Guinea-pigging;
Healthy human subjects for drug-safety trials are in demand. But is it a liv-
ing?

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On September 11, 2001, James Rockwell was camped out in a clinical-research unit on the eleventh floor of a Philadelphia hospital, where he had enrolled as a subject in a high-paying drug study. As a rule, studies that involve invasive medical procedures are more lucrative-the more uncomfortable, the better the pay-and in this study subjects had a fibre-optic tube inserted in their mouths and down their esophaguses so that researchers could examine their gastrointestinal tracts.

Rockwell had enrolled in many previous studies at corporate sites at places like Wyeth and GlaxoSmithKline. But the atmosphere there felt professional, bureaucratic, and cold. This unit was in a university hospital, not a corporate lab, and the staff had a casual attitude toward regulations and procedures. "The Animal House of research units" is what Rockwell calls it. "I'm standing in the hallway juggling," he says. "I'm up at five in the morning watching movies." Although study guidelines called for stringent dietary restrictions, the subjects got so hungry that one of them picked the lock on the food closet. "We got giant boxes of cookies and ran into the lounge and put them in the couch," Rockwell says. "This one guy was putting them in the ceiling tiles." Rockwell has little confidence in the data that the study produced. "The most integral part of the study was the diet restriction," he says, "and we were just gorging ourselves at 2 A.M. on Cheez Doodles."

On the morning of September 11th, nearly a month into the five-week study, the subjects gathered around a television and watched the news of the terrorist attacks through a drug-induced haze. "We were all high on Versed after getting endoscopies," Rockwell says. He and the other subjects began to wonder if they should go home. But a mass departure would have ruined the study. "The doctors were, like, 'No, no!' " Rockwell recalls. "'No one's going home, everything's fine!' " Rockwell stayed until the end of the study and was paid seventy-five hundred dollars. He used the money to make a down payment on a house.

Rockwell is a wiry thirty-year-old massage-therapy student with a pierced nose; he seems to bounce in his seat as he speaks, radiating enthusiasm. Over the years, he estimates, he has enrolled in more than twenty studies for money. The Philadelphia area offers plenty of opportunities for aspiring human subjects. It is home to four medical schools and is part of a drug-industry corridor that stretches into New Jersey. Bristol-Myers Squibb regularly sends a van to pick up volunteers at the Trenton train station.

Today, fees as high as the one that Rockwell received aren't unusual. The best-paying studies are longer, in-patient trials, where subjects are often required to check into a research facility for days or even weeks at a time, so that their
diet can be controlled, their blood and urine checked regularly, and their medical status carefully monitored. Occasionally, they also undergo invasive procedures, like a bronchoscopy or a biopsy, or something else unpleasant, such as being deprived of sleep, wearing a rectal probe, or having allergens sprayed in their faces. Because such studies require a fair amount of time in a research unit, the subjects are usually people who need money and have a lot of time to spare: the unemployed, college students, contract workers, ex-cons, or young people living on the margins who have decided that testing drugs is better than punching a clock with the wage slaves. In some cities, like Philadelphia and Austin, the drug-testing economy has produced a community of semi-professional research subjects, who enroll in one study after another. Some of them do nothing else. For them, "guinea-pigging," as they call it, has become a job. Many of them say that they know people who have been travelling around the country doing studies for fifteen years or longer. "It's crazy and it's sad," one drug-trial veteran told me. "For me, this is not a life. But it is a life for a lot of these people."

Most drug studies used to take place in medical schools and teaching hospitals. Pharmaceutical companies developed the drugs, but they contracted with academic physicians to carry out the clinical testing. According to The New England Journal of Medicine, as recently as 1991 eighty per cent of industry-sponsored trials were conducted in academic health centers. Academic health centers had a lot to offer pharmaceutical companies: academic researchers who could design the trials, publications in academic journals that could help market the products, and a pool of potential subjects on whom the drugs could be tested. But, in the past decade, the pharmaceutical industry has been testing more drugs, the trials have grown more complex, and the financial pressure to bring drugs to market swiftly has intensified. Impatient with the slow pace of academic bureaucracies, pharmaceutical companies have moved trials to the private sector, where more than seventy per cent of them are now conducted.

This has spurred the growth of businesses that specialize in various parts of the commercial-research enterprise. The largest of the new businesses are called "contract research organizations," and include Quintiles, Covance, Parexel, and P.P.D. (Pharmaceutical Product Development), a company that has operations in thirty countries, including India, Israel, and South Africa. (About fifty per cent of clinical trials are now conducted outside the United States and Western Europe.) These firms are hired to shepherd a product through every aspect of its development, from subject recruitment and testing through F.D.A. approval. Speed is critical: a patent lasts twenty years, and a drug company's aim is to get the drug on the shelves as early in the life of the patent as possible. When, in 2000, the Office of the Inspector General of the Department of Health and Human Services asked one researcher what sponsors were looking for, he replied, "No. 1-rapid enrollment. No. 2-rapid enrollment. No. 3-rapid enrollment." The result has been to broaden the range of subjects who are used and to increase the rates of pay they receive.

Most professional guinea pigs are involved in Phase I clinical trials, in which the safety of a potential drug is tested, typically by giving it to healthy subjects and studying any side effects that it produces. (Phase II trials aim at determining dosing requirements and demonstrating therapeutic efficacy; Phase III trials are on a larger scale and usually compare a drug's results with standard treatments.) The better trial sites offer such amenities as video games, pool tables, and wireless Internet access. If all goes well, a guinea pig can get paid to spend a week watching "The Lord of the Rings" and playing Halo with his friends, in exchange for wearing a hep-lock catheter on one arm and eating institutional food. Nathaniel Miller, a Philadelphia trial veteran who started doing studies to fund his political activism, was once paid fifteen hundred dollars in exchange for three days and two G.I. endoscopies at Temple University, where he was given a private room with a television. "It was like a hotel," he says, "except that twice they came in and stuck a tube down my nose."

The shift to the market has created a new dynamic. The relationship between testers and test subjects has become, more nakedly than ever, a business transaction. Guinea pigs are the first to admit this. "Nobody's doing this out of the goodness of their heart," Miller says. Unlike subjects in later-stage clinical trials, who are usually sick and might enroll in a study to gain access to a new drug, people in healthy-volunteer studies cannot expect any therapeutic benefit to balance the risks they take. As guinea pigs see it, their reason for taking the drugs is no different from that of the clinical investigators who administer them, and who are compensated handsomely for their efforts. This raises an ethical question: what happens when both parties involved in a trial see the enterprise primarily as a way of making money?

In May of 2006, Miami-Dade County ordered the demolition of a former Holiday Inn, citing various fire and safety violations. It had been the largest drug-testing site in North America, with six hundred and seventy-five beds. The operation closed down that year, shortly after the financial magazine Bloomberg Markets reported that the building's owner, SFBC International, was paying undocumented immigrants to participate in drug trials under ethically dubious conditions. The medical director of the clinic got her degree from a school in the Caribbean and was not licensed to practice. Some of the studies had been approved by a commercial ethical-review board owned by the wife of an SFBC vice-president. (The company, which has since changed its name to PharmaNet Development Group, says that it re-
quired subjects to provide proof of their legal status, and that the practice of medicine wasn't part of the medical director's duties. Last August, the company paid $28.5 million to settle a class-action lawsuit.)

"It was a human-subjects bazaar," says Kenneth Goodman, a bioethicist at the University of Miami who visited the site. The motel was in a downtrodden neighborhood; according to later reports, paint was peeling from the walls, and there were seven or eight subjects in a room. Goodman says that the waiting area was filled with potential subjects, mainly African-American and Hispanic; administrative staff members worked behind a window, like gas-station attendants, passing documents through a hole in the glass.

The SFBC scandal was not the first of its kind. In 1996, the Wall Street Journal reported that the Eli Lilly company was using homeless alcoholics from a local shelter to test experimental drugs at budget rates at its testing site in Indianapolis. (Lilly's executive director of clinical pharmacology told the Journal that the homeless people were driven by "altruism," and that they enrolled in trials because they "want to help society." The company says that it now requires subjects to provide proof of residence.) The Lilly clinic, the Journal reported, had developed such a reputation for admitting the down-and-out that subjects travelled to Indianapolis from all over the country to participate in studies.

How did the largest clinical-trial unit on the continent recruit undocumented immigrants to a dilapidated motel for ten years without anyone noticing? Part of the answer has to do with our system of oversight. Before the nineteen-seventies, medical research was poorly regulated; many Phase I subjects were prisoners. Reforms were instituted after congressional investigations into abuses like the four-decade Tuskegee syphilis studies, in which researchers studied, instead of treating, syphilis infections in African-American men. For the past three decades, institutional review boards, or I.R.B.s, have been the primary mechanism for protecting subjects in drug trials. F.D.A. regulations require that any study in support of a new drug be approved by an I.R.B. Until recently, I.R.B.s were based in universities and teaching hospitals, and were made up primarily of faculty members who volunteered to review the research studies being conducted in their own institutions. Now that most drug studies take place outside academic settings, research sponsors can submit their proposed studies to for-profit I.R.B.s, which will review the ethics of a study in exchange for a fee. These boards are subject to the same financial pressures faced by virtually everyone in the business. They compete for clients by promising a fast review. And if one for-profit I.R.B. concludes that a study is unethical the sponsor can simply take it to another.

Moreover, because I.R.B.s scrutinize studies only on paper, they are seldom in a position to comment on conditions at a study site. Most of the standards that SFBC violated in Miami, for example, would not be covered in an ordinary off-site ethics review. I.R.B.s ask questions like "Have the subjects been adequately informed of what the study involves?" They do not generally ask if the sponsors are recruiting undocumented immigrants or if the study site poses a fire hazard. At some trial sites, guinea pigs are housed in circumstances that would drive away anyone with better options. Guinea pigs told me about sites that skimp on meals and hot water, or that require subjects to bring their own towels and blankets. A few sites have a reputation for recruiting subjects who are threatening or dangerous but work cheaply.

Few people realize how little oversight the federal government provides for the protection of subjects in privately sponsored studies. The Office for Human Research Protections, in the Department of Health and Human Services, has jurisdiction only over research funded by the department. The F.D.A. oversees drug safety, but, according to a 2007 H.H.S. report, it conducts "more inspections that verify clinical trial data than inspections that focus on human-subject protections." In 2005, F.D.A. inspectors were finally given a code number for reporting "failure to protect the rights, safety, and welfare of subjects," and an agency spokesman says that they plan to make more human-subject-safety inspections in the future, but so far they have cited only one investigator for a violation. (He had held a subject in his research unit against her will.) In any case, the F.D.A. inspects only about one per cent of clinical trials.

Most guinea pigs rely on their wits—or on word of mouth from other subjects—to determine which studies are safe. Some avoid particular kinds of studies, such as trials for heart drugs or psychiatric drugs. Others have developed relationships with certain recruiters, whom they trust to tell them which studies to avoid. In general, guinea pigs figure that sponsors have a financial incentive to keep them healthy. "The companies don't give two shits about me or my personal well-being," Nathaniel Miller says. "But it's not in their interest for anything to go wrong." That's true, but companies also have an interest in things going well as cheaply as possible, and this can lead to hazardous tradeoffs.

The most notorious recent disaster for healthy volunteers took place in March, 2006, at a testing site run by Parexel at Northwick Park Hospital, outside London; subjects were offered two thousand pounds to enroll in a Phase I trial of a monoclonal antibody, a prospective treatment for rheumatoid arthritis and multiple sclerosis. Six of the volunteers had to be rushed to a nearby intensive-care unit after suffering life-threatening reactions—severe inflammation, organ failure.
They were hospitalized for weeks, and one subject's fingers and toes were amputated. All the subjects have reportedly been left with long-term disabilities.

The Northwick Park episode was not an isolated incident. Traci Johnson, a previously healthy nineteen-year-old student, committed suicide in a safety study of Eli Lilly's antidepressant Cymbalta in January of 2004. (Lilly denies that its product was to blame.) I spoke to an Iraqi living in Canada who began doing trials when he immigrated. He was living in a hostel and needed money to buy a car. A friend told him, "This thing is like fast cash." When he enrolled in an immunosuppressant trial at a Montreal-based subsidiary of SFBC, he found himself in a bed next to a subject who was coughing up blood. Despite his complaints, he was not moved to a different bed for nine days. He and eight other subjects later tested positive for tuberculosis.

A decade ago, shortly after I began teaching bioethics and philosophy at the University of Minnesota, I got a phone call from a psychiatrist named Faruk Abuzzahab. He wanted to know if he could sit in on an ethics class that I was teaching. There had been some trouble in a research study that he had conducted, it seemed, and the state licensing board had ordered him to take a class in medical ethics.

Despite some misgivings about my class being used as an instrument of punishment, I agreed. He seemed affable enough on the phone, explaining that he had been a faculty member at the university before going into private practice, and had once chaired the Minnesota Psychiatric Society's ethics committee.

I did not give much more thought to Abuzzahab until about three years ago, when a for-profit testing site called Prism Research opened in St. Paul. Prism was advertising for healthy subjects in a local alternative weekly. I discovered, on the company's Web site, that Abuzzahab was one of its researchers. A few more clicks revealed that he was also conducting studies at his private practice, Clinical Psychopharmacology Consultants. I began to wonder what, exactly, the incident was that had brought him to my class.

As it turned out, the disciplinary action was a response to the injuries or deaths of forty-six patients under Abuzzahab's supervision. Seventeen of them had been research subjects in studies that he was conducting. These were not healthy-volunteer studies. According to the board, Abuzzahab had "enrolled psychiatrically disturbed and vulnerable patients into investigational drug studies without ensuring that they met eligibility criteria to be in the study and then kept them in the study after their conditions deteriorated." The board had judged Abuzzahab a danger to the public and suspended his license, citing "a reckless, if not willful, disregard of the patients' welfare."

One case, which was reported in the Boston Globe, concerned a forty-one-year-old woman named Susan Endersbe, who had struggled for years with schizophrenia and suicidal thoughts. She had been doing well on her medication, however, until Abuzzahab enrolled her in a trial of an experimental anti-psychotic drug. In the trial, she was taken off her regular medication and became suicidal. When Abuzzahab gave her a day pass to leave the hospital unsupervised, she threw herself into the Mississippi River and drowned. In another case cited by the board, Abuzzahab had prescribed a "large supply of potentially lethal medications" to a woman with a history of substance abuse, "shortly after a serious suicide attempt." She committed suicide by taking an overdose.

The public portion of Abuzzahab's disciplinary file is freely available from the Minnesota licensing board, and has been posted on the Web site of Circare, a watchdog group that documents research abuse. When I ran a Google search on "Faruk Abuzzahab," the first hit I got was a 1998 article in the Globe on his trial disasters. Yet none of this seems to have derailed Abuzzahab's research career. Even after his suspension, the Times has reported, he continued to supervise drug trials, and to receive payments from at least a dozen drug companies. In 2003, the American Psychiatric Association awarded him a Distinguished Life Fellowship.

The U.S. regulatory system is built on the tacit assumption that the main threat to research subjects comes from overly ambitious academic researchers, who might be tempted to gamble with subjects' health in the pursuit of medical knowledge or academic fame. The system was intended to check this sort of intellectual ambition, mainly by insuring that studies are reviewed in advance by boards made up of the researcher's academic peers. But, like most physicians supervising clinical trials today, Abuzzahab does not work in an academic setting. The studies conducted at for-profit sites such as Prism are not the natural domain of academically ambitious researchers. They are rarely published and, even if they were, would bring little intellectual credit to the physicians carrying them out, because they are designed by the industry sponsor. A researcher like Abuzzahab would not become famous by supervising subjects in studies like these. But he might become rich.

Abuzzahab represents a new, entrepreneurial breed of physician-researcher; in fact, many of his colleagues have moved even farther from the academic realm. In 1994, according to the Tufts Center for Drug Development, seventy per
cent of clinical researchers were affiliated with academic medical centers. By 2006, that figure had dropped to thirty-six per cent. The work can be lucrative, and some sponsors offer researchers additional financial incentives to recruit subjects. One doctor told the Department of Health and Human Services that he was offered twelve thousand dollars for each subject that he could enroll in a trial, plus a thirty-thousand-dollar bonus and an additional six thousand dollars per subject after the first six.

Some of the people conducting clinical trials have little training in how to conduct research. And, as the Abuzzahab case suggests, not all drug companies are especially selective about the researchers they hire. In 2001, the F.D.A. asked the pharmaceutical company Sanofi-Aventis to perform new studies of the antibiotic Ketek, which was suspected of causing liver failure. Reports later revealed that the top-recruiting investigator hired by P.P.D., the firm contracted to conduct the studies, was a graduate of an offshore medical school who tested the antibiotic on clients in an obesity clinic she ran in Alabama. She was sentenced to five years in federal prison for fraud. Another top-recruiting investigator was arrested when the police found him carrying a loaded semiautomatic handgun, and hiding cocaine in his underwear.

In early December of 2002, a man named Bob Helms took part in an industry-sponsored "drug delivery" study. Helms and his fellow guinea pigs were required to take a new anti-anxiety drug and, later, to defecate into a small basket. The unfortunate clinic staff members then searched for the remains of the tablet to determine how much had been absorbed by the body.

The guinea pigs were paid thirty-three hundred dollars and were required to live in the unit for five periods of four days each. But before the end of the first period, Helms says, the guinea pigs decided that they were getting a raw deal. The process of fecal collection was smelly and unpleasant; the amount of time allowed outside the unit had been shortened from three days to thirty-six hours; and the subjects were required to abstain from alcohol, even though the study—because of unexpected delays—was taking place over the Christmas and New Year's holidays. The guinea pigs wanted a raise.

Since the staff was collecting their feces, Helms suggested that the guinea pigs all swallow notes that said "More money." This idea was rejected. Instead, they presented a one-page memo to the staff, detailing their concerns and requesting a pay increase of eleven hundred dollars. When the memo was ignored, they began hinting that they might decamp for a better-paying study at another site. Eventually, the clinic agreed to pay each subject an additional eight hundred dollars.

Helms is a pioneer in the world of guinea-pig activism. A fifty-year-old housepainter and former union organizer, he has a calm, measured demeanor that masks a deep dissident streak. Before he started guinea-pigging, in the nineteen-nineties, he worked as a caregiver for mentally retarded adults living in group homes. There Helms began to understand the difficulties in organizing health-care workers who were employed by the same company but in far-flung locations—in this case, group homes that were spread over two hundred miles of suburbs. "The other organizers told me right off the bat that I could not organize workers who might meet each other once a year at best," Helms says. "How could we ask them to take risks together? They were strangers."

Helms saw that guinea pigs faced a similar problem, and, in 1996, he started a jobzine for research subjects called Guinea Pig Zero. With a mixture of reporting, advocacy, and dark humor (a cartoon in an early issue shows a young man surrounded by I.V. bags and syringes, exclaiming, "No more fast food work for me-I've got a career in science!")), Guinea Pig Zero published the sort of information that guinea pigs really wanted to know—how well a study paid, the competence of the venipuncturist, the quality of the food. It even published report cards, grading research units from A to F. "Overcrowding, no hot showers, sleeping in an easy chair, incredibly cheap shit for dinner, creepy guys from New York jails—all these are a poor man's worries," Helms says. "Where are these things in the regulators' paperwork?" Guinea Pig Zero was not aimed at sick people who sign up for studies in order to get new treatment. It was aimed at poor people who sign up for studies in order to get money.

And here is where its perspective diverged most radically from the traditional ethical perspective. Guinea Pig Zero assumed that subjects should get more money, while many ethicists and regulators argued that they should get none at all. The standard worry expressed by ethicists is that money tempts subjects to take part in dangerous, painful, or degrading studies against their better judgment. F.D.A. guidelines instruct review boards to make sure that payment is not "coercive" and does not exert an "undue influence" on subjects. It's a reasonable worry. "If there were a study where they cut off your leg and sewed it back on and you got twenty thousand dollars, people would be fighting to get into that study," a Philadelphia activist and clinical-trial veteran who writes under the name Dave Onion says.
Of course, ethicists generally prefer that subjects take part in studies for altruistic reasons. Yet, if sponsors relied solely on altruism, studies on healthy subjects would probably come to a halt. The result is an uneasy compromise: guinea pigs are paid to test drugs, but everyone pretends that guinea-pigging is not really a job. I.R.B.s allow sponsors to pay guinea pigs, but, consistent with F.D.A. guidelines, insist on their keeping the amount low. Sponsors refer to the money as "compensation" rather than as "wages," but guinea pigs must pay taxes, and they are given no retirement benefits, disability insurance, workmen's compensation, or overtime pay. And, because so many guinea pigs are uninsured, they are testing the safety of drugs that they will probably not be able to afford once the drugs have been approved. "I'm not going to get the benefit of the health care that is developed by this research," Helms says, "because I am not in the economic class to get health insurance."

Guinea pigs can't even count on having their medical care paid for if they are injured in a study. According to a recent survey in *The New England Journal of Medicine*, only sixteen per cent of academic medical centers in the United States provided free care to subjects injured in trials. None of them compensated injured subjects for pain or lost wages. No systematic data are available for private testing sites, but the provisions typically found in consent forms are not encouraging. A consent form for a recent study of Genentech's immunosuppressant drug Raptiva told participants that they would be treated for any injuries the drug caused, but stipulated that "the cost of such treatment will not be reimbursed."

Some sponsors withhold most of the payment until the studies are over. Guinea pigs who drop out after deciding that a surgical procedure is too disagreeable, or that a drug seems unpleasant or dangerous, must forfeit the bulk of their paycheck. Two years ago, when SFBC conducted a two-month study of the pain medication Palladone, it offered subjects twenty-four hundred dollars. But most of that was paid only after the last of the study's four confinement periods. A guinea pig could spend nearly two months in the study, including twelve days and nights in the SFBC unit, and get only six hundred dollars. SFBC even reserved the right to withhold payments from subjects whom it dropped from the study because of a drug's side effects.

Guinea-pig activists recognize that they are indispensable to the pharmaceutical industry; a guinea-pig walkout in the middle of a trial could wreak financial havoc on the sponsor. Yet the conditions of guinea-pigging make any exercise of power difficult. Not only are those in a particular trial likely to be strangers; if they complain to the sponsor about conditions, they risk being excluded from future studies. And, according to *Bloomberg*, when illegal-immigrant guinea pigs at SFBC talked to the press, managers threatened to have them deported.

Lawsuits on behalf of injured subjects are growing, though, and they have begun to target not just research sponsors but also institutional review boards and bioethicists. Alan Milstein, an attorney in Philadelphia, has pioneered this area of law, most notably with successful litigation against the University of Pennsylvania on behalf of the family of Jesse Gelsinger, who died in a gene-therapy trial in 1999. Milstein has represented volunteers injured at commercial sites, but most guinea pigs are in no position to hire a lawyer. "This is not something you or I do," Milstein says. "This is something the poor do so that the rich can get better drugs."

During our early years of medical school, my classmates and I were given a course in physical diagnosis. Usually, we practiced on one another. Each of us would percuss a classmate's chest, or listen to his heart with a stethoscope. But some procedures were considered too personal to practice on a classmate. For some of these, we were assigned a "model patient"—someone from the community who was "compensated" in exchange for undergoing an examination.

This was how I performed my first rectal exam. A large group of us were led into a room, where our model patient was bent over an examining table with his pants around his ankles. One by one, we approached him nervously from behind, inserted a gloved, lubricated finger into his rectum, and felt around for the prostate. "Thank you," we all said politely to the model patient as we removed our index fingers from his anus. The model patient stared straight ahead, saying nothing.

What made the experience oddly disturbing was not just the forced, pseudo normality of the instruction, or the fact that the exam could have been done more privately, but the instrumentality of the encounter: a pretend "patient" bending over naked for anonymous strangers in exchange for money. The fact that the model patient had been paid did not make his work seem any less degrading. (Tipping him would have made it even worse.)

Perhaps there is something inherently disconcerting about the idea of turning drug testing into a job. Guinea pigs do not do things in exchange for money so much as they allow things to be done to them. There are not many other jobs where that is the case. Meanwhile, our patchwork regulatory system insures that no one institution is keeping track of how many deaths and injuries befall healthy subjects in clinical trials. Nobody appears to be tracking how many clinical...
investigators are incompetent, or have lost their licenses, or have questionable disciplinary records. Nobody is monitoring the effect that so many trials have on the health of professional guinea pigs. In fact, nobody is even entirely certain whether the trials generate reliable data. A professional guinea pig who does a dozen drug-safety trials a year is not exactly representative of the population that will be taking the drugs once they have been approved.

The safety of new drugs has always depended on the willingness of someone to test them, and it seems inevitable that the job will fall to people who have no better options. Guinea-pigging requires no training or skill, and in a thoroughly commercial environment, where there can be no pretense of humanitarian motivation, it is hard to think of it as meaningful work. As Dave Onion puts it, "You don't go home and say to yourself, 'Now, that was a good day.'"