Interview with Carl C. Peck

by John Swann

JS: Start. Okay, and start here. Okay. Terrific. So my name is John Swann. I'm from the FDA History Office and I'm here doing an oral history with Dr. Carl C. Peck. We're in San Luis Obispo, California, and Dr. Peck, thank you so much for sitting down to carry out this reflection of your life and career. Particularly, your career at the Food and Drug Administration. What we often do in our oral histories is we start off by getting a picture of our interviewee, and sort of where they came from and where their interests developed, that eventually brought them to the Food and Drug Administration. So in your case, we'll of course start with where you were born and your early education and take it from there.

CP: So it's a great pleasure, John, to be talking with you, given -- especially since we went to the same university, the University of Kansas. So I was born in 1942 in Kansas and remained in Kansas until I ended my undergraduate years. I lived most of my youth in Concordia, Kansas, a little town north of Salina. A small farming community. Parents were both farm kids raised, schooled in single-room schools. And very early on, I developed an interest in science. I took radios apart. I tried to understand radio waves. I became a hand moderator, a novice, and then general class. I could do Morse code. Still can. And imagined, over time, that I would become a physicist. I had a very strong interest in math. I used to do math doodling when we were at church, which was more often than I would like to be. And so I entered the University of Kansas in 1960, summer of 1960. My first course was a calculus course, and I can't tell you how thrilled I was to take that course. It was magic. And I feel a thrill to this day at the experience I had taking that calculus course. I also had an English course that taught me I needed to learn a lot more about how to express myself. So my undergraduate years were focused on -- in the early period -- on engineering physics, and that was my thrust with a broadening through the Western Civilization program at Kansas University, which caused, among other things, me to

have a language requirement. Having grown up in a little town where one of the doctors had studied in Germany in the 1930s which was, at that time, the Mecca of medical science and research and teaching, I recall he told me once in his office, he said, "Son, if you ever go into medicine, you're going to have to learn German and you're going to have to go to Germany to learn medicine." Curiously, when I faced this language requirement, I thought, well, why not German? And so I struggled through German, which came in handy when I decided to change my major to mathematics and chemistry and go to medical school. I had been going to summer school each year. I was able to graduate in three years, apply for a full-ride scholarship and was awarded one to study physical chemistry in Germany. So I had the language requirement to begin -- to take that fellowship and that scholarship in Germany. And that's what I did during 1963 and 1964.

I then returned to Kansas University and spent four years in medical school there. I recall that great pleasure in interviewing patients and being at the bedside with patients, and imagined actually, part of the time, that I would become a country doctor. Had a great experience in Quinter, Kansas in a preceptorship with two doctors out there who had been medics during World War II and the VA, the GI Bill had permitted them to go to medical school. Hesterman and somebody else was -- they had their own hospital. It was a really thrilling six weeks that I spent with them. But we had the Vietnam War under way. I had already been in ROTC, and it was clear that if I had not been aiming at medical school, that I would already be in uniform in Vietnam. But I got a deferment and went to medical school, then, at the University of Kansas. I spent four years there.

JS: That was starting in 1968?

CP: That was 1964.

JS: 1964.

CP: 1964 to 1968. Having mastered German during that year, it was a real struggle at first, but I picked it up pretty quickly. It gave me interest in other languages, and so I took

Spanish while I was in medical school and spent six weeks in Mexico City studying vectorcardiography with a famous cardiologist. And then later on, I spent six weeks in Colombia, South America. Medellin actually, at the time, was safe, and I studied tropical diseases there.

JS: Was this -- this must have been pretty unusual, though, to be doing this during medical school, wasn't it? Or was this somehow incorporated into your -- the education of a physician there?

CP: Well, I think [inaudible] faculty that thought that doctors ought to be broad, and there was the opportunity through the medical school to take these two six-week periods off. The one in Mexico City and the one in Colombia. And both of them had a little bit of support from the university to do that. I also recall the thrill of studying anatomy and physiology. Those two reinforced my interest in the whole person. The whole system, as opposed to focusing in a particular organ area. And so eventually I decided to study internal medicine, because that offered me the opportunity to go more into depth into all of the systems of the body. Nonetheless, I was also a little bored with clinic medicine; endless hypertension, diabetes, obesity. We had only weak therapies that we could offer them, and I was always trying to find some way to use math and physiology and physics to improve their medical care. It became pretty clear, during the latter parts of medical school and during my internal medicine training, that medical practice wasn't going to be sufficient. That I needed an outlet for doing research in one sort or another. So I joined the US Army as a fourth-year medical student. The reason I joined, as opposed to waiting to be assigned -- at the time, I had a deferment from the draft, but clearly, once you get your medical degree back then, if you didn't have an internship or a residency or didn't have a residency selected, you were automatically drawn into one of the medical services of the military. And I had heard through some faculty at Kansas University that if you join a service and get to know them during your senior year through focus groups and stuff, you would have a better chance of influencing your career, your assignments. Not really

sure that was true, but it turns out that I then took an Army internship at Tripler Army Medical Center in Hawaii, which sounds glamorous, but I didn't get to the beach at all during that year.

We had a steady flow of Vietnam casualties coming in with Malaria and various infectious diseases and various trauma. It was a fabulous year. I really, really enjoyed that year because it was just day and night, frequent call and learning, learning, learning. Then I had the opportunity to continue -- I was in the Army. I was a US Army Lieutenant, but then I had a chance to take a residency in a military teaching hospital. The military, at that time -- Army, Navy, and Air Force -- had teaching hospitals, beyond the famous ones, Walter Reed Army Medical Center and the Naval National Medical Center. One of them was in San Francisco. It was called Letterman Army Medical Center, and they offered an internal medicine residency. I went to Walter Reed and I went to San Francisco to interview. And I realized that the faculty were as good as you could get anywhere in the world, because there was a plan called the Berry Plan that young specialists could engage -- instead of going, being assigned to Vietnam, they could take a teaching position in a military hospital as their military service. So we had fabulous people from the best medical schools as teachers in those days. So I took an internal medicine residency in Letterman Army Medical Center from 1969 to 1972.

JS: Let me ask, when you started this, did you have in mind what you wanted to do during this residency? What your longer term interests were? Or was this still a bit up in the air?

CP: I was still toying with the idea of becoming an internist and practicing internal medicine. But I learned some things about myself. I remember, my first assignment was on an oncology ward. And I remember the resident that I took over 12 cases from was eager to leave, and a little sloppy. And what he left me were these terribly complicated patients with very dense medical records that were unorganized and in manila folders, and they were older people with multiple diseases on 10 or 20 drugs. They were very complicated, and I really -- just to understand what was going on, I really had to dig in, like going to a library and doing a research project. And I learned that I enjoyed that. I enjoyed taking a sort of chaotic record and

investigating the essence of it and coming up with a crisp problem list, a crisp number of drugs they were taking, crosschecking the potentials for drug-drug interactions and so forth. And that -- I realized that that's not something that you have time to do in medical practice. I really enjoyed that. I also was beginning to review the medical literature, but my math background, I could see that there were a lot of flaws in the statistical parts of it. I'd taken some statistics. And what eventually happened that really drew me into my career direction was, I gave a lecture at Letterman Army Medical Center while I was on the neurology service. The residents were expected to periodically give a lecture on some [inaudible] that they had researched. And I took the tack of criticizing contemporary medical articles, with respect to the quality of the statistical methods. I eventually published a little paper on that, within the medical community of the US Army teaching hospitals. It's the first publication I think I have listed on my CV.

There was a medical student from UCSF who was rotating through the hospital on that service. His name was Mike Roysin. Turned out to be a famous anesthesiologist later on. He came up to me afterwards and he said, "You know, Carl," he says, "You sound just like Ken Melman." I said, "Well, who's that?" "Well, he's a professor of medicine at UCSF here in San Francisco, and head of the Division of Clinical Pharmacology. And they study drugs and clinical trials and they have individuals over there who are using math and physics and quantitative methods to understand drug action in humans. You should make contact with him." And so I called Ken Melman. And I said, "Mike Roysin," who he knew, "had recommended I call you." And he says, "Sure, young man." He says, "Why don't you come over and give us a lecture?" To this day, I'm thinking, that really was audacious of me to actually agree to do that. Because who I met over there were full faculty people publishing in the peer-reviewed literature and postdocs that were working with him, and I was there to criticize the quality of the papers that they were publishing. I did it, and there was a person in the audience -- and they were polite, but dutifully critical to us. It was good feedback. I had some things right and some things wrong, but there was harmony. And one of the individuals who was there was Lewis Sheiner. Lew Sheiner was a

physician internist who had a very strong interest in math and physics, statistics like myself. And he was working in a field called pharmacokinetics. It's the application of mathematics to drug action in humans. It deals with using math equations to model the time course of drug action and drugs in the body. He said, he says, "You're pretty interesting to me, because we have some common interests. What do you say we do a project together?" And I said, "Sure. Why not?" He had the idea that you could take a blood level, draw a blood sample or two from a patient, analyze the drug for the concentration of the drug, and then predict or forecast the time course of concentrations in the blood after each dose, and match that up with the clinical outcome.

And he was studying the drug Digoxin. But he says, "We don't have enough patients. Do you think you would have some patients over there at Letterman?" So I said, "Sure, I work in the cardiology clinic. I could drum up a few patients who are taking Digoxin." And so we did a clinical trial that year, the two of us. We basically were evaluating whether we could predict certain parts, certain aspects of pharmacokinetics in patients by just drawing one blood level. We'd give them a dose and we'd draw one blood level and then see if we could put that into a model and predict their future blood levels. We did that. It turns out that the data -- there was so much noise in the data, due to the fact that patients sometimes don't take their drug as they're prescribed, so-called nonadherence to the prescription, that we didn't publish that study, but the data went into another study that eventually got published. Well, I experienced the thrill of research and the thrill of applying math, and I took an additional statistics course during that year. And so by the end of my last year as an internal medicine resident, even though I'd been Chief resident and had the opportunity, then, to go to Walter Reed and be on the staff, I persuaded the Army to send me over to UCSF for two years for a post-doctoral research fellowship in clinical pharmacology. So very impactfully in my career, from 1972 to 1974, I spent full time at UCSF in the Division of Clinical Pharmacology; learning pharmacokinetics, taking multiple statistics courses, and working with Dr. Lew Sheiner. Fortuitously during that year, we published a paper that put together all of the data that we had together between us

[inaudible] forecasting for blood levels. And Lew gave me the opportunity to be the first author, and it got accepted for publication in the New England Journal of Medicine, which was sort of amazing. And, of course, that was a thrill, too. So by the end of 1974, I was an internist and a clinical pharmacologist, and I definitely wanted to pursue my career. But the options were to go to Vietnam, go to Walter Reed on the faculty, or go into what was known, at the time, as the Medical Research and Development Command of the US Army.

JS: What was that function?

CP: Right. So it turns out that the military services have always been doing medical research. There's been funding for research on diseases that are of particular concern to soldiers. And many advances in civilian medicine have come from the military medicine. For example, during World War II, there was a serious problem with Malaria in the Pacific Theater, and so the government supported a great deal of academic and military research on Malaria. As we were talking earlier, I've learned that Francis Kelsey and her husband, both pharmacologists, have papers that were published during that period of time on Malaria -- antimalarial pharmacology. So I discovered that -- well, I knew that there was a research laboratory at Letterman Army Medical Center, and so I looked into it more closely and it was called Letterman Army Institute of Research. It was doing research in a variety of areas and they had an opening, oddly enough, in the Blood Research Division. The problem that the military faced in Vietnam was supply of blood. The blood came from the United States. At the time, the shelf life of bank blood was two weeks. And so you can imagine the difficulty of harvesting blood, checking its quality, putting it into blood bags and Air Evacing it to Vietnam, storing it there, and having it available. So, typically, blood drawn on the east coast, there would only be one or two days of shelf life left by the time it got to Vietnam and available in the field. So the military was tasked with -- the R&D command was tasked with extending the shelf life of blood. And that's what the goal of that division was, was to permit it to go longer. During the six years that I was in that laboratory, we achieved an extension to six-week storage. I was part of a team. Eventually, I inherited the

leadership position, because the Chief of the division went on to become an Institute Director. And so, I don't know, roughly 1978 or so, I became Chief of the Blood and Research Division at Letterman Army Institute of Research.

What I was mostly interested in at the time was the migration of one of the chemicals in the blood bag into blood and what happened once blood was infused to the humans. Plastic blood bags are flexible, and they have what's known as a plasticizer in it. And the plasticizer is a chemical. It's called DEHP, Di(2-ethylhexyl) phthalate, and because blood is stored at a relatively warm temperature, a substantial amount migrates into blood. It's lipid soluble and it migrates into blood. And so every time a human gets a unit of bank blood, they get about 10 milligrams of DEHP. It's a common problem in drug storage containers is the issue of what's in the plastic or the paper or whatever, the blister pack, that can actually attach to your drug and then get into the body. So part of the FDA's remit is to be sure that the packaging and the interaction of the packaging with the product is safe. So that gave me a wonderful opportunity to learn the analytical methods for DEHP. I did a lot of laboratory work during those years to investigate it in non-human primates. At that time, we used African Green monkeys. And by the time that period of my career was over, I published several papers on the pharmacokinetics and metabolism of DEHP in primates, in non-human primates. So that was the first six years of my career. Still in San Francisco, practicing clinical pharmacology research.

JS: By the way, I have to ask. Basically, how did the laboratory find a way to extend the shelf life from two weeks to six weeks? That's incredible.

CP: Right. Well, blood cells are living cells and you can keep them alive for a while. They require oxygen. They require a way to give off Co2, and they're -- the metabolic machinery in there for maintaining life of the red cell is operative if you supply it with the right materials. We discovered that adenine, which is a constituent, I think it's an amino compound, that is key to mitochondrial oxygen support. And along with glucose and the buffer that is normally in CPD

adenine -- that's citrate-phosphate-dextrose-adenine and glucose -- was able to extend the useful life of a blood cell from two weeks to six weeks. It was a major advance.

JS: It sounds like it. And at one time, of course, blood banking was done with glass bottles. Is that right? But at some point, between World War II and Vietnam, we changed to using the --

CP: The plastic bottles.

JS: The plastic bags that you were talking about.

CP: Yeah. Well, and before the glass bottles it was human to human.

JS: True. Now, during this period from basically from about -- up to 1980, when you were in San Francisco, you had a [inaudible] appointment though at USCF, though, did you not?

CP: That's right. Once one is trained in a specialty and then a subspecialty, there's an opportunity to engage in teaching and continue research through a local university. And so even though I was not paid by UCSF, I maintained an academic appointment and my duties were to come over to UCSF one half-day each week and to teach medical students and house staff and postdoc researchers principles of rational therapeutics. And then the other special things that I was interested in; computing and medical statistics and applications of mathematics. So that was an opportunity for me to continue work with Dr. Lew Sheiner and to write abstracts and papers and give presentations. So basically, I've always maintained, even though I had a primary appointment, not always in the university, I always maintained an academic appointment because it's a good way to continue learning, and to enjoy the scholarly life.

JS: Right. While you were in San Francisco during these 11 or 12 years or so, obviously you've talked about your research interests that -- and this is obviously the -- this carves out what's going to be your interest for the rest of your career, really.

CP: Absolutely.

JS: You've talked about your teaching interest. By the way, I guess I should ask. So when you were teaching the students, and even staff, I suppose, at UCSF about rational

therapeutics. This is a pharmacological-based approach to therapeutics, is it? Now, they're not talking about actual drugs, therapeutics of certain diseases. This is basically an approach on drug action and how that's taken into account when making therapeutic decisions. Is that right or is it something beyond that?

CP: Yeah. The general principles are applicable across all conditions and with respect to all medical therapeutics. So for example, principle number one is you have to get the diagnosis correct. You don't want to give a drug for the wrong purpose. So having a full understanding of the pathophysiology and the patient is sort of step number one. And in fact, there are situations in which there's no need for therapy or if therapy's warranted, the therapies aren't appropriate for the patient. So you have to understand the patient and the disease and then you have to understand the variation in the drugs that are available and sort of match up the right drug with the right patient. And then it's a matter of the dosing regimen. That is giving the right dose at the right time for the right duration of time. And underneath that is getting the amount and concentration of the drug to the site of action that would be beneficial and to minimize the exposure of that drug to other sites of action where it might cause mischief. Side effects. So those are the basic principles, along with the requirement to monitor, periodically, the consequences of your therapeutic decisions. So I've written papers on the general principles and chapters on that subject, and it's a -- in a way, it's a philosophical approach. First, do no harm. But before you can know whether or not you could even do harm, you have to understand the patient and what's available for them.

JS: Okay. So that's very helpful.

CP: It fits with FDA's philosophy, as well.

JS: It does. During these years, too, your clinical responsibilities change, I assume, based on what you've said so far. So those probably decrease during this period. And plus I assume you have some -- a variety of administrative other responsibilities, at least at Letterman

perhaps. But in terms of your clinical, does your clinical work -- can you say something about that while during your San Francisco years? Does that --

CP: Sure. Well, basically beginning in 1968 with my internship, rotating internship in Hawaii and then three years of residency, full time medical practice. I recall after, I had a little bit of time after the end of my residency in which I took a locum tenens and practiced medicine for six weeks in Eureka, California. And I rather enjoyed that, but also was reminded, at the time, that it wouldn't be -- I'd be bored over time with the repetitive nature and the lack of opportunity for research. I failed to mention that during that last year, I had an opportunity to go abroad again through the Army. I had a brief period of time when I was in southeast Asia and Malaysia. Kuala Lumpur, Malaysia, in a tropical disease laboratory, undertaking a clinical trial of an antimalarial. That was definitely instructive for me, because not only did I have patients that had Malaria and was able to evaluate the consequences of our drug trial, but I myself got Malaria, and I was pretty ill. I was Air Evaced to Bangkok and spent four weeks in a military hospital being worked up and treated for Dengue, actually. The Malaria wasn't recognized. And two years later, while I was -- maybe it was three years later, while I was a young scientist at the Letterman Army Institute of Research, one night while I was moonlighting in an emergency room over in Alameda, I suddenly had this full spectrum of the signs and symptoms of Malaria and had to get a substitute and go home and try to recover. And a few days later, the diagnosis was made of Vivax Malaria and I was treated successfully and I've never had it in the meantime. So that's real up close and personal with understanding a disease that I really know a lot about and I've published on that.

During my years at Letterman Army Institute of Research, I spent one half-day a week in a clinic. Most of the time, it was at an oncology clinic. And then I spent a half a day over at UCSF. So I actually had a one day a week when I was either doing clinical work or research work or academic work. I require very little sleep, and I work most weekends, so this didn't cut into my duties. And I actually -- we'll get into what happened from 1980 to 1987 in a minute, but

I kept that style of a half -- of seeing patients until I went to FDA. Up until 1987, I spent either half a day a week in a clinic or when I was in Washington, I had a period of time when I was the attending physician on a medical ward at Walter Reed Army Medical Center or at the Naval Medical Center. Usually it was one of each during the year. I'd like to take a break now and --

JS: Okay. Let's pause this.

CP: Use the restroom.

JS: Start with that and turn this on. Okay. And, great. And we're back. So, in -- now, you've spent over a dozen years or so in San Francisco, but in 1980, you make a big move. A big move, certainly geographically, and maybe in other ways. And that's to the Uniformed Services University of the Health Sciences in Bethesda, Maryland. Now, certainly I'm interested in hearing why you made that decision. Certainly the fact that this was probably the place where you trained physicians and health practitioners who go into the armed services, and the fact, probably, that you were going to direct their clinical pharmacology program might have had something to do with it. But could you say a little bit about what kind of led you to take that position? And also, I'm curious if perhaps your thinking about, based on your earlier work that you developed in San Francisco on pharmacokinetics, pharmacodynamics and so on, to what extent maybe that maybe got even further distilled at USUHS, in terms of your thinking about the construction of clinical trial and how these sciences could play an important role there? But I guess, first, maybe what led you to Bethesda?

CP: [Inaudible] I'm going to close the door here. Getting a little bit of noise from the construction. My wife just arrived. So looking back on my career, I realized a while back that I have made a change, a substantial change, somewhere around every 7 to 10 years, that sort of a time constant. I've talked to other people about this, and this happens in a lot of careers. There comes a time when you become less interested in what you've been doing, less thrilled about it, less inspired, or you figure that you have achieved your goals. So in the late '70s, I was beginning to feel that blood product research, the work that I was doing there was sort of maxing

out my interest, so I was looking around. Since I was a US Army Major at that time, as it turns out, every time I decided to take a new assignment during those early years, I incurred additional obligatory years. If I'd have gone into the Vietnam period, I would have had two years and that would have been up. But by taking a residency, I incurred some additional payback time. But by the late '70s, I paid back all of my time and I could have left the service, taken an academic position someplace. So I was teetering with that to do at the time. And I heard about the new military medical school in Washington DC, the Uniformed Services University of the Health Sciences, the Dean of whom was a very well-known infectious disease person and whose work I knew. And I learned that a very well-known pharmacologist from Stanford had just gone to head up the new pharmacology department. And it became known to me through him that they were looking to set up a clinical pharmacology unit there. I had toyed with going to Washington a couple other times. Walter Reed Army Institute of Research had tried to recruit me, and it intrigued me and my wife. So we basically made the decision to -- also, I was at about my 10-year period in the military and that's a period of time where you've invested a lot of time in the military. If you have a reason to stay in 10 more years, then you get a little retirement.

So all of that sort of came together and I thought, well, this looks pretty interesting; it's well-funded, it sits right next to the NIH campus. It'd be a way to grow. So Lew Aronow and I spoke and he was, he's still living, a very well-known pharmacologist and a very fatherly chairman of the department, and I knew that we would harmonize and that he would be very supportive. So that's what -- we made that decision. We moved to Washington DC in January of 1980. And my duty was to teach clinical pharmacology principles of rational decision making to second-year medical students, and Lew agreed that I'd set up a research laboratory and that I would establish a postdoctoral research fellowship. So all the things that would [inaudible] a young academic to build and to establish something new. And the resources were perfect for that. I did exactly that. I established a laboratory. I had been working on a novel idea of mine, and that was capturing chemicals that reached the surface of the skin for diagnostic purposes. It

turns out that the skin's the largest organ in your body, and it's relatively impermeable. Although the outer layer of skin has the thickness of Scotch tape, it basically keeps water in and a lot of the bad stuff in the environment out. It's an amazing barrier, but it's not a simple barrier. There's several layers. There's living layer and there's some dead layer and there's a bunch of elements to it. There's hair and there's some various kinds of sweat glands and so forth. But the reason you and I are relatively pink is because there's a huge river of water just underneath that layer of Scotch tape. And that river of water, the capillaries that's causing the skin color, is full of interesting information. In fact, when you drink alcohol, alcohol vaporizes from the surface of your skin all over your body because it exits the capillaries and moves across the lake of water in between that and the outer surface. And it comes out in molecular form. So it was well-known that the human body emits a lot of gas. This is not intestinal gas. This is just gas from coming off the surface of the skin.

In fact, that's such an important thing that when I was at Wright-Patterson Air Force Base in 1962 in the nuclear physics department, I actually toured a part of the base where they were evaluating human's gas emission for space travel. The concern was, look, there's all sorts of stuff coming off of the skin. What do we do with that stuff? How do we clean it out? Is it going to be harmful to the other people? If you're confined to a closet-level space with another human that's airtight for six weeks, what are you going to do with it? So they had chambers where they were actually -- they'd have a person in a chamber and he would be completely in the chamber with a tight seal around the neck, and they would pass very pure argon gas through [inaudible] and collect the gas at the other side and run that through a mass spectrometer. And they discovered thousands of gases coming off of the human body, various cell organic compounds. Well, I thought, well, that's a good diagnostic portal. Then I asked the question, and this was a leap, what about non-volatile chemicals? Do they ever reach the surface of the skin?

JS: Just one moment. I have to turn this over. Okay.

CP: So I asked the question, do non-volatile chemicals ever reach the surface of the skin? And there I discovered, in the agricultural research literature, a very interesting paper in which horses had been given a sulfonamide and put in a barn where they were sweating -- horses sweat -- and someone came along and wiped off the sweat and discovered that they could detect sulfonamide in the sweat. So I thought, okay, let's look at that literature. Well, it turns out that it was already well-known that human sweat has a trace of a whole lot of stuff that we're exposed to. Then I asked the question, what about in the absence of sweat? Could something reach the surface of the skin? And for that purpose I invented, and I have the patents on this, a device, which is essentially a sink, creates a sink condition on the surface of the skin, and a liquid bridge across which anything that reached the surface of the skin could move into the sink. We used activated charcoal and an aqua gel and we demonstrated that that was a feasible diagnostic approach. I wrote a very complex mathematical theoretical paper on this subject, which I was always very proud of. Nobody's ever read it because it was very obscure. And Lew Aronow was interested in this. He said, "Yeah. We can fund that." So I went after some funds from NIH and the Air Force, and so for the next six years that was my research area, was skin. I learned -- researched everything I could possibly learn about skin. And that's where I ran into the work of Higuchi, from Kansas. Because he had developed the idea of transdermal drug delivery systems. So what I was doing was researching the outward migration of chemicals from inside the body, instead of migration from a device on the surface into the body. So I had a handful of papers on that and it was a wonderful experience [inaudible] how to do that. I eventually formed a small company to exploit the information, exploit that, and we worked on that during the 1990s, but it didn’t turn out to be sufficiently feasible for me to make it into a commercial product.

JS: But this transdermal work you were doing. This was during your time at --

CP: At Uniformed Services. Right, right. And it brought me into some broader areas of mathematical modeling. I learned about physiologically-based modeling for pharmacokinetics. The traditional approach to pharmacokinetics is to envision the body as a

tank, and you put the drug in a tank of fluid and you measure the concentration and you measure its exit properties and you run a differential equation to explain that. Well, that's a very crude approximation to the human body. Another approach is called physiologically-based modeling, PBPK. And it actually involves anatomically correct, physiologically correct connections between organs in the body and blood flow. And so they're much more complicated models, but it's a much more realistic representation of the body. I often explain that the body is basically a collection of pipes, pumps, and tanks. And that's what physiologically-based modeling is. The liver is a tank, the heart is a pump, the brain is a tank. You can connect them mathematically, and it's turning out now to be an incredibly fruitful approach to modeling and forecasting and it's used at FDA. It's used in the drug industry. That was my first opportunity to sort of get that technology and understanding into my -- so, that was the research end. And I attracted students and postdocs to work in my laboratory with me on that and we published papers. I established a research fellowship. These were mostly internists. Pediatricians who had trained at Walter Reed Army Medical Center or the Navy, and who got permission from the service to get trained up in clinical pharmacology, and to undertake, then, military research and medical research using the advanced methods that we were developing in clinical pharmacology. So that was the seven years that I spent at Uniformed Services University teaching and researching and publishing.

JS: Did you enjoy teaching?

CP: I did. I did. I enjoyed it a lot, but only at the -- I would have been a terrible lecturer to 500 students. The most satisfying teaching is with three to five students who are voluntarily there because they're inspired by the subject. And so teaching at the postdoc level was a lot of fun. Of course, I taught medical students. It was less joyful, but I dutifully put together my various courses. There's an anecdote that probably is not worth sharing too much, but I believe that the Uniformed Services University is the best medical school in the country, and I'll tell you why. The students are so top. Most of them come from the academies, where they had an engineering degree. They mostly have had one or two tours of duty. They're family-

oriented. They're in their late 20s. They're serious. They stand at attention when the professor walks into the room. They listen and they work their rear-ends off. And during the summertime, they have duty. They're off providing medical care as medics and so forth in military situations. If you ever find yourself in the emergency room and you look up the doctor and he says, "I trained at Uniformed Services University." You can have a lot of confidence that that individual's going to know what's going on. I've taught at Stanford, UCSF, Georgetown. We've had these students come by the bedside and so forth, and they just don't hold a candle from, on clinical grounds. Now, of course, these great universities attract research-oriented people and so forth. But I've always been proud of the work of the Uniformed Services University. And they have good teachers, because they're over Walter Reed and Naval National Medical Center and NIH.

JS: Of course, now they're combined in one site.

CP: Right. They are.

JS: So, as you were saying before, this is -- we're approaching here an end of another seven or eight-year period.

CP: That's right.

JS: And I found it interesting. I've looked at some of the interviews that you did when you were leaving the agency and when you look back, and you mentioned that you hadn't really been a close follower of FDA. But -- and the position you were, you took at the agency was one completely unlike -- now, I'm sure there are elements of it that really mirrored much of what you had done before, but in the breadth of the position, the vast responsibilities of the position of Director of the Center for Drug Evaluation and Research, this was one with just responsibilities that -- I think it's hard for people to appreciate unless you've been at the agency and seen some of the things that the FDA is responsible for. But you had not been a follower of the FDA. Now, it wasn't a big move. It was just a few miles up Rockville Pike to where the FDA headquarters was from USUHS. But in terms of what the job entailed, it was a huge change. So what was it that attracted you to FDA? And how did this come about in the first place?

CP: Right. Well, I'm so glad you asked because I myself find this a very unlikely and interesting story. Indeed, I had not been watching FDA very closely. I had not been a student of FDA. I not had -- yeah, I'd consulted with drug companies on very specific pharmacokinetic statistical clinical issues over the years. I'd been involved in some clinical trials. But I didn't really have much of a clue, and I was subject to the biases that the many people have with respect to what they read in the newspapers about the FDA. But I was in Washington DC, and of course, FDA is always in the news, and so I was more aware of FDA. And a few years before I left the university and went to FDA, I -- an FDA reviewer came to me. His name was John Harder, and he said, "Carl, or Dr. Peck," he says, "I'm a reviewer at FDA. Basically I'm an academic. I had an early career in academics but I got interested in drug development and worked for a couple drug companies and now I'm Head of the Rheumatology Drug Review Section of the FDA. But I need an academic outlook. Could I come over here a half a day and enjoy your library and teach some medical students and you and I could engage on various things?" I said, "Sure." So I got to know Dr. John Harder. And what I learned about Harder was that he was a terribly rigorous scientist and had a bit of fame in his own right. He had invented alternate day steroids, as a safe way of giving steroids chronically. He was in research at Harvard in the late '50s, early '60s. So he was somebody from FDA that I really had a lot of regard for, and I began to think about, gee, what I read in the newspapers about the bureaucrats at FDA that never are willing to approve a drug, there's something missing here because this guy is really something. So and then I realized a couple of other facts. One is a predecessor of mine in the job, Dr. Dick Crout, had been a very well-known academic, and I knew him from my clinical pharmacology days. And so I said, "Well, jeez, if that guy could leave academia and go to FDA, that must be something."

Then there was a Commissioner who had a somewhat short-lived Commissionership, as often Commissioners do, who also was a well-known clinical pharmacologist. That was Arthur Hayes. And so I began to become aware of the fact that FDA wasn't exactly what the media was

purporting it to be. There was even an advisory committee held at Uniformed Services University just down the hall from me in the auditorium that I slipped into one day in late 2005, I think it was. And it was on an AIDS drug. And this advisory committee was very interesting. They had experts from FDA and experts from the drug company and from academia giving talks. So slowly I became aware that FDA was something not as described in the media. And then John Harder came to me in the summer of 2006 and he said --

JS: Now, which year?

CP: Thank you. I get these decades wrong at times. 1986. Thank you. And he said, "You know, there's a rumor that Hank Meyer," who was Head of the Center for Drugs and Biologics. The two had been combined in the early '80s for reasons of not being able to find, apparently, properly a replacement for Dick Crout, "and they're looking for a new director. Why don't you think about doing this?" And I said, "You've got to be kidding me, John. I'd never do that. I'm a division director. I've never been a department director. I've never been a Dean. I don't really enjoy management. I like research, I like teaching, I like math, blah, blah, blah." John kept working on me, and so he said, "Well, at least do this." He says, "Why don't you talk to a few people at FDA?" He said, "You've heard of Bob Temple and you've heard of Bob O'Neill. These are colleagues of mine. I think you'd enjoy meeting them." So I went to talk to them, and to the last one, they said they were amazed that I was inquiring, because I think they didn't think there was a chance in the universe that I would ever be considered because of my lack of experience at the senior managerial level. But I was very impressed with Bob Temple. Very impressed with Bob O'Neil and some others that I interviewed with. And they were just -- these were just informal requests that I made of them. All the while, my colleagues, Lew Sheiner and -- well, actually, Lew's an exception, but most of the other people that I talked to who were friends of mine saying, "That's a dead end. Why would you do that? Why would you ever go to FDA?" And it began to dawn on me that, well, maybe there are some things wrong with the FDA, but think about it. I could have a look at everything that's going on in the industry, and I could learn

what's going on in drug development. And these guys that work at FDA are no slouches. They're really impressive people. Most of them had an academic career. Most of them have tons of papers, and some of them continue to put paper.

So I finally became convinced that I should throw my hat in the ring. That was the fall of 1986. So I did. I went through the motions of announcing to whoever the recruiter was that I would be interested. Then there was silence. A long period of silence. I think I announced, I submitted a letter of interest in September of 1986 and by late November, I was just bumping over 20 years in the service. I could leave and I could take position and my wife was urging me to look around and wondered why I would ever think about continuing government service now that we had this opportunity to actually invest in stock and take a meal from a -- and so, I made an inquiry at FDA. And Stuart Nightingale was the head person in the Commissioner's office who was the point of contact, and he said, "Well, I'll make an inquiry." Before he could make the inquiry, the news came out that the then Commissioner, Frank Young, that his son had incurred a very serious cervical fracture in a wrestling match. Jonathan. Jonathan Young. And that the Commissioner was very distracted and that they were putting the recruitment for the [inaudible] director on hold. And of course, everybody was worried about this young man and sympathetic to the Commissioner. So basically nothing happened for the next several months. In about March, I was getting pressure from Barbara and [inaudible] my own pressures, because I'd made it known that I was looking around, thinking about doing something else. Meanwhile, I had also heard that, gosh, there was a lot of people applying for this thing. 65 or something like that was the number I was told. Now, I have no idea if that was true. At the time, I can't imagine that -- it doesn't seem to be a very popular position to me. It didn't seem to be like -- but there were people who were interested who knew more than I did, maybe, about what the opportunity was.

So I inquired at Stuart again, and he said, "Well," he says, "this thing is not going anywhere." He says, "I'll inquire." Nothing happened again for about two months, and finally I called Stu and I said, "You know, I just think that it's been bumping up on three-quarters of the

year since I applied for this thing." And I was imagining all the time that -- I must not be competitive, because I hadn't heard anything. And then Stuart said, "Well, it just turns out you've been named in the top five and Frank Young would like to meet with you." But he said, "First, you have to go through the normal interview process." And I said, "What's that?" He says, "Well, you've got to [inaudible] three days and we want you to interview with, I don't know, 25 or so different people in the center." Actually, and Center for Biologics and the Center for Drugs. Because at the time, the position being offered was a replacement for Hank Young as Director of the Center for Drugs and Biologics.

JS: Hank Meyer.

CP: Hank -- oh, sorry. Hank Meyer.

JS: Right.

CP: Who am I thinking of Hank Young? That's Frank Young. Yeah, Hank Meyer. Thanks. Thanks for correcting me here.

JS: But still, the point is though it's still of this combined center.

CP: It's a combined center.

JS: Combined Biologics and Drugs Center, right?

CP: That's right. So I knew that I could feel comfortable with small molecules, the drug center. Because I'd studied that all along and I felt -- the biologics was a very different thing. I had almost no experience, but I did have experience in blood products. And I had a sense for that. But I knew very little about biotech, genetics, any of that stuff. Nonetheless, I went through the interview process. It was a three-day process and I remember going to biologics. At the time, the interviews were held in, I think it was building nine of the NIH Center. And I had actually been there during my CPD adenine clinical trial stage in the late '70s. So I knew a little bit about that. It was a very different kind of center. It was research oriented, and that appealed to me. So I didn't think it was disingenuous to apply for that, but I was also aware that the two centers had never really merged. There was lots of acrimony and the biologics thought that they

were just a bunch of bureaucrats over there in drugs, and drugs thought they were just a bunch of researchers and didn't know anything about drug regulation, blah, blah, blah. So it had never been a happy -- So, in the early summertime, I interviewed with Frank Young, and we hit it off immediately. I was still stunned at why I was even in the running. We were down to three. Two or three. As it turns out, the deputy to Hank Meyer was one of the candidates.

JS: That would be Paul Parkman.

CP: Paul Parkman. A very fine scientist and wonderful human being who I got to know in time. I hadn't known him at all, but I knew that he was as much a misfit for drugs as I was for biologics. Because he was very famous, actually, for working in vaccines and so forth. But so, in fact, even during the interview process, his deputy, who I interviewed with, asked me if I didn't just want to throw the hat in and be Paul's deputy. I said, "Well," at the time, I said, "That's really not what I'm applying for. We can talk about that later." So, Frank Young really appealed to me because he had been a medical school Dean before that at Einstein Medical Center and -- oh, wait, no.

JS: Rochester.

CP: Rochester. It was Kessler who had been at Einstein. It was research oriented. He asked me a lot of questions about research. Seemed to be quite interested in my knowledge in statistics and clinical pharmacology. So I knew I wasn't going to be dismissed out of hand, but still wasn't really confident that I would get the job. Meantime, Barbara was not really happy about all this and nobody was really very supportive of it. And then --

JS: Do you want to get a drink? Do you want to take a rest for a drink?

CP: I want to just finish this thought. And then I got a call from Frank Young's office. Stu said, "The Commissioner wants to talk to you about ideas he's got." And I went into the room and Frank said, he said, "It's a really hard decision between you and Paul." And I was thinking, "Oh, shit. Poop, here it comes. I'm going to be looking for a job someplace." And he said, "Carl," he says, "I'm thinking about splitting the centers off again and making one of them a center for

drugs and the other a center for biologics. What would you think about what? Would you want to give up biologics?" And it didn't take me long to say, "You know, Frank, I really feel comfortable in drugs. I think I could do a great job with drugs, and I think Paul Parkman could do a great job." And so it was settled at that point.

JS: So I just want to make sure I understand. At the time you were applying, this was still very much a combined center.

CP: That's right. It was a combined center, and that's what the job was. And it was, I think -- I had to -- I have never been so thankful to a human in my life as I am to Frank Young for having the, whatever insight he had to give me this opportunity and to craft it. And I think it was a brilliant move on his part, because Paul did a fine job with biologics and he was on the horse already and ready to go. And the biologics staff was ever so happy to not have to divide the director's time with drugs. And the drug side seemed to be happy enough, although I was a real unknown. There was one little nuance. Barbara, frankly, wasn't really happy about my agreeing, and I let that be known to Frank Young. And let me tell you what happened. Frank Young came over to our home one evening after dinner and spent 30 minutes persuading Barbara that we should take this job. I can't believe it to this day that he did that, but he did. He really had made a decision that I would be a good person for this job. And I don't know to this day. He always seemed very happy with the innovations I brought and with the little bit of tutorial from him, he became very comfortable with all of my decisions. He was very supportive when the congressional hearings and all. But I have to tell you, Frank Young saw something in me and in the opportunity that I think was way over the top. I don't know quite how he came about this, but it became the definitive job in my life. Unbelievable opportunity and wonderful period of time.

JS: We'll get into the priorities you had and what you did once you started there, but I'm curious, when you were interviewing in this process and talking with the Commissioner, did he make known to you whether -- if he had priorities for the drugs area? Or if the administration had priorities for the drugs area?

CP: Well, there were definitely priorities and I slipped right into novel ideas about them. For example, he was very frustrated with the AIDS crisis. And there was a -- he was frustrated with the anti-infectious division. With the way they were being bureaucratic and legalistic and insisting on randomized placebo control trials and turning down -- he basically felt that the center was reactionary and not -- and he asked me for what my ideas were, and I said, "Well, listen, I come with a set of skills in clinical pharmacology that I think could be brought to bear on this. We can use pharmacokinetics and we can use flexible clinical trial designs and we can use dose response trials and not have to use a placebo." So I laid these kind of things out and that appealed to him. And I realized that I could be creative in this job. I didn't -- no Center Director who takes this job ever has any idea what the job description actually involves. I didn't know anything about the congressional hearings. I knew very little about the inability to move a reactionary reviewer from one part of the agency to another, let alone fire them. But I could see that I could bring to the center an influence that hadn't been there before. And I think Frank Young recognized that, too. In fact, long before I took -- long before I started into the actual job, he and I made a bunch of decisions. For example, we made a recruitment decision for what to do with the prison director of anti-infectives and who to replace that person with. And we selected a young reviewer by the name of Cooper, and she turned out to be fabulous.

JS: We're going to talk about that, too. Do you want to take a pause?

CP: Yeah, I think we ought to probably have a bite to eat.

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