Phase III trial would require 363 patients, of which Rossi had found only half. But in February TransMID met with yet another obstacle. Celtic Pharma decided to terminate Phase III testing "on commercial grounds," citing the unlikelihood that the drug would meet efficacy requirements in the late-stage patients it was testing on. TransMID's future is once again unclear; Celtic may undertake new trials in patients with early-stage tumors, sell TransMID to yet another sponsor, or terminate the drug's development altogether. The 143 patients already enrolled in Phase III testing will have to petition the company if they want more of the drug.

As drug approval progresses in fits and starts, patients are liable to fall into the gaps. When Gotschall's tumor returned in 2002, Phase II of the clinical trials had concluded, and production of TransMID had been halted during a merger. There was simply no new drug to give him.

Rossi petitioned the FDA for permission to dispense some TransMID left over from Phase II, but the FDA would not grant permission to use the remaining drug without potency and stability analyses. TransMID's backers ordered the relevant tests. When those results were in, Rossi reapplied for permission. The process took over 3 months. "By the time we got approval to use the Phase II material," recalls Rossi, "they gave John only days to live." Gotschall finally got the treatment, his tumor rapidly growing. He died six months later.

In the nexus between men like Gotschall, who surrendered himself to the whims of researchers, and Abigail Burroughs, who never got the chance, lie uncomfortable truths about drug experimentation and patients. At the very least, men like Frank Burroughs and Steve Walker force us to acknowledge what we give up by insisting on the cold order of randomized trials; they cast the trade-off in the starkest of terms, because the lives of people they loved were part of what was traded. Whereas patients once had the right to treat their bodies as laboratories, their selves as subjects, the right to experiment on individuals is no longer the province of the individuals themselves. Patients fight for the right to be test subjects for others, and consider themselves lucky to be chosen.

At the end of our last long interview, after Walker delivered his usual hyperarticulate assessment of the cruelty of the clinical trial system, capped off with another description of his wife's final days, his voice grew suddenly weary. "God, I hate talking about this," he said quietly. Patients of the present and future should hope he keeps talking. Perfect information comes at a cost. And as Walker keeps reminding researchers who don't want to listen, that cost does not fall on everyone equally.

Kerry Howley is a senior editor of Reason.

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