4 April 2014

Dear IRB Panel Members,

We would like to introduce a project for continued panel member education and development. Each month we will distribute articles on current research ethics topics for your consideration. Additionally we are launching “board shorts”— brief visual summaries of regulations and policies that we hope will be useful as quick reference reminders. These materials will be distributed at panel meetings and posted to the Information for Panel Members section of the IRB Website:

http://www.irb.northwestern.edu/members

Your feedback and suggestions for topics are very welcome!

Sincerely,

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Living With Cancer: The Cost of Trials

By SUSAN GUBAR

March 20, 2014, 4:41 pm

Susan Gubar writes about life with ovarian cancer.

A recent CT scan made me realize that the clinical trial extending my life effectively excludes all but the most privileged cancer patients.

I used to weasel out of scans. Chalk it up to trepidation about radiation and possible kidney damage, along with paranoid suspicions that such scans don’t yield definitive pictures. My oncologist and I had agreed to fudge on frequent testing. But the clinical trial did not.

When I registered for the CT, a woman wearing a badge that read “financial navigator” handed me the requisite forms to sign. I explained that the CT should be billed to the Phase I trial, since I was undergoing it so the investigators could measure the efficacy of their drug. Unable to reach the trial administrator by phone, she asked, “Can we put it down as a self-pay since you can change it afterwards?”

The clock was ticking. I would need to start drinking the gallons of what I call Kool-Aid, the drink that people under 140 pounds need to gulp during the two hours before an abdominal CT. I knew that I had to concede but wanted to know how much it would cost. “Oh,” she replied, “I
couldn’t say.”

I signed the form and, after receiving the paper bracelet, trudged down to the basement and began the long haul of swilling and waiting. The Kool-Aid — in science-speak, the gastrografin contrast solution — brought to mind my friend Judy, vomiting the barium milkshake she had to ingest in a different hospital. It was impossible to keep down, she reported, but her oncologist insisted on it. I touted the less viscous Kool-Aid and she asked a hospital radiologist who replied, “Sure, you could try that instead.” We shook our heads in disbelief at his nonchalance.

Running repeatedly to the bathroom, I thanked my lucky stars that I did not need to take the drugs prescribed for people with allergic reactions to this test. The CT would be brief and painless, I knew, and therefore none of the anxiety of the first few scans plagued me as the technician accompanied me down the hall to the scanner.

“I can’t tell when I can get a nurse to access your port,” she said, positioning me on the narrow plank facing the gaping mouth of the huge machine. “There were massive cutbacks two months ago. Would you rather wait or have me stick you?”

At least I was fully clothed while making this decision. Praying a vein would work, I eyed the triangular bar hanging from a pulley over my head while the technician established a line and took cover in another room.

The conveyor belt moved me so deep into the bowels of the cave-like mechanism that the overhead metal bar, which I clutched with upraised hands, clanged against it. Only my head remained just outside of the giant doughnut.

“Take a breath and hold,” a mechanical female voice said. Did they change it to a male voice for men? I wondered.
Conveyed back out, I heard, "Breathe."

Through the IV line, the technician injected another contrast agent that, she told me, would give me an awful taste in my mouth and make me feel as if I were wetting my pants, and then the process was repeated.

"Take a breath and hold."

"Breathe."

After the technician removed the needle in my arm, I limped out of the hospital determined to control my nausea with peppermint. Although I had not eaten for some 20 hours, I asked my husband to stop the car on the way home only to use a gas station restroom.

The nausea I had felt that day returned some time later when I received a bill for $4,567. Because standard practice of care for recurrent ovarian cancer includes a CT every three months, the trial did not cover the cost of this scan. At registration, I had been thinking in terms of the trial paying or me paying. Instead of saying "self-pay," I should have handed the "financial navigator" my insurance cards. Adjustments would have to be made with billing services.

My mistake at registration revealed the exorbitant price of the CT, which otherwise would have been masked by the incomprehensible maze of paperwork sent by providers. The trial exacts large expenses: it requires that people have periodic scans and does not pay for them.

How could patients who are under-insured or not insured at all be included in such a clinical trial? How could people working for the minimum wage afford $18,268 a year for CTs? If the trial were in a remote hospital, travel and lodging would raise that price tag, as would the need to take days off from work for recurrent blood tests.

Now I understand why low-income patients are underrepresented in
cancer trials, although they bear a disproportionate burden of cancer mortality. For economic status is of course a barrier not only to trials but also, more alarmingly, to detection and treatment.

I made the call to billing services. I took a breath and got put on hold.

Susan Gubar is a distinguished emerita professor of English at Indiana University and the author of “Memoir of a Debulked Woman,” which explores her experience with ovarian cancer.
The Future of Biomedical Research

Witner appearig before the.
House Subcommittee on Labor — NIH — Education Appropriations

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

March 26, 2014

Good morning, Mr. Chairman and distinguished Members of the Subcommittee. I am Francis S. Collins, M.D., Ph.D., Director of the National Institutes of Health (NIH). It is an honor to appear before you today to provide an overview of NIH’s critical role in enhancing our nation’s health through scientific discovery.

As the nation’s biomedical research agency, NIH’s mission is to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance human health, lengthen life, and reduce illness and disability. I can report to you that NIH leadership, employees, and grantees continue to believe passionately in this mission.

Before I discuss the tremendous strides we have made and the exciting scientific opportunities on the horizon, I want to thank you, Mr. Chairman, and Ranking Member DeLauro, as well as your colleagues, for the recent Fiscal Year (FY) 2014 Omnibus Appropriations bill. The Subcommittee came together in a bipartisan way to increase funding for NIH and we are truly grateful for your action. The past year has been challenging for us: the sequester reduced funding for groundbreaking medical research and affected the morale of the scientific community. This impact was further exacerbated by the shutdown.

There is much good news to report about the science that we support. NIH has been advancing our understanding of health and disease for more than a century; scientific and technological breakthroughs generated by NIH-supported research are behind much of the gains our country has enjoyed in health and longevity. For example, death rates from heart attacks have fallen by more than 60 percent over the past 40 years, while deaths from strokes have declined 70 percent. Cancer death rates have been dropping about 1 percent annually for the past 15 years—life expectancy gains that save the nation billions of dollars. HIV/AIDS treatment and prevention now enable us to envision the first AIDS-free generation since this virus emerged more than 30 years ago. NIH research also has given us vaccines to protect against an array of life-threatening diseases, including cervical cancer, influenza, and meningitis. We can look forward to a future in which advanced prevention and treatment strategies such as these allow everyone to have a significantly better chance of living a long and healthy life.

These statistics tell you how far we have come—but our aim is to go even further, faster. Let me describe a few of the many areas in which NIH-supported research is opening up extraordinary opportunities to improve the health of the American public.

A major program that began this year is the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, for which thanks are due to this Subcommittee for its FY 2014 support. NIH is a major player in this pioneering multi-agency venture that will enable the creation of new tools capable of examining the activity of billions of nerve cells, networks, and pathways in real time. By measuring activity at the scale of circuits and networks in living organisms, we can begin to decode sensory experience and, potentially, even memory, emotion, and thought. Successful pursuit of the BRAIN Initiative will revolutionize neuroscience, providing a foundational platform for major advances in Alzheimer’s disease, autism, schizophrenia, epilepsy, traumatic brain injury, and many other brain disorders.

As technology allows us to tackle mind-boggling tasks like recording the activity of billions of nerve cells in the brain or determining the DNA sequence of tens of thousands of human genomes, researchers are generating enormous quantities of data at an unprecedented pace. The challenge posed by this revolution is how to store, retrieve, integrate, and analyze this mountain of complex data—and transform it into knowledge that can improve human health. To address this challenge that affects virtually all areas of biomedical research, we have just launched the Big Data to Knowledge (BD2K) Initiative. The goals of BD2K are to develop and disseminate new analytical methods and software, enhance training of data scientists, and facilitate broader use and sharing of complex biomedical datasets. With sustained investment and effort, we will overcome the challenges associated with Big Data to accelerate real-world applications of basic science discoveries.

We are also excited about another area of intense interest: the development of therapeutics. Recent advances in genomics, proteomics, imaging, and other...
Technologies have led to the recent discovery of more than a thousand risk factors for disease — biological insights that ought to hold promise as targets for drugs. But drug development is a terribly difficult and failure-prone business. To the dismay of researchers, drug companies, and patients, the vast majority of drugs entering the development pipeline fall by the wayside. The most distressing failures occur when a drug is found to be ineffective in the later stages of development — in Phase II or Phase III clinical studies — after years of work and millions of dollars have already been spent. A major reason for such failures is that scientists often have not had enough information to choose the right biological targets. If a drug is aimed at the wrong target, it won't work against the disease it was intended to treat.

With that challenge in mind, we were thrilled last month to launch the Accelerating Medicines Partnership (AMP). This unprecedented public-private effort will use cutting-edge scientific approaches to sift through a very long list of potential therapeutic targets, and choose those most likely to lead to success. Besides NIA, the AMP partners include the FDA, 10 biopharmaceutical firms and a number of non-profits, including patient advocacy groups. This pre-competitive partnership, which will share all data openly, will initially focus on three disease areas that are ripe for discovery: Alzheimer’s disease, type 2 diabetes, and the autoimmune disorders, lupus and rheumatoid arthritis. Through this team effort, we believe we can reach our shared goals of treating and curing disease faster.

Preventing disease is another top priority, and influenza is one area of prevention in which we are poised for rapid progress. Currently, to provide protection against the rapidly evolving influenza virus, a new vaccine must be produced each year and we all need to get an annual flu shot. Also, despite best efforts, the vaccine isn’t always ideal. In an average year, the flu claims up to 49,000 American lives and costs the U.S. economy about $87 billion. But it does not have to be that way. NIH-funded researchers are now working on a universal flu vaccine — designed to protect people against virtually all strains of the flu for extended periods of time and, thus, potentially reduce the need for annual flu shots. Of critical importance, such a vaccine could also protect against a future global flu pandemic.

While we are several years away from having a universal flu vaccine available to the public, our researchers have already demonstrated proof of concept and are testing a number of approaches, including two-stage "prime boost" vaccines and inulin nanoparticles. Clearly, the prospect of a universal flu vaccine is not science fiction. Early clinical studies are already underway. With sustained investment, the United States may be a few years away from realizing its potential to benefit our health and our economy.

As impressive as a universal flu vaccine would be, it is not the only trick we are teaching our immune systems. We are also aiming to harness the body’s own immune system to fight cancer. Until recently, our weapons for attacking cancer have been largely limited to surgery, radiation, and chemotherapy — treatments that carry risks and cause adverse side effects. Now, after years of intense basic and translational research, we have an exciting new possibility: cancer immunotherapy.

Researchers have long been puzzled by the uncanny ability of cancer cells to evade the immune response. What stops the body from waging its own “war on cancer?” As it turns out, our bodies have built-in checkpoints to prevent our immune systems from going into overdrive and killing healthy cells. Now, NIH-funded researchers have discovered a way to genetically modify certain white blood cells called T-cells — the soldiers of the immune system — to attack tumor cells. In this new approach, T-cells are collected from cancer patients and engineered in the lab to produce specific proteins on their surface, called chimeric antigen receptors (CARs). When the modified cells are infused back into patients, they multiply and, with guidance from their newly engineered receptors, seek and destroy tumor cells. Promising results in patients with leukemia prompted Science magazine to name this its 2013 Breakthrough of the Year.

Today, I have provided a very brief overview of NIH’s past successes and continuing commitment to basic, translational, and clinical research. Our nation has never witnessed a time of greater promise for advances in medicine. With your support, we can anticipate a future of accelerating discovery across NIH’s broad research landscape, from fundamental scientific inquiry to human clinical trials. The “National Institutes of Hope” is ready to move forward.

This concludes my testimony, Mr. Chairman. I look forward to your questions.
Crowdsourcing medical decisions: Ethicists worry Josh Hardy case may set bad precedent

By Ariana Eunjung Cha, Published: March 23

Just hours after social-media supporters of a dying 7-year-old boy pressured a reluctant biotech company into giving him an experimental medication, the backlash began.

Is "it rite to save 1 child an[d] not the rest?" wondered one commenter on a news forum. "It's really not fair to the thousands of others that were turned down just because they didn't make a big public outcry," said another.

The Herald-Sun newspaper in Durham, N.C., where the company that makes the drug is based, said it was glad for the boy's sake that he was able to get the medicine. "But the process leaves us pained," the editorial board wrote. "This is no way to make healthcare decisions."

The story of how Joshua Hardy — a first-grader from Fredericksburg, Va., who is fighting off an infection after getting a bone-marrow transplant — got access to an unapproved treatment when others with similar requests were turned down highlights the ethical conundrums facing doctors, companies and regulators in the era of Facebook and Twitter.

In the days leading up to the drug company's change of heart March 11, contrasting photos of Josh — smiling in baseball outfits and then lying in his hospital bed with tubes sticking out of his body — were all over the Internet. He has beaten cancer four times since he was 9 months old. But the disease has left his body without much of an immune system, and in February he was infected with a virus that left him close to death.
Nearly 20,000 people signed a petition supporting “compassionate use” for Josh, which allows a drug to be administered outside of a clinical trial. Hundreds bombarded Chimerix, a small, publicly traded company that makes the drug, with e-mails and calls on the boy’s behalf. Even Washington Redskins quarterback Robert Griffin III took sides, tweeting to his 1.12 million-plus followers to “#savejosh.”

Critics of the strategy say they sympathize with Josh’s parents and admire them for being willing to do anything to save their child, but they decry the crowdsourcing of medical decisions and warn that the case may set a dangerous precedent.

“You couldn’t get a more troubling and impossible-to-resolve moral dilemma than this one,” said Arthur Caplan, director of the division of medical ethics at New York University’s Langone Medical Center.

From the perspective of the public and future patients, it’s best for the company to focus on getting the drug approved as soon as possible so that the largest number of people can be helped, Caplan said. But from a patient’s point of view, getting immediate access to the drug is what’s important.

“It’s a trade-off between the public good versus self-interest,” Caplan said. “They conflict. There is no way of getting around it.”

Richard Plotkin, a 69-year-old retired trial lawyer from New Jersey who started the Max Cure Foundation after his grandson was diagnosed with lymphoma at age 4 and who was at the center of efforts to save Josh, defends the campaign as necessary.

“I knew we had at the latest until the end of the week before the boy would die, and the best way to make a company change its mind — fast — is to get the public involved,” Plotkin said.

The parents of 11-year-old Sarah Murnaghan also have faced intense criticism. The girl received two lung transplants (the first one failed) last June after her parents launched a Change.org petition that got more than 370,000 signatories and sued in an effort to get their daughter an organ more quickly.

Janet Murnaghan said she knows that not everyone agrees with the way her daughter’s case was resolved — a judge ordered the transplant network to put her on the adult list, and she jumped to the top because of the severity of her condition — but she believes it did the public good by demanding that patients and their families have a larger voice in how organs are allocated.

Since the early days of the AIDS epidemic, patients with life-threatening conditions have become increasingly vocal about demanding access to drugs still in development. The Food and Drug Administration in 1987 created new rules, amended in 2009, for expanded access or compassionate use to allow what it says is “broad and equitable access” to those treatments. But the program remains limited. Since 2009, the agency has approved an average of 1,030 applications each year; each request may be for multiple patients.

Most patients’ requests never make it to that stage.

Before the FDA gets involved, companies must agree to allow their drug to be used. But many companies are reluctant to do so for a host of reasons — legal, financial and logistical — and, in most cases, they hold firm despite intense public pressure.

Andrea Sloan, 45, a lawyer whose case drew the support of several Texas legislators as well as Newt Gingrich,
died Jan. 1 while fighting for access to a drug to treat ovarian cancer made by BioMarin Pharmaceutical. Nick Auden, a Denver father of three with melanoma who was able to gather 500,000 signatures for a petition for compassionate use of a Merck drug, died in November without getting the treatment. He was 41.

The companies argue that if something goes wrong with a patient who gets a drug outside the clinical-trial process, it could slow down their larger development program while the FDA investigates. Moreover, insurance companies typically won’t pay for unapproved treatments, so either the drug companies have to bear the costs or give the treatment only to those who can afford it. The companies also often create only a small supply of a drug for clinical trials; making more or diverting it could be time-consuming and costly.

Even if those challenges can be overcome, companies say, there are ethical issues.

Kenneth Moch, chief executive of Chimerix, which makes the drug that the Hardys were seeking, said that until 2012 the company had a large compassionate-use program but had to discontinue it to focus its limited resources — it has only 60 employees and is not profitable — on getting the drug approved.

During the past two years, Chimerix has nonetheless received 200 applications for compassionate use, and 80 were for adenovirus infections like the one Josh has. All of the requests were turned down. “Every one of those is heart-wrenching. But making it available for one child, whatever the reason, as an exception is not equitable distribution,” he said.

Chimerix turned down the Hardys’ requests, too. But after several days of intense phone calls with officials at the FDA’s Division of Anti-Viral Products — who heard about Josh’s plight through the media — they worked out a solution.

Instead of getting the drug through the compassionate-use program, Josh got it through the clinical-trial process. Although he wasn’t eligible for the trial in progress — it is for adults with a different condition — the FDA offered to immediately green-light a new clinical trial that would be designed for pediatric patients with Josh’s condition.

In this way, medical experts say, the FDA created a wall that would allow Chimerix to give Josh and up to 19 other children the drug for free without opening the floodgates to others.

The deal was also a big win for Chimerix: No only did it solve its public relations crisis, it allowed the company to cut through the red tape that is typically required to get another clinical trial approved. The company’s stock has soared nearly 29 percent since the news was announced Tuesday.

“There is no doubt that the social media campaign by the Hardys helped accelerate the dialogue,” Moch said.

Josh, who on Wednesday received his second dose of the treatment — an antiviral drug called brincidofovir — remains in intensive care at St. Jude Children’s Research Hospital in Memphis.

His mother, Aimee Hardy, wrote hopefully on Facebook that the virus in Josh’s blood is replicating more slowly, and he is in less pain than before. “Glory to God,” she said, “the medicine is working.”
§46.205(a)
- Each individual providing consent must be fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- The consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
- Preclinical and/or clinical studies have been conducted and provided data for assessing potential risks to neonates.
- Researchers will have no part in determining the viability of a neonate.

Uncertain Viability §46.205(b)

Approvable if:
- The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and
- Any risk is the least possible for achieving that objective.

OR
- The purpose of the research is the development of important knowledge which cannot be obtained by other means, and
- No added risk to the neonate from the research.

Either Parent Consents
- If neither parent is able to consent, a parent's legally authorized representative may.

Non-Viable §46.205(c)

Approvable if:
- Vital functions of the neonate will not be artificially maintained.
- The research will not terminate the heartbeat or respiration of the neonate.
- There will be no added risk to the neonate resulting from the research.
- The purpose of the research is the development of important knowledge that cannot be obtained by other means.

Both Parents Consent
- If either parent is unable to consent, one parent will suffice.

Viable §46.205(d)

Follow Subpart D: Additional Protections for Children