Regional Oral History Office
The Bancroft Library

University of California
Berkeley, California

Program in Bioscience and Biotechnology Studies

WILLIAM D. YOUNG
DIRECTOR OF MANUFACTURING AT GENENTECH

An Interview Conducted by
Sally Hughes
in 2004

Since 1954 the Regional Oral History Office has been interviewing leading participants in or well-placed witnesses to major events in the development of northern California, the West, and the nation. Oral history is a method of collecting historical information through tape-recorded interviews between a narrator with firsthand knowledge of historically significant events and a well-informed interviewer, with the goal of preserving substantive additions to the historical record. The tape recording is transcribed, lightly edited for continuity and clarity, and reviewed by the interviewee. The corrected manuscript is indexed, bound with photographs and illustrative materials, and placed in The Bancroft Library at the University of California, Berkeley, and in other research collections for scholarly use. Because it is primary material, oral history is not intended to present the final, verified, or complete narrative of events. It is a spoken account, offered by the interviewee in response to questioning, and as such it is reflective, partisan, deeply involved, and irreplaceable.

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William Young, 2000

TABLE OF CONTENTS—William D. Young

Biotechnology Series History vii

Biotechnology Series List ix

Interview History xi

Interview 1: April 12, 2004
Tape 1, Side A 1
Family background and early life in Kentucky
Eli Lilly & Co.
Employment in process engineering at Eli Lilly & Co.—Field sales of antibiotics—Running biochemistry of antibiotics at a Lilly plant in Puerto Rico—Lilly's relationship with Genentech on recombinant human insulin—Supervising recombinant insulin development at Lilly

Tape 1, Side B 10
Dealing with the NIH guidelines and the Recombinant DNA Advisory Committee
Employment at Genentech
Learning that Lilly refused to buy Genentech—Bob Swanson, Genentech culture, and benchmarks—Brian Sheehan as the first hire in manufacturing; disagreements with Swanson —Developing, processing, and testing human growth hormone

Tape 2, Side A 20
Genentech reduces its focus to human health products—More on Genentech culture—Strengthening development science —Swanson's stress on informal access, ho-ho's—Herbert Boyer's motives for involvement in Genentech; criticism; Nobel Prize—Genentech-Lilly-UC litigation—Genentech's aggressive patenting strategy; comparison with Lilly—Swanson's FIPCO ambition—Genentech's early partnerships in Japan

Tape 2, Side B 29
More on human growth hormone—Tissue plasminogen activator (tPA)

Interview 2: June 23, 2004
Tape 3, Side A 31
Benchmarks and avoiding quarterly losses—Scaling up and purifying tPA—A plant for tPA production—Overestimating the market for tPA—Applying tPA innovations to Pulmozyme, Herceptin, and Rituxan—Pricing tPA

Tape 3, Side B 40

Streptokinase, tPA, and the GUSTO trial—TPA and FDA approval—Hoffmann La Roche acquires Genentech—Roche's early agreement with Genentech on alpha-interferon—Kirk Raab's hiring and role in the Roche acquisition—Swanson and Raab clash—Beating Roche's put—Increased support for R & D—More on tPA

Tape 4, Side A 50

Genentech rejects vaccines as a business—Difficulty in pricing biotech drugs—Walter Cronkite's visit to Genentech—David Martin and others as head of Genentech research—Moving from cloning genes for existing proteins to innovating new drugs—The board of directors—Publication and patenting policies—Levinson becomes CEO—FDA criticism regarding aggressive marketing practices—Young as Chief Operating Officer

Tape 4, Side B 59

Young becomes CEO of ViroLogic

BIOTECHNOLOGY SERIES HISTORY—Sally Smith Hughes, Ph.D.

Genesis of the Program in Bioscience and Biotechnology Studies

In 1996 The Bancroft Library launched the forerunner of the Program in Bioscience and Biotechnology Studies. The Bancroft has strong holdings in the history of the physical sciences--the papers of E.O. Lawrence, Luis Alvarez, Edwin McMillan, and other campus figures in physics and chemistry, as well as a number of related oral histories. Yet, although the university is located next to the greatest concentration of biotechnology companies in the world, the Bancroft had no coordinated program to document the industry or its origins in academic biology.

When Charles Faulhaber arrived in 1995 as the Library's new director, he agreed on the need to establish a Bancroft program to capture and preserve the collective memory and papers of university and corporate scientists who created the biotechnology industry. Documenting and preserving the history of a science and industry which influences virtually every field of the life sciences and generates constant public interest and controversy is vital for a proper understanding of science and business in the late twentieth and early twenty-first centuries.

The Bancroft Library is the ideal location to carry out this historical endeavor. It offers the combination of experienced oral history and archival personnel and technical resources to execute a coordinated oral history, archival, and Internet program. It has an established oral history series in the biological sciences, an archival division called the History of Science and Technology Program, and the expertise to develop comprehensive records management and to digitalize documents for presentation on the Web in the California Digital Library. It also has longstanding cooperative arrangements with UC San Francisco and Stanford University, the other research universities in the San Francisco Bay Area.

In April 1996, Daniel E. Koshland, Jr. provided seed money for a center at The Bancroft Library for historical research on the biological sciences and biotechnology. And then, in early 2001, the Program in Bioscience and Biotechnology Studies was given great impetus by Genentech’s major pledge to support documentation of the biotechnology industry. Thanks to these generous gifts, the Bancroft is building an integrated collection of research materials--oral history transcripts, personal papers, and archival collections--related to the history of the biological sciences and biotechnology in university and industry settings. A board composed of distinguished figures in academia and industry advises on the direction of the oral history and archival components. The Program's initial concentration is on the San Francisco Bay Area and northern California. But its ultimate aim is to document the growth of molecular biology as an independent field of the life

sciences, and the subsequent revolution which established biotechnology as a key contribution of American science and industry.

Oral History Process

The oral history methodology used in this program is that of the Regional Oral History Office, founded in 1954 and producer of over 2,000 oral histories. The method consists of research in primary and secondary sources; systematic recorded interviews; transcription, light editing by the interviewer, and review and approval by the interviewee; library deposition of bound volumes of transcripts with table of contents, introduction, interview history, and index; cataloging in UC Berkeley and national online library networks; and, in most cases, digital presentation at http://bancroft.berkeley.edu/ROHO/projects/biosci.

Sally Smith Hughes, Ph.D.
Historian of Science

Regional Oral History Office
The Bancroft Library
University of California, Berkeley
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ORAL HISTORIES ON BIOTECHNOLOGY

Program in Bioscience and Biotechnology Studies
Regional Oral History Office, The Bancroft Library
University of California, Berkeley

Paul Berg, Ph.D., *A Stanford Professor's Career in Biochemistry, Science Politics, and the Biotechnology Industry*, 2000

Mary Betlach, Ph.D., *Early Cloning and Recombinant DNA Technology at Herbert W. Boyer's UCSF Laboratory*, 2002

Herbert W. Boyer, Ph.D., *Recombinant DNA Science at UCSF and Its Commercialization at Genentech*, 2001

Roberto Crea, Ph.D., *DNA Chemistry at the Dawn of Commercial Biotechnology*, 2004

David V. Goeddel, Ph.D., *Scientist at Genentech*, CEO at Tularik, 2003

Herbert L. Heyneker, Ph.D., *Molecular Geneticist at UCSF and Genentech, Entrepreneur in Biotechnology*, 2004

Irving S. Johnson, Ph.D., *Eli Lilly & the Rise of Biotechnology*, 2006

Thomas J. Kiley, *Genentech Legal Counsel and Vice President, 1976-1988, and Entrepreneur*, 2002

Dennis G. Kleid, Ph.D., *Scientist and Patent Agent at Genentech*, 2002

Arthur Kornberg, M.D., *Biochemistry at Stanford, Biotechnology at DNAX*, 1998

Laurence Lasky, Ph.D., *Vaccine and Adhesion Molecule Research at Genentech*, 2005

Fred A. Middleton, *First Chief Financial Officer at Genentech, 1978-1984*, 2002

Diane Pennica, Ph.D., *t-PA and Other Research Contributions at Genentech*, 2003

Thomas J. Perkins, *Kleiner Perkins, Venture Capital, and the Chairmanship of Genentech*, *1976-1995,* 2002

G. Kirk Raab, *CEO at Genentech*, 1990-1995, 2003

George B. Rathmann, Ph.D., *Chairman, CEO, and President of Amgen, 1980–1988*, 2004

Regional Characteristics of Biotechnology in the United States: Perspectives of Three Industry Insiders (Hugh D'Andrade, David Holveck, and Edward Penhoet), 2001

Niels Reimers, *Stanford's Office of Technology Licensing and the Cohen/Boyer Cloning Patents*, 1998

William J. Rutter, Ph.D., *The Department of Biochemistry and the Molecular Approach to Biomedicine at the University of California, San Francisco, volume I*, 1998

Richard Scheller, Ph.D., *Conducting Research in Academia, Directing Research at Genentech*, 2002

Robert A. Swanson, *Co-founder, CEO, and Chairman of Genentech, 1976-1996*, 2001

Axel Ullrich, Ph. D., *Molecular Biologist at UCSF and Genentech,* 2006

Daniel G. Yansura, *Senior Scientist at Genentech*, 2002

William Young, *Director of Manufacturing at Genentech*, 2006

Oral histories in process:

Brook Byers
Ronald Cape
Stanley N. Cohen
Donald Glaser
James Gower
William Green
Irving Johnson
Keiichi Itakura
Daniel E. Koshland, Jr.
Arthur Levinson
Edward Penhoet
Arthur Riggs
William J. Rutter, volume II
Mickey Urdea
Pablo Valenzuela
Keith R. Yamamoto

INTERVIEW HISTORY—William D. Young

Of all the narrators in the Genentech oral history series, Bill Young has one of the longest perspective on the company's evolution, beginning with his arrival in 1980 at the time of its IPO through his departure in 1999 to join ViroLogic as chairman and CEO. Trained as a chemical engineer, Young was hired in the mid-1960s by the pharmaceutical giant, Eli Lilly, where he held positions in production and process engineering for fourteen years. In 1980, he surprised his superiors at Lilly by abandoning a secure future to join an upstart company called Genentech which was partnering with Lilly on human insulin and growth hormone. He welcomed the freedom and flexibility of a small company and also the challenges of "scaling up" human insulin and other products for eventual marketing. He proceeded to put manufacturing and process science at Genentech on its feet and to rise to direct all of the company's development, operations, and commercial functions. In 1997, Young was named chief operating officer, an indication of his value to the company. The reader will find in the oral history intriguing discussion of the origins and creation of corporate culture; patenting strategy; the development, pricing, and marketing of tissue plasminogen activator (tPA); Hoffmann La Roche's acquisition of Genentech, and much more.

Two interviews were conducted in Young's unpretentious office at ViroLogic in South San Francisco, the room's informality reflecting the personality of the man himself and the culture he had found compatible at Genentech and now fostered at ViroLogic. (In 2005, the company's name became Monogram Biosciences.) Young's fluid and lively comments augment the contents of other oral histories in this series, particularly regarding the Kirk Raab years and the Roche acquisition. By agreement with Genentech regarding the oral histories it supports, its legal department received transcripts of all interviews to review solely for current legal issues. As in all instances to date, no changes were requested.

The Regional Oral History Office was established in 1954 to record the lives of persons who have contributed significantly to the history of California and the West. The series list of completed oral histories documenting the history of bioscience and biotechnology is included in this volume. The Regional Oral History Office is a division of The Bancroft Library and is under the direction of Richard Cándida Smith.

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The Bancroft Library
University of California, Berkeley
April 2006

[Interview #1: April 12, 2004]
[Begin Tape 1, Side A] ##[1]

Hughes: Start with your grandparents, please, and tell me a little about where they came from and what they did.

Young: Well, my paternal grandparents actually were from Scotland, and the family grew up in a little town outside of Glasgow, Darvel and Newmilns, which are little dots in the road in Ayreshire, Scotland. They were blue collar workers who I am sure had a tough economic time in the twenties, sent one of their sons over, the eldest who actually turns out is my father William Young, to scout out America and build a better life for the family. He came over first and established himself in the Northeast, in Buffalo, New York, and then kind of recruited the rest of the kids who were a couple of other brothers and a sister to come over and the grandparents to come over. So they all immigrated in the mid-twenties and then established themselves in various businesses, in Cleveland, in Buffalo, and in Pennsylvania. My grandfather actually stayed about three weeks and said, "You know, I don't like America," and then went back.

Hughes: [laughs] And meanwhile—

Young: Meanwhile, everyone stayed but none of the family after that would talk about him, so we don't know what happened to him when he went back to Scotland. Maybe he had a girlfriend or something; nobody really knows. My wife, Sherry Young, and I on a trip to Scotland about ten years ago actually tried to find him and evidence of him but couldn't, in the town where they were all from. We found a lot of other Youngs and McInnes, which was the maternal side of my grandparents. But at any rate that is the story of how they got here.

My father and mother, Ruth Ringmacher, then met in Buffalo and married and then later moved to eastern Pennsylvania, actually to Wilkesboro, and that is where I was born. I was an only child. Then my father passed away when I was about four years old, and we moved to Louisville, Kentucky which was the home of my mother's aunt and uncle, who then took us in, and I spent, up until I went to college, growing up in Louisville. I ended up going to Purdue University, which is in Indiana, for my bachelor's degree [1966]. Then I got an MBA [1971] from Indiana University, but that was partly the proximity between Indiana and Louisville.

1.## This symbol indicates that a tape segment has begun or ended.

Hughes: That was the reason for Purdue.

Young: Yeah. And also my uncle had gone to Purdue as well.

Hughes: Oh, I see. Did he become a father figure?

Young: No, not really because he was out of the house early. So really the father figure was my great uncle, George Cook, who was the head of the household that we lived in. Then my mother remarried when I was about thirteen, so then I had a stepfather from that point on. I went to Purdue because I was quite interested in math and chemistry and in science and ended up wanting to be an engineer. So I went to Purdue, and I graduated as a chemical engineer in 1966 actually, a long time ago. Actually just like Tom Kiley.

Hughes: Did you know what you wanted to do with chemical engineering?

Young: Well, I actually didn't. I thought it was a great discipline because it emphasized what I like to do in math and science, but I also had an English minor because I wanted to be a little more rounded than just engineering. In those days the education for chemical engineers was primarily in the heavy industry, so it was petroleum refining and chemical manufacturing and those sorts of things. As I interviewed in my senior year, those were the kinds of companies that I talked to. So ending up at Texaco or Chevron or DuPont was a more likely course. I was walking by the recruiting office one day and saw a recruiting ad for Eli Lilly, which was a pharmaceutical company headquartered in Indianapolis. Actually, it had operations in West Lafayette where Purdue was, and I thought, oh, gee that might be interesting. So I ended up talking with them and, as it turned out, ended up going there and getting excited about the pharmaceutical industry. But it was not part of a plan; it was one of those things in life where you get some good luck by having fallen into that. So they actually hired me as a young engineer working in one of their engineering groups that dealt with the technology around injectable drugs, and that was the first thing that I learned about.

Hughes: What appealed to you about Eli Lilly that made it more attractive than DuPont or some of the other companies?

Young: Well, I think that the drug and health care businesses had appealed to me because you thought, not only can you do some interesting engineering work. But you can also potentially help people and be on that side of the equation that is more direct than some of the other industries. I guess it was also helped by the fact that my fiancée at the time was from Indianapolis, and her parents were there and were kind of encouraging me to stay closer to home. But I don't think that was the main draw. I think the main draw was, hey, this is kind of a neat company. In those days drug companies were very much influenced by their founders. Eli Lilly's grandson was still there in the company, and so you had this

kind of, “Hey, we have a good culture here, and we are going to do good things for mankind, etc. as part of it.”

I also worked for and with the very first chemical engineer Lilly had ever hired, a guy named Sam McCormick. Sam was a director by the time he was thirty. He was a very influential guy within the company, and he taught me a lot about doing research in the library, about thinking through problems, about just how to go about establishing myself and working within an industrial company, which most people out of college don’t really know how to do. Sam had this whole habit of sort of latching on to young engineers that were coming in, kind of mentoring for a few years and the turning them loose within the company. He was just absolutely great, and I will never forget the things that he taught me. He would go out and buy me handbooks that he thought I should have as I went about the things that I was involved in. So teaming up with him was quite a wonderful thing for a young engineer because I might have floundered around by myself for a long time.

Hughes: And rather unusual I would think. Other corporate cultures, would they have such mentoring?

Young: Maybe not.

Hughes: It was almost an academic approach wasn’t it?

Young: Yeah, that is right. It was not a formal mentoring program that he had. It was more something that he just liked to do and had done it for a lot of young engineers coming in over the years. Because he was a long- time employee, he had access to a lot of the senior people around Lilly, and so he could open a lot of doors for you that you might find it difficult to open.

After a couple of years Sam got involved with the building of a new manufacturing facility that was going to be built on a green-field site west of Indianapolis about sixty miles. It was just absolutely full of new technology. The idea was, okay we are going to start with a green-field site; we have two new antibiotics that we are going to make there. At that time Lilly was one of the top companies in the world in antibiotic production and that is at a time where the U.S. industry was preeminent in antibiotics. Now it is all kind of moved overseas. But then Lilly and a number of other companies had developed penicillin technology from growing it in bottles to these large facilities. They had pioneered a lot of that at the end of World War II. Actually, that is why Sam had come there and what he had done first. Now we were moving off into more sophisticated antibiotics. What they wanted to do at this site was to implement a lot of new ideas and technology that they had on the drawing boards but didn’t want to retrofit an existing plant, they wanted to do it here.

Hughes: And so the injectables were almost all antibiotics?

Young: Oh, no. They were all different products. When I joined, we had 900 different products on their price list. But they probably had five or six top products. So they had insulin, the Darvon products, analgesics, cephalosporin antibiotics. There was a whole family of antibiotics, including the cephalosporins, that were big money makers for them. The new plant was to make an antibiotic that was actually used for growth promoting effects for cattle. And also a product called penicillin V which is a version of penicillin that they produce. Because one was a product aimed at agricultural use, it needed to be made very cheaply.

Hughes: Did that become your problem?

Young: It became my problem because Sam picked some of the people he mentored, and I ended up in charge of the design, construction, and start-up of the purification part of that plant. We worked for about a year before we ever even broke ground there, working on designing a brand new process to produce this particular antibiotic. Sam was right in the middle of that, and it was his project. There were several other engineers that were doing other parts of the operations. So as an example of the new technology we put in—some of which by the way didn't work out so well, but you don't know that when you are doing it. For fermentation for microorganisms of the type that made this particular antibiotic, you need to put a lot of aeration through the fermenter and a lot of agitation. So the real costs there are the raw materials plus horsepower to run the agitation system. You are talking about fifty- a hundred-thousand-gallon reactors and also compressors to compress the air that you need for aeration.

The typical fermenter was a kind of vertical fermenter so you had to pump the air all the way down, and the fermenter had to overcome all of the hydrostatic pressure to be able to pump the air through it. So you needed these giant compressors. So anyway, the innovation there was, we took the fermenters and turned them on their side so they were horizontal. We used natural gas-driven engines to drive the agitators and the air compressors. Because the fermenters were turned on their side, the height of liquid inside was much lower. So you needed a different class of compressors which could be lower pressure to be able to provide air to the microorganisms. So the whole thing was kind of energy efficient. Then instead of putting expensive jackets and cooling systems in, we kind of ran the water down the side of the fermenter to cool it. So great innovations. Not all of them worked so well. Among other things, because you had exposed aeration systems instead of jacketed tanks, they were very prone to contamination. Because you used low-pressure compressors, you got no killing effect on ambient bacteria going through the compressor because you were only compressing to about 15 psi. So we got a lot of contamination problems, and I think the natural gas crisis hit in the early seventies with the huge cost of energy, if you remember back in the boycott days.

Hughes: Right, I remember.

Young: It was right at the wrong time to have natural-gas-driven power. Anyway it was wonderfully innovative, a lot of the stuff we did. It took probably like an extra year to get the whole place started, and a few years later it was running great. That was my first real significant project in new plant construction—hiring the people, starting it up, going through all of that. I still lived in the south side of Indianapolis then and wore out several cars driving back and forth during the starting-out phase. But it was just a terrific experience for a young engineer to go through that at such an early stage because you learned a lot of things you should have done better, but also got really involved. It was just great. I loved the construction phase where you were dealing with the contractors and all of that. During the start-up phase, I remember crawling into evaporators, and I probably did things that I would shudder to do now in trying to trouble shoot things. We had these giant pieces of equipment that we would be crawling in, trying to find out what was wrong. That was in the late sixties to early seventies.

Then in about ‘72 or so I actually took a break in between assignments, and they sent me out to field sales. They had a program at Lilly which I think is a very good one where people from the home office train you as a detail salesman, drug sales rep, and then they send you out to territory for three months. The person in that territory comes to the home office and works in marketing and learns that side of the business. They call it the switch program. They probably still do it. So I got really exposed to talking to doctors and actually selling the products. You go through the regular training just like everybody else. Then you decide, is this really something that I want? Which most people decide it isn’t. That was a good experience then. In the mid-seventies I had several assignments in the antibiotic development operation.

In about ‘75 I got involved with a project in Puerto Rico where Lilly was building another manufacturing site. In the seventies and eighties, all the major pharmaceutical companies had major operations in Puerto Rico because there was a provision in the tax code, section 936, which allowed companies to basically shelter profits by manufacturing in Puerto Rico. Since Puerto Rico is part of the United States, they had this agreement with the U.S. to do that. Everybody had operations there. Lilly had several already, and this was a whole new operation that they wanted to build there. So I was part of the engineering design team, led that. Then when it came time to actually run the plant, I went down to Puerto Rico to actually do the construction and then run the biochemical part of that facility. That was also a great experience because you got a chance to hire and train the people. It was a 200-person company so you were very close to all the things going on. You are right in there with them. The top management layer was from the States but everyone else was Puerto Rican. We hired Puerto Rican engineers and brought them to Indianapolis to train them and went back with them.

Hughes: Did that involve a lot of innovation as well?

Young: No, we were more careful this time. The process actually ran in Indianapolis, and we pretty much took it down there identical to the way we ran it. And it was to make a brand new antibiotic, an aminoglycoside which was called Tobramycin, which is actually a very well-used antibiotic now, that Lilly had not been aggressively developing, but with this plant decided to. We actually bought an old brewery that had gone out of business. I remember going in it the first day. It was like a time wrap because the brewery had gone bankrupt and everybody's calendar was turned to August, and this was probably December. It was like they dropped everything and didn't come in the next day. We took out the brewery equipment and put in our stuff and basically remodeled it.

Hughes: So you just wanted the structure?

Young: We just wanted the land, basically, and the building.

Hughes: How much accommodation has to be made to the organism which is producing the antibiotic? I mean, how generalizable is an antibiotic fermentation facility?

Young: It is usually very generalized with respect to the fermentation facilities. So the part where you are growing the organism, you can use for different antibiotics. But like in biotech the part that's usually pretty customized is the purification. Purification techniques were just then getting more sophisticated, and we actually had chromatography steps in the process and much more sophisticated and analytical techniques than had been used up to that point for this particular product. We had an ion-exchange separation, we had filtration ion exchange, or maybe it was centrifugation—I can't remember. And then chromatography to purify the antibiotic away from a lot of its similar contaminants, crystallizing in bulk, etc, etc. So we had a pretty good process. The plant was really self contained. That was my first real exposure to waste treatment and the issues around that. It was mostly the microorganisms that you were finished with that you had to get rid of, and how to treat those. Of course we had a lot of issues with that. It was in an industrial area east of San Juan called Carolina, but there were a lot of residential areas around it. So if the plant didn't smell great that week, we got complaints, and we had to deal with those. We actually had to put in a lot of specialized pollution-control equipment after we got there because typically antibiotic fermentations don't smell that great. You are actually blowing all that air through, and you have exhaust that someplace.

Hughes: How forward looking was Lilly in adopting new technology?

Young: Oh, I think they were very forward thinking. They had strong process development people that really worked hard to look at the latest technologies and developed a lot of it there. That was one bias that I took with me to Genentech because it is as important to have extremely strong science and engineering on the development end as it is on the research end. So when I got to Genentech I knew that was one of the things that I wanted to build because I

knew it was critical. I knew the industry would be doing a lot of new things that hadn't been done before, and we needed the best brain power that we could get.

So anyway, that was Puerto Rico, and I was there about four or five years. I actually met my wife there. She was working for the Royal Bank of Canada down there, and we met on the beach one day, got married, and I honestly didn't want to leave there. I thought it was a great lifestyle. This was the late '70s. I thought, oh, this is pretty nice. It is warm all the time, we only get pestered by people in Indianapolis in February, and the rest of the time they leave us alone. The culture of the place was great because we had hired all of the people. You get very close to them, because Puerto Ricans are very family oriented so they will invite you to their homes and we would have pig barbecues on the beach. So it was great, really great. And you are really close to the eastern Caribbean, so you have got the Virgin Islands and the whole Antilles Islands chain to go visit and play around on.

We had the plant started and we were running fine and I had been there a few years. One day I got a call from the personnel people. They said, "Look you have been down there quite a while. If you stay down there for much longer we are going to forget about you." I think that is an issue for developing leaders in organizations; your mentors keep track of you for a while, but eventually you lose them. They actually wanted to get me back to Indianapolis because they figured that I would go totally native if I stayed out.

Hughes: But that speaks well of you, does it not?

Young: Yeah, I think it does.

Hughes: Some people they could have cared less about.

Young: The person that called me was Joe Cook, who later left and is now CEO and maybe chairman of Amylin. So he eventually himself went into biotech. He said, "We have this project that we have just started, and we signed an agreement with this crazy California company. It is something about genetic engineering. I don't really understand it very well, but they thought maybe you would like to come back and explore working on that project. We thought it was going to be a long time, but these guys keep achieving the benchmarks that we set. So our management up here think maybe we should get our act together a little bit, because maybe it will be ready to develop before we thought it was."

Hughes: Do you mean that the feeling was, "We will contract with these guys, but they are probably not going to make these benchmarks, and we don't really have to worry about it."

Young: Oh, yes. Well, I think that Lilly wanted it to work. At that point Lilly was— I think they still are—the number-one producer of insulin in the world. They had

probably 80 percent of the U.S. market. I think they still do. There were two trends going on in insulin then. One trend was towards more highly purified, more human-like insulins, and the [other] insulin that people were gravitating towards was a more highly purified porcine insulin which has one amino acid different than human. But it is still not exactly human.

Hughes: You mean, getting away from the bovine?

Young: Yes, getting a little more away from the bovine. So there was a recognition that side effects were probably caused at least in part by the animal origin, and so the closer you could get to human—the more purified the better. So there was that trend going on, and so they had been doing a lot of work on improving the purification technologies, etc. The other thing that they were worried about is that the supply of insulin was primarily from the pancreases of cattle and pigs. That was staying fairly constant, if not declining, but the number of diabetics was increasing with increased diagnosis and more older people who develop a need for insulin. So they could see a time where the supply was getting tighter and tighter, and they were having to go to the international sources, etc, etc. This was before you got into all the mad cow and adventitious agents issues or anything like that. But Lilly was worried about supplies, so they were exploring options for making insulin in other ways, and making them by genetic engineering was one of the ways

Hughes: Was Irving Johnson in charge of that?

Young: Yes, absolutely. Irv had an up and down career there. He would be in charge of everything and then politically things would be stripped away, and then he would go start some whole new initiative. I don't know if you interviewed him for this.

Hughes: I did.

Young: He is a wonderful guy.

This was in '78, so I am twenty-eight or thirty so I am young. But I have been down there [in Puerto Rico] for a while. I came up, and I actually was going to a wedding in Chicago, and Lilly said, "Why don't you stop by in Indianapolis and talk to Irv Johnson and some of the people you worked with in development and kind of see what is going on. See if you would be interested in it." So I did. And Irv got me really excited about coming back and working on really what was the first recombinant product that anybody had tried to develop. The people in Lilly research had worked on some technology to take the two insulin chains apart and put them back together, so they had that piece. So he went through the whole thing with me about how exciting this would be and actually hooked me. So I said, "Okay, I will do that." So I called my wife back to Indianapolis, and this was probably in '78. I remember my wife said, "You know, I haven't lived in the

States." She had been moving around with her parents in the Caribbean for most of her life and didn't have a winter coat, she didn't have shoes that cover your foot. And it was like one of the coldest winters in Indianapolis history that we moved back right in the dead of winter. I used to call her up in the afternoon and wonder if she was still there because it was really twenty below zero for weeks on end. I remember that was a really bad time. But I got very excited about the whole project. I worked on the side where we developed the whole process and then actually designed the first plant. We broke ground for that in probably 1980.

Hughes: Tell me what the steps were once you got the organisms from Genentech. I understand at least the first batch, the organisms, there was an A-chain producing organism and a B-chain producing organism.

Young: Right. We didn't know how to do two things at that point with bacteria which have since been learned. We didn't learn how to secrete proteins out of a cell. So these were all intercellular. The second thing we didn't know was how to make the whole molecule. We only knew how to make each chain. The way it was made was there was an expression vector made where you made the A-chain attached to a piece of protein that you had to cleave off with cyanogen bromide. So it was a chemical cleavage site. So the whole process was two fermentations make the A-chain like the B-chain, purify it, cleave it, re-purify it to get the chains, put the chains together, and then crystallize it.

Hughes: Yes. And all that was happening at Eli Lilly?

Young: 100 percent of that was happening at Eli Lilly because at that time Genentech had just fifty people or less. They did some work but didn't really have any development capabilities, or manufacturing for that matter, so Lilly had to do the vast majority of the development. What Genentech furnished was the cells with the expression plasmids and all that. So they did the expression work. Naïve as we were, we thought in those days, once you get the fermentation and the microbiology done, the rest is easy. Well, it isn't so easy. Part of what convinced me that to move into a company focusing totally on biotechnology would be a good thing for me, which happened later, was I would go to our people in fermentation and say, "I have got this problem. We have got to get a scientist on this. Give me your best guy. I want so and so for this project." "Oh, my best guy is working on a new antibiotic that is coming out." "Well, what about your second best guy. What about so and so?" "No, he is working on some problem in manufacturing." You know, you kind of get the fifth best man. And not everybody at Lilly was totally oriented toward the Genentech project, although it had a high profile when you really got down in the ranks and started recruiting people. We worked hard to recruit a great team and did a lot of development. And we did figure out that it was more than just putting plasmids in cells and fermenting them; you had a lot of development to do. But we did design a

process and naturally started construction at the point where I left to join Genentech.

[End Tape 1 Side A] ##
[Begin Tape 1 Side B]

Young: We also had to face the issues around scale-up in those days. People may remember that none of the scientists involved in the early genetic engineering days knew what was going to happen with these organisms once they got loose. There was an Asilomar meeting in about ‘76 where NIH set up the Recombinant DNA Advisory Committee to look at what people wanted to do experimentally and so forth. The committee is now I think still in existence but does mostly gene therapy kinds of things.

Hughes: Right.

Young: But then it was all around safety. Of course many, many experiments, and experiments since then, have proven that you really can’t do much harm with these recombinant organisms. But we didn’t know that then. So we had to design at Lilly a fermentation system in the laboratory that actually was all contained and was actually run under negative pressure so nothing would get out. It was a challenge for something were you are trying to keep the ambient organisms out of it.

Hughes: Were you designing all that?

Young: Yes, I was doing all that. I remember going to a Recombinant DNA Advisory Committee [RAC] meeting to discuss our contained systems and how they work and get permission to scale-up because there was a restriction on doing experiments in fermenters bigger than ten liters. If you wanted to do that you had to go get these exceptions. So we had to validate this one hundred-liter contained fermenter that we had so we could do experiments in it. So it was quite an interesting event. Later the scale-up restrictions got relaxed. But that was all going on at the time we were trying to develop the technology.

Hughes: Had the Lilly hierarchy anticipated all these problems? Both the scientific development problems and these more political problems? Did they really know what they were getting into?

Young: I don’t think there was in the realm of people like Irv Johnson and Neal Pettinga, who was Irv’s boss, who was the senior VP in charge of research and other things there. I think they were used to dealing with new issues and technology issues. I don’t know if they were surprised or not, but they certainly worked at it as, these are problems that can be solved and let’s go solve them

Hughes: And the same with the political issue?

Young: I think so, yes. I mean, Lilly worked hard, we made presentations to the RAC, and we sent out information, and we worked hard to design the systems and validate them so that we could show that we were taking all the necessary precautions on something that really wasn't that harmful to begin with. But we didn't know that then.

Hughes: Do you remember that industry wasn't technically covered by the NIH guidelines?

Young: We were voluntarily covered. That is right.

Hughes: What was that about?

Young: I think we wanted to be good guys. We said, "Look, we don't know the answers to these questions either. We want to work through the issues with you." I think the best policy for any regulatory agency you deal with is collaboration. So we just said voluntarily we want to comply. It may have been voluntary, but the FDA said, "We want you to comply." So it wasn't quite voluntary. FDA was saying, hey we are going to look for compliance to RAC as part of your application.

Hughes: I see. There was certainly some pressure there.

Young: Yes, but at any rate that was the background. As a part of the collaboration with Genentech, [their] people would come [to Lilly]. There weren't very many, but you would meet them and give them your names and present and that kind of thing.

Hughes: Who was it usually?

Young: The guys that I remember coming to Lilly were [Robert] Swanson, [Thomas] Kiley, Mike Ross—who was an early scientist and is still around and now in venture capital. I don't know if you have interviewed him.

Hughes: No, I haven't.

Young: There was a manufacturing guy named Brian Sheehan that Bob had hired. Those are the people that I remember. You would have meetings and discuss where the technology was in the collaboration, '78, '79.

Hughes: And did you feel that was a meeting of peers?

Young: Oh, yes. Bob as you know from talking to him is very engaging and charismatic, and he would kind of seek out people—you didn't know it at the time—"Oh, what is your background? What do you do around here?" And the next thing you know, you get a call from a recruiter. So in 1980 I am getting these recruiting

calls from somebody called Anita Howe, who was Genentech's recruiter in those days. She is calling and she is saying, "Gee, a company would be interested in you." And I have no idea who it is or why, but pretty soon I find out it is Genentech. That was probably the summer of '80. So I said, "Maybe I would be interested." So I end up coming out to California, and I had never been to California. I get very interested in what they are doing, but on the other side I had a great career at Lilly. I had many different assignments, all interesting, all fun, I was on a good track. In those days in drug companies you never left. They were quite paternalistic; the tradition was you go there, and that was where you would spend your career. There were many, many career people around you who would periodically retire, but they spent their whole career there. Unless you died or got fired or you did something dishonest, that was about the only way out. But nobody left to go to another company, almost nobody.

I finally decided to come to Genentech and I think the main reasons were around, "Hey, I think biotechnology is going to be terrific area to be in, it fits my background perfectly, because I have always been interested in a lot of sciences. I've got the engineering background, I have been doing this sort of work anyway at Lilly. But at Lilly biotechnology is going to be competing with every other thing that they are doing." Here is a way to have a pure play. Plus it is a really innovative company.

Hughes: Had you been paying any particular attention to Genentech as a company?

Young: No, only the interactions that we had because of the insulin projects. I knew they were small and they were starting and it was a new field.

Hughes: Well, they were hot onto their IPO [initial public offering] in the summer of 1980.

Young: Yes, but I didn't know it.

Hughes: That was not a consideration?

Young: Well, I was kind of a reluctant hire. But Bob kept at it and was very persistent.

Hughes: It was Bob that was at it?

Young: It was Bob, yes. I remember I brought Sherry out on one of the trips, and he and Judy took us to "Beach Blanket Babylon" and went to dinner and did the whole North Beach tour. Bob was recruiting heavily. Eventually I decided to go. I think it was on the positive, being a part of a very exciting industry, but second, I said, "If I don't do this and this is really successful, I am going to be kicking myself for the rest of my life." So in the end I decided to do it, and Sherry never ever said what she thought I should do. She was great; she said, "It is up to you; it is your career. Go wherever you want." After I decided, she said "If I had to stay in

Indianapolis one more winter, I would probably kill you!" [laughter] But she didn't say that during the process. So anyway, we went, and I remember going to my boss, Fred Lloyd, to tell him that I was leaving. Of course this was a very hectic time for the project. They could not believe it. They said, "How could you do this?" It almost made me feel guilty. "You can't go there; we have spent all this time developing you." I said, "Well, that is what I have decided to do." I remember Neil Pettinga, Irv Johnson's boss, called me in. I went in and talked to him, and he said, "I know you told us that you want to do this, but I just want to tell you that we know a lot about Genentech. They actually tried to sell the whole company to us six months ago, and here is the file on all the stuff that we looked at and why we decided not to do that. And you've got to read this." So he gives me this thick file, and of course I didn't know anything of this. So I looked through the file and said, "Well, that is fine but I am still going." They did their best, and then they said, "Well, can you work a couple more months so we can get a replacement and have time for you to transfer the project."

Hughes: That is amazing.

Young: Yes. Well they didn't know what to do. Nobody ever left so they didn't have a system.

Hughes: I meant you, too. I think that took some courage to have Lilly, a company that you obviously respected, saying, "We are not going to buy Genentech because of—" whatever flaws they found, and you still persisted.

Young: Yes, I still went. I did work about another six weeks. They selected a replacement, John Kehoe, and I got him up to speed and all that, and then moved to California. Bob had said all along, "Well, I can't tell you why, but you need to get out here before September."

Hughes: Was that the IPO?

Young: Yes. [laughing]. He never told me it was an IPO, but he said, "You need to be here before such and such a date."

Hughes: What about salary and stock options and all that? Was any of that a draw? What were the main draws?

Young: I didn't even know what stock options were. Money was not the draw. They gave me a nice increase. They helped me relocate. In those days I think I was making— I think the first salary at Genentech was like $70,000. So it was not a huge amount of money. Maybe I was making $60,000 or near that. The options were nice, but I didn't really know how they worked anyway, because Lilly didn't have stock options. They had stock awards they would give you directly, but there was no real stock option program there.

Hughes: Was that something that biotech created?

Young: Well, I think that a lot of the stuff that Bob did, I found out later, he borrowed from high tech[nology]—a lot of the cultural values and the things that the company did.

Hughes: Why high tech? Because they were innovative?

Young: They did a lot of that, yes. And I will get into that in a second here. I think Bob was very good at borrowing the value, culture, atmospheric things that he thought would be innovative, and he was right. It established Genentech early as part of the culture, plus some other things too from academics and things that really weren't part of high tech. Of course, I loved all of the people I met at Genentech, all bright, all really motivated. They don't know what they are doing either but they think it is going to be fun.

Hughes: [laughs] What was your impression of the culture? Can you compare Lilly to Genentech?

Young: Genentech was very informal, very academic feeling, scientists running around, Bob being the cheerleader, encouraging people. There was an early on, very important culture which most biotech companies don't have now—discipline. Bob gets criticized for this a lot, but I think it instilled a lot of discipline in the company. We set up a lot of agreements with benchmarks and did it in such a way where we never wanted to lose money. So this was after we were public. So we would sell off parts of the world or get collaborative agreements that would allow us to take revenue in. It was such a quarterly discipline that we wanted to achieve those benchmarks to avoid losing money. Maybe one quarter the company lost money from the time it started till Roche [acquisition]. But it always made those.

Hughes: Is that for PR value? That makes a company look good to outsiders?

Young: A part of it was Bob saying, "Look, money is hard to get; we want to avoid dilution; we want to get as much value built as we can. I am sure that he was thinking that way. But the side effect of it was, this is a great way to instill discipline in the organization, to achieve its goals, and meet these [benchmarks]. That will play into some decisions made later on which may or may not have been in our best interest, but it still drove us to do a lot of things. And I think it is a discipline that a lot of biotech companies now don't have because they are used to losing money and so they just keep losing it. There is not the drive in there that that provided us. So anyway, that is what I thought it accomplished.

Hughes: Was it pretty true that up and down the line Genentech employees took it seriously to meet benchmarks?

Young: Oh, absolutely, absolutely. It started with the people in research in molecular biology, the Dave Goeddels and those kind of folks who I am sure you have also talked to. They had an incredible discipline to achieve the goals that they set out, and they did it. Part of it was the money goal, and part of it was the competitive goal. And probably competition was the majority of it for people like Dave: I want to be the first guy to clone insulin or clone interferon or whatever it was. He basically wanted to win. So all that drive was really built in because of the kind of person he is. The early molecular biologists who came to the company were all very competitive people. Molecular biology was a kind of hot science area in those days. They had it partly in them but also I think the company discipline and all that played a role; Bob's focus on goals and all that played a role. So it was a great place to be. It was very chaotic and a lot of different personalities entered the organization. As I reflect on it now, "Here is a company that is built on hiring executives and technical people from all their [corporate] partners." [laughs]. So you have all these different company backgrounds coming in and trying to make one company out of that. It was very chaotic from that point of view but also very exciting. I remember I went to my very first offsite meeting at Silverado. Bob's wife [Judy] at that time worked for Amfac who owned Silverado, I think, as one of their properties. So we used to handle a lot of our offsites up there. So I go to this meeting and we are like 3:00 in the morning and I am listening to one of the scientists, Roberto Crea, who is actually the organic chemist in research talking about how his role had changed, and he wasn't very valuable anymore, and what should we do about that? Because the technology was evolving so quickly, the stuff that was critical a year ago (DNA synthesis) now was old hat and was on to something else. So you have this very rapidly evolving technology, and the place where the spotlight is shining is shifting, and the tension is on the resources and some people got along and some people couldn't.

Hughes: Well, tell me what you found when you arrived. You were in charge of development. What was there and what needed to be changed?

Young: Well, we can talk about all of the wonderful things about Bob's character that I respect. He was very forward thinking; he would have to be to start this company in the first place at time where people were telling him that this [recombinant DNA technology] was a long way off. So he was always kind of on things earlier than everybody else, and so the very first executive he hired was a manufacturing guy. He thought, "I am going to be a fully integrated company; I need a manufacturing guy."

Hughes: But there was nothing to manufacture.

Young: Right. That didn't bother Bob. He just wanted one. The first executive he hired was a guy named Brian Sheehan, I think from Squibb, who was kind of a fermentation-manufacturing guy. That was very innovative and very early. But Brian was probably the wrong guy for the company. Bob and he didn't see eye to

eye. Actually, there was a phase in the ‘70s early on as the company started to grow, way before I got there, where Brian actually tried to wrest the company away from Bob, and they basically had a huge falling out.

Hughes: Oh, really?

Young: Yes, and Bob fired him. He wanted to become CEO. He was, I think, trying to recruit the board on his side. He later took his marbles and went and started his own company right down the road from Genentech, and that company was not successful.

Hughes: The first defector. He used some of Genentech’s technology?

Young: To be honest, I can’t remember what it was based on, but it was probably very similar to what Genentech was trying to do. So, that kind of soured Bob on manufacturing people a little bit. He really wanted me. He met me at Lilly and thought I was great. When I was recruited, I said, “Well Bob, why don’t you give me a VP title and I will come for sure.” “Well, you know, I am not quite sure, the last guy wasn’t—” I overcame that very quickly, but he was a little apprehensive because of [the experience with Sheehan].

So my first job was manufacturing and process sciences, and there was virtually nothing there. There was a handful of people who worked for Brian. There was a little pilot plant that actually had been built in the original building, Building 1, that didn’t work. It was equipment that was actually bought from Lilly. I remember when Genentech bought it from us, being very happy because we could never get it to work either [laughter]. Genentech said, “Here, see if you can make something out of that.” They were building a pilot plant also in the same building but farther down in the building. I said, “This is not going to be enough” They had an animal facility in one part of it, and they had parenteral manufacturing, and I said, “You can’t put these things together. This isn’t going to work. Let’s change what we are doing here.” You have a lot of influence, because I think they are glad that somebody who really knows how it needs to be done is there.

Hughes: Well, what had Sheehan been doing?

Young: He had not been doing much. He could get very little to actually work. He had not built much of a science group. He mostly had been fighting with Bob. There were a few good scientists there in process development, some good operations people running the pilot plant, but it did not run very well. Really what we needed was a lot more development capability because we had processes going through.

Hughes: You said earlier that science was important in development. Was that something that you had to convince Swanson of?

Young: I think the popular opinion of operations is that it is more mechanistic. But it isn't. In biotechnology it is still true today: the science is important and, as difficult as it is, the basic research end. If you have the right brain power and know how to design the processes, you can make it work. But no amount of good operational skill is going to overcome that process. So that is more the thrust that I had and we had. So I am looking and I am saying, "Now I have got to build this up. I got some kind of a nucleus here, but I don't have the right people." And in the meantime you are also trying to advance the business. So it is not just sit back and build the organization, you have to be doing the work at the same time.

Hughes: Were you given the authority to hire the people you needed?

Young: Oh, yes. I think Bob was always very good at listening to what you needed and then making sure you had it. At that point the organization was moving to more of a development mode. So his task was he had to kind of calm the research people down who saw the spotlight now shifting. So it was more what you could do for them versus what you needed to do for the company. But Bob was very supportive.

Hughes: Were these developments revolving around growth hormone?

Young: Yes. We weren't doing any insulin, or very little insulin work. Genentech's decision was, OK, the next product we are going to take forward on our own is growth hormone. So it was basically all involved with growth hormone. The first growth hormone product, Protropin, was an intercellular growth hormone that you had to purify out of this kind of gemisch of *E.coli.* It was an *E.coli* process. Everything those days was in bacteria and that is what we had to do. You would express the protein. You'd have a glob of it there. You'd have to dissolve and purify it out of the cell, purify the cellular components away. The very first thing I got into there was, they were getting ready to go to the clinic [clinical trials], and so we purified growth hormone. Protropin, because of the intricacies of the way *E.coli* express proteins, there was an extra amino acid on the end of it. So there was an extra methionine which is kind of a start signal for bacteria, and we didn't know how to cleave that off. We actually had it on growth hormone. So Genentech's original human growth hormone was actually one amino acid extra with this one.

Hughes: Did that worry you?

Young: Yes. It worried us, but we didn't know a lot about antibody responses or reactions in those days. So we had a phase 1 drug trial, and we hired as head of clinical this guy Bob Swift. He was the first head, and we were getting ready to go to the clinic, and we said, "Okay, the first safety study we are going to do in Genentech volunteers." So this had to be '81 or '82.

Hughes: And was that acceptable protocol?

Young: You would never do that again. But then we rounded up Genentech volunteers, and I was an alternate. I was qualified, but I said, "Well, if you don't need me, I'd just as soon not do this." It was a safety study. The idea was to get injections of growth hormone. It was a blinded study. In those days, the pituitary-derived growth hormone was still on the market, and then we had Protropin. We had, I don't know, a dozen Genentech volunteers to be split between these two drugs to do a dose response and do the phase 1 study.

Hughes: Which was just for toxicity?

Young: Yes.

Hughes: Because you can't measure growth.

Young: No. We were looking for safety and probably the pharmacologic half-life and that kind of thing. We were basically doing that in healthy adult male volunteers. The analytical techniques at the time were fairly crude by today's standards, but then they were the best that protein chemists had. Protein chemistry, you are doing research, you are working at something, you are thinking it is pure if it is like 90 percent pure. The coomassie-stained gels and the way at looking at purifying material then were pretty crude, but it looked 100 percent pure to us. We thought this was pretty good stuff. We had done a lot of work to purify it with all the new technology that was available then. But of course nobody had every purified a human protein from bacteria before. So we inject all these patients and—

Hughes: But you had with insulin.

Young: Well, insulin was Lilly's, right?

Hughes: Oh, yes.

Young: Actually there are some intricacies in growth hormone that weren't true in insulin. Insulin, if you remember, the purification was very extensive because you were taking each chain, purifying it, cleaving it, purifying it again, putting it together, purifying it again. So it went through a lot of purification.

Hughes: Three steps at least

Young: Yes, so probably that saved insulin. And then you crystallize it. Where growth hormone you can't really crystallize. So you have a lot of purification steps that had to be done because of the way you process it that probably didn't have to be in the growth hormone process. But we thought the growth hormone was pure. So we inject all these volunteers, and the control was the pituitary growth

hormone. So half of them came down with these big welts and they had fevers, and we are saying, "Great. The pituitary stuff is really bad. Our stuff is really pure." That went on a couple more times, and we said, "You know, maybe we should break the blind and look at this before we get too much farther." Well it was the Protropin that was giving the rash.

Hughes: And was it the methionine?

Young: It wasn't the methionine. We did a lot of work to prove down the road that that wasn't the case. It was *E.coli* contaminants that we couldn't detect most likely that were there. That led to a huge effort on the part of Genentech to develop better technology for looking at pyrogenicity. You do the rabbit pyrogen tests, but it doesn't show up in rabbits because growth hormone suppresses the pyrogen response in rabbits, where it doesn't it humans. Of course we didn't know all that at the time we were doing it. So you didn't see it in those tests but you did in humans. We also didn't have the right analytical technology so we had to develop a lot of gel-based technology to tag the *E. coli* proteins to be able to detect them so we could purify them.

Hughes: Were your development people doing that?

Young: No, by then development people had been hired in assay development or in process sciences to work together. To make a long story short, developing those processes for the early proteins was much before analytical technology so we could see what we were doing. And if you can detect something, then you can figure out how to get rid of it. But that all had to be developed at the same time. They were some of the best scientists that you could find to do that stuff in biochemistry and in analytical technology and in process development. And then eventually we figured out how to purify it well enough. Then a successor generation, a process scientist Jim Swartz, figured out how to secrete growth hormone into the periplasm of the *E.coli* and also cleave off the methionine, so now we had human growth hormone. That became a second generation product. Because you were getting it quickly away from all the intracellular components of *E.coli*, the purification was much easier. Of course we know a lot about that. Neutropin was developed later. But there was so much prejudice against Protropin. The FDA had this theory that it was in the methionine, and we had to do a huge amount of work to prove that that really wasn't the fault.

Hughes: How was Eli Lilly entering into this story?

Young: They had a parallel project of their own, developing human growth hormone. Later, the two companies got into a battle over the appropriation of Genentech technology in the human growth hormone [project at Lilly]. And that ultimately got settled. When I was there [at Lilly] working on insulin, we were [also] working on growth hormone.

[End Tape 1 Side B] ##
[Begin Tape 2 Side A]

Young: I worked with a subsequent license to Monsanto, and that was also in the early eighties. In fact I worked a lot on that project. The idea was to use growth hormone in dairy cattle to increase milk production. Monsanto actually sells now a bovine growth hormone. Of course there was a lot of controversy over that.

Hughes: Cost-cutting measures had to be applied? You said earlier that when you are dealing with animal products—

Young: Well, in Genentech's early days, we thought that biotechnology could solve any problem. So we said, "Look we are going to spread a very wide net." We had an agricultural division, and we had an industrial group. Even in research we had an industrial biocatalysis group working on use of biotechnology to do industrial products. And then we had the human health stuff. Oh, and the animal health. We had a joint venture with Hewlett Packard in instrument development. We had a wide map. It dawned on us after a few years, you know, this human health stuff is pretty hard, and we should probably be focusing on that. In the industrial and animal side, it is not like you are curing someone of cancer. There is an economic value—the animal is worth so much. There are economic solutions that you have to fight against, and maybe this is not the place we ought to be. Maybe we should really concentrate on curing disease and be on that side. About the mid-eighties or so we started moving in different directions on all of those functions. So we ended up forming a company called Genencor which still exists. Incidentally, they are now getting into human health. That was a joint venture between Genentech and Corning to have an outlet for our industrial ideas and projects, and that turned out to be pretty successful.

Hughes: Where was the board figuring in this? I think it was [David] Packard, saying—there is some really nice quote which I can't quite remember.

Young: Young companies die of indigestion, not starvation.

Hughes: Yes.

Young: Yes, he was great. He would come out with his one-liners, and we would all say, "Oh, Mr. Packard, you are right on." I think the board was influencing the thinking about what to do with all of these other ideas. And the company, to its credit, Swanson and the management, which I was a part of, we started peeling those [programs] back and finding different ways to focus. That all happened in the eighties. We started Genencor, so we got that out of Genentech. They basically were designing enzymes. They have an enzyme that is in Tide which was genetically engineered. Ultimately, Genentech and Corning both sold their interest in Genencor to new owners. The animal health stuff—we licensed

bovine growth hormone to Monsanto, and then we basically got out of animal health.

Hughes: Who do was mainly responsible for that refocusing?

Young: Well, I think it was Bob, the board, the management group. I don't know that there was a single person. I think it just sort of dawned on us at the same time that this was too much. We had to really focus here. [Human] health was hard enough. In fact, even in health you have to focus.

Hughes: Well, it is not a given that a company comes to that conclusion.

Young: No, it is not.

Hughes: Look at what Cetus was doing, and Amgen, too.

Young: Oh yes. Amgen had dye for blue jeans and all kinds of stuff in their portfolio. I think as Genentech hired more of us from the drug industry, that also influenced how we were thinking about things. Because we [from industry] were saying, "Hey, there is an economic equation here; biotechnology is going to take a while to develop where it can meet that economic test, where in health there isn't. You cure the disease or not." So I think that was part of it. But it was a gradual realization on everyone's part that we needed to do that. Kirk [Raab] came in eighty-five. He obviously was not interested in all of these other tangible things and helped also to influence the focus. So I don't know that it was any one person. I think that it was part of a gradual realization that this was the right course for the company. That is what happened.

Hughes: You were going to say something about Swanson's models for what he was trying to do with Genentech. You mentioned high tech.

Young: The culture?

Hughes: I guess it was just the culture.

Young: Bob probably doesn't get a lot of credit for this, but I will give it to him. He set a lot of the cultural values that biotech uses today, and when you look at them in more detail, they all have a reason, a purpose, an outcome. I think he freely borrowed from wherever he could borrow them. So some of them are borrowed from the high tech industry, which had in California a tradition of being more informal, etc. But Bob really glommed onto those. I remember hearing Jim Treibig, who founded Tandem Computers, also out of Kleiner-Perkins, speak once where Bob brought him in. He was talking about the culture he had at Tandem, and it was all the same stuff we where doing. I know from that that Bob and Jim were friends and colleagues, and I know that Bob borrowed this. The additional twist in the culture thing is that we had very, very strong science

emphasis and almost an academic science atmosphere. I think [Herbert W.] Boyer was also part of this. The things I remember that in my own company [Virologic] now I still strive to emphasize and want people to do: first is that all good things of biotechnology come out of good science. The way to get that good science is to allow scientists the freedom to have their own careers develop and flourish. So, therefore, you want them to publish. You want them to go to meetings. You want them to feel that they have a status of being peers to other scientists in academia or other industries. Now at that point in time that [culture] was very anti-drug company. Drug company scientists were not allowed to publish unless it was work that no one was interested in. They didn't go to meetings. They basically followed the path of keeping everything a secret.

Hughes: That is what you had experienced at Lilly?

Young: That is what I had experienced at Lilly, and the scientists at Lilly weren't that great. Now I come to a place [Genentech] where they are great, and they are young, and they are aggressive. I think a lot of it was the influence of Herb and Bob in setting that tone right. Secondly, it was a tradition in the drug companies, and in academia too for that matter, that young scientists do some work, but the department head is the one on the paper, he is the lead author. The scientist may be in there somewhere. And Bob and Herb said, "No, we are not doing it that way. If you do the work, you'll be the lead author, and you get the credit." To their credit, they didn't stick their own names on as author. He [Swanson] understood what it meant to develop a scientific career and what that could bring to the company. That was pretty far-thinking in those days. First of all, it was a little pragmatic because it allows you to recruit scientists, but there were many untold benefits because Genentech to this day has an incredibly strong scientific reputation. It is cited in more papers—You ask people what the strength of the company is, and that is it, or one of the strengths. That was all, in my mind, from setting that early culture and making it stick and not just giving it lip service but really doing it.

Hughes: Yes. But that could have been intimidating to you, too, that the weight of the company was on the research, not on what came after.

Young: Well no, that is why I corrected [my statement] that [good science] was the only value; good science and good everything else also came. I think Genentech was also recognized as the leading manufacturer of biotech products in the world, with the best technology. But that came from not only having the science and process sciences but also in the operational excellence.

Hughes: Would it be fair to say that the shift really begin to have momentum when you arrived?

Young: On the operation side, sure, because there was no—but I also was a timely hire because that was when they were really getting into that stuff. We recruited lots of people from the industry who had the background to make that work.

Hughes: Was there any friction with the scientists who up until then had been the top dogs?

Young: Yes, sure. There were always issues of pecking order and who was getting the attention, and the fact that development scientists maybe look a little different, work a little differently than they do in research. The science is important but the way it is expressed may be different. So development science probably doesn't publish as much as a research scientist, or his expression of creativity and progress probably comes more from internal reports or patents or things of that sort. More of their work is trade secret; there aren't the forums to publish; you can't get a process published in *Nature* like you can on the research side. One of the early-on things that we spent a lot of time doing, and a lot of this catalyzed from when Dave Martin came in the early eighties, was developing scientific career ladders. [We made] sure that we called them the same thing, and the quality was a high, that they were able to accommodate different work and the needs of different work in the ladders we established in the science center.

Hughes: How would Dave have known how to do that?

Young: He didn't. He had to have my help to do it. But, you know, we did a lot of that together. It wasn't just the manufacturing development or process development people we were hiring. We were also hiring people in pharmacology and clinical research and other areas of the company downstream of research. Yes, of course it is chaotic when you bring lots of people from different backgrounds with different perspectives into an organization and try to have one crucible to make the company out of it. They all have a different background and different perceptions that they have to accommodate to each other.

Hughes: Is that one reason that Genentech culture looms so large, as an attempt to blend all of these heterogeneous elements?

Young: Yes, well, I think it was certainly done in the crucible of having all that come together. But other aspects of what Bob established were also important in making that accommodation go faster. Another thing he emphasized was a very informal environment—unlike the drug companies. I will always remember my experience at Lilly fondly but also with some of the things that they didn't do so well. I was a young engineer, I am a developing manager there, I have a lot of responsibility. You never, ever saw the senior management around the company. They lived on the top floor in the office building. They have their own elevator; they have their own cafeteria; they have their own parking. You went to see them; they never went out into the organization. There was no real touch from them in the company, and if you had an issue you would go up there.

Bob didn't want that. He emphasized informality so people have an easy time interacting. We made sure that executives offices were sprinkled around their functions wherever they were working but not all kind of together. I am sure that that has all changed now. Everybody had the same size office, by and large. There was no committee which decided, based on your level, how many potted plants you had. Everybody had the same, and you had it kind of based on need, not on your status in the company. There was no reserve parking. We wouldn't have lunch at all when I first got there. But there was no separate dining. We actually towed Swanson's car one time. [What's the rest of this story?] He said, "Look, you get here at six o'clock in the morning, and you deserve the best parking place." And then we had the Friday ho-ho's, the biz—we call them the biz here; Genentech calls them ho-ho's. A lot of biotech companies copy that. But the purpose of that was people working all week, they are working in their areas, they get together to interchanged ideas, they get to see each other, and they interact. And in the early days, that is exactly what it was. Management always went so you could talk to people. Lots of times you would be introducing people who had just gotten to Genentech to people they should know. We talked about projects that they should know about. So it was an incredibly productive the way they do it. Now, as the companies get bigger, those ho-ho's are less practical and other things happen. But all of those things you see still in people. To this day, I won't let people in this company [Virologic] build an office that is bigger than our standard, which is this size. It is the kind of thing which puts barriers between people, and you don't want barriers. In a technology organization, the guy in the lab is the one with the knowledge, so you want to make sure that the people are free to interact. And Bob was very strong at that.

Hughes: Did he have models for all of those elements?

Young: I think a lot of the office informality, Friday parties, came from high tech. But the emphasis on science integration and came more from academic research. It's a blend of those— kind of the best things in those. Swanson was a great man [laughs].

Hughes: Yes, I am getting that from you.

Young: Not perfect, but great.

Hughes: What about Tom Perkins? How does he figure in this early story?

Young: Well, Tom was chairman of the board and was the obvious sponsor of Bob in the early days. I don't know if Bob talked about this: people don't know that I think Tom had actually fired Bob from Kleiner-Perkins, and Bob was out kind of on his own. He was actually on welfare, and he was trying to figure out how to start a company. The story of him going around is true, where he went around to try to get Cetus people interested in starting a biotech company and then eventually ran into Boyer and got one started, and then Tom provided the initial funding.

Hughes: Well, it brings up something you said earlier where you pointed to Swanson as far thinking. Putting Swanson in the context of starting out on this venture, how much of it was foresighted and how much of it was, here is a technology that I have got to glom onto, and I have got to have something to do.

Young: Oh, no, I don't think it was that. There were a lot of alternatives. He could have done things with high tech which was hot then. You had PC [personal computer] companies starting; there was a lot going on out here. I think that he really believed that this was a technology that could make people's lives better, and make drugs and make a successful company.

Hughes: But what about the timeline? A lot of people around the mid-seventies were saying, "Yes, this is a great technology but it is going to take a long time before we have products."

Young: Yes, that is what they were saying. And that is what everybody but Boyer said.

Hughes: Was it Boyer telling Swanson, "I don't think the timeline is so long."?

Young: I don't think he knew either. He said, "Hey, this might be kind of fun." Herb up to that time had spent his whole career working on a restriction enzyme called EcoR1, and he was very narrowly focused. Herb is kind of an optimistic guy who probably thought, why not try it? And I am sure that if you haven't talked to him already—

Hughes: Oh, I have talked to him.

Young: He will talk about those early days better than I. But the lore that we were told after we got there was, "No, he just wanted to take a flyer. He thought that was good. Maybe I could borrow my $500 from you, Bob, and start the company. This might be kind of fun." I heard Herb say many times later: if he knew when he started that it was going to be as hard as it turned out to be, he probably wouldn't have done it. But he didn't know, so the naivete was part of the reason he was receptive.

Hughes: Also, he wasn't taking that much of a risk.

Young: Right.

Hughes: He had his position at UCSF.

Young: Well, I think he was as it turned out. His risk was really academic reputation risk. Because he was one of the first scientists, really good scientist to go to biotechnology. Now, he didn't actually go there, but he was a founder.

Hughes: He was still seen as a founder

Young: He was still criticized a lot by his fellow academics who later went and started their own companies. But at that point that was the first time that anybody had done that. He did take a lot of heat and maybe didn't get the Nobel Prize because of that—who knows. But that was kind of a bad thing to do in those days. It was not pure. You are going to work with a company, you are going to try to make money, that is not what we [academics] do. So it was a new model.

Hughes: I wonder how much he thought that through at the very beginning. Could he have anticipated how much criticism he would get? Because you are very right, he was really the center of the storm.

Young: Oh, yes. And later I think he was actually interviewed by the Nobel committee, and they didn't elect to award him a prize. He should get the Nobel Prize—he and Stan Cohen. They put the two pieces of this technology together so this can be done, and we can actually make something that no one knows how to make. I don't how much more fundamental you get than this. And starting a huge industry. I can't understand why the Nobel committee doesn't do that and doesn't like that. But that is their problem.

But at any rate, I think he did take a lot of personal risks. Herb never actually worked in the company. He stayed at UCSF until he retired. I think he did one sabbatical with us for the summer, but by in large stayed on the board, stayed there. A lot of the early work was done in his lab [at UCSF], but he never actually worked day to day at the company.

Hughes: And would you say that he was a rare presence at Genentech, very unlike Swanson who at least in the early days was wandering around the corridors?

Young: Yes, Herb wasn't there. At least in my recollection, he wasn't there that much. The way I remember him from those days and the way he is today, because we are personal friends, he is exactly the same, as far as I am concerned. Same gentle guy, same thoughtful approach to things. All that has happened, I don't think has changed the basic Herb Boyer. He is also very lucky [laughs].

Hughes: Oh, oh, he is very lucky [laughs].

Young: But luck is a part of this business, too.

Hughes: Oh, of course it is. What position were you in when this litigation did come forward?

Young: With Lilly?

Hughes: Yes. You had been an insider at Lilly, working on this project and then an insider at Genentech.

Young: You know, I can't honestly remember. I think there were a couple of rounds of [litigation], too.

Hughes: Yes, there were.

Young: I think Lilly did, and then UC sued Lilly and Genentech.

Hughes: Yes, a very complicated case.

Young: I remember giving a bunch of depositions. I don't remember much of the detail at this point. I think that the thing to emphasis here is Genentech realized—Tom Kiley was a big part of that, maybe Bob also—that patents were going to play a major role. This was innovative stuff. We needed to be aggressive, and so Genentech has been aggressive at filing and enforcing its patents and settling them when they needed to. I think that started with the first microorganism patent back in those days. We didn't even know back in those days whether these sorts of patents were even going to be issued by the patent office, so thank goodness that they did. Now the intellectual property situation in biotechnology probably needs another round of sorting out because there are so many patents, and they all interact and intersect, and almost everything you do, you are running into other people's IPs. That may be counterproductive to innovation rather than promoting it. So maybe another look at this is actually required. People should still get protection for innovative ideas, but now people patent stuff without even the data to support them. But that is a whole other story.

But then they thought that [IP] is really important to emphasize—got some early possessions, lost some, won some. But that was always important. We had to put some processes in place to make sure this happened in the early eighties, because it was pretty freewheeling science. But we did absolutely everything we could to make sure that before people spoke, the patent got filed, and there were lots of times where the patent people were writing stuff up in the middle of the night before the paper went in or whatever.

Hughes: And that was true in Research and Development as well?

Young: Yes, but most of the innovative, early patents were around cloning something, so there was no serious restriction. But yes, it was true everywhere.

Hughes: The emphasis around patenting was much stronger when you moved to Genentech, is that not true? What was the status of IP at Lilly?

Young: Oh no, they were very strong on it also. But I think the difference was that Lilly was *so* strong on its patenting emphasis that they wouldn't let their scientists talk about anything. So they kept everything a secret. If they didn't patent it, it was trade secret. So it left their scientists with no ability to talk about anything meaningful. That was more the tradition of the drug industry. On Genentech's

side, they said, “Let’s do both. Let’s get our scientists to publish and speak and get our data out there, but let’s make sure we protect it before we do this. So it put more of pressure on the patent attorneys to write the stuff up and get it thought through and get it filed than taking it out on the scientists by just saying, “No, we are not kidding, we are not going to let you talk about this.”

Hughes: And trade secrecy was less of an issue?

Young: Yes. We knew we had trade secrets but we worried about them a little bit less. We figured, well we are going to out-innovate everybody anyway. We have better people. We don’t need to deal with it, but we did keep some things in-house.

Hughes: Do you think we have said enough about insulin and growth hormone?

Young: Probably, yes. Growth hormone were that later we—it is like anything, it is a product that continues to be the subject of innovation. So later Genentech developed technology to develop a liquid form of growth hormone, which doesn’t sound like much but was very difficult to do for a protein. Having a lyopholized or freeze-dried form is a much more stable form for any protein, and to make a liquid form that will sit on the shelf for eighteen months and be stable, you had to learn a lot about what all the degradation profiles and even more analytical technology. That took several years to actually develop. So they did finally develop that, and that allows you to put it in a needle injector and do other things. They also developed some sustained-release forms which allow you to have one shot at once—one every day or whenever. There is continual innovation and evolution of the technology even today. We can talk at the next session about the building of the process sciences and the various stages we went though there and what we learned how to do. Probably one of the last things we learned how to do is the formulation part of it really well, and really started to getting to advance formulations. That took a whole different set of technology.

Hughes: We are about out of time, but let me just ask one more question. One of the things that I remember Swanson emphasizing when we were talking is his concept of a FIPCO, fully integrated pharmaceutical company. How early were you aware that he had that idea?

Young: For me, it was part of the coming on to work.

Hughes: So really early.

Young: Oh, yes. He wanted to do that very early, but he wanted to do everything else too. In my mind, it was always part of the excitement was him wanting to build a company that could do it all. And again, this is part of Bob’s early—just two other really quick pieces about him thinking ahead. We hired a sales

representative because we thought we were going to get approval for growth hormone, and it got delayed a couple of years. But we hired a sale representative like a year before even the earliest date we could approval. So he was already getting those sales organization going. He was also in the early eighties one of the first, probably the first biotech executive, to visit Japan. His view was, hey, Japan is going to be really important. We need to partner with them. There is a whole world over there. He was making trips to Japan in the eighties and also in the late seventies to the extent that the Tokyo papers would feature him in the headlines, "Swanson from Genentech Here This Week."

Hughes: Oh, really! [laughs]

Young: Yes! He was absolutely way ahead. Of course, we were nowhere near ready to produce; we could barely do it here.

Hughes: Was that somewhat because of Japanese consumer patterns? Japan had a well developed fermentation industry.

Young: That was part of his idea, sure. And he made me visit several Japanese companies, big fermenters, and yes I think that was part of it. But he had this vision that Japanese companies can play a major role. How did he put it? "Well, they don't know how to innovate, but they know how to make it perfect." So it was like we need them for the optimization. He was good at really thinking ahead and getting into some of these things. Sometimes it was too early for the company, frankly. It got us spending time on things where maybe we would have been better off getting our own act together. But overall he was putting himself out there.

Hughes: Were you aware throughout that growth hormone project that that was the test case for this FIPCO idea?

Young: Yes, of course. Oh, yes.

[End Tape 2 Side A] ##
[Begin Tape 2 Side B]

Young: It was really a question of let's make a drug that everybody already knows how to use, that we already know is efficacious, and all we are doing is making a human copy of that drug. In the case of insulin we are filling the need for supply, a molecule that is more like the human. In the case of growth hormone, it is the same issue. We didn't know it at the time when we were working on the growth hormone that there was going to be episodes of Creuzfeld-Jacob disease, that the pituitary product would be taken off the market. We thought that this was kind of a demonstration project, and I know the early market forecast for growth hormone for Genentech was a few million dollars a years. That's all we thought we would sell. So we thought the one salesman could do it. [laughs]

Hughes: I thought I had heard that initially Swanson said that he didn't want anything to do with growth hormone.

Young: Yes, he may have. They thought the market was too small. So what happened was, as we developed it, they had cases of Creuzfeld-Jacob disease so they yanked all of the pituitary hormone off the market and now we are sitting here with the only application for human growth hormone, so the FDA approved it. If it hadn't been for that, we probably would still be arguing about methionine on the molecule. But that gave them the motivation. The risk profile was now reversed because they had put something out for these kids who were going to be forever short and growth hormone deficient. So that really tilted the whole thing for us.

A lot of the stories about our interactions with people at FDA with the human growth hormone and the difficulties that we had, we can do that at the next session. Just to set this up, at that time we are building our process development and manufacturing capabilities. We are now starting to think about what new innovative products we want to develop. One story that I think is particularly interesting is the whole story around the development of tPA [tissue plasminogen activator] and how that got discovered, and what we did there, and what challenges that brought. Because that project really, I think, leap frogged the company into the big time. The product itself didn't do as well as we had hoped, but the technology developed to make tPA you can find now in every monoclonal antibody that Genentech produces, in Herceptin, in Rituxan, in Pulmozyme for cystic fibrosis, in Avastin for cancer. It is basically the foundation technology for all of Genentech's work and many other companies' now in all these antibody products. We had no idea how to make tPA. We had no technology for mammalian cell culturing. We didn't know what the issues were, and we had to make a huge conversion from an *E.coli* company to a mammalian cell company, and in a very short time. So that in itself was a pretty interesting story, and someday somebody is going to write a book about it. Maybe it will be Kiley because he knows how to do these things.

Hughes: [laughs] Well, good. Let's stop there and we will continue.

[End Tape 2 Side B] ##

[Interview #2: June 23, 2004]
[Begin Tape 3 Side A] ##

Hughes: Mr. Young, last time we covered insulin and growth hormone, and I think this time we should talk about tPA, not only from the development standpoint, but also how it related to the Roche acquisition.

Young: Yes, that would be good. The development of all the technology surrounding making tPA and making enough for the market, I always think of it as kind of a project that was similar to making penicillin during World War II, because it was a great discovery, but no one knew how to mass produce it. Or the Manhattan Project, or other things that are major efforts of science to get something that hadn't been done before done. I think the manufacture of tPA fills the bill there because tPA was the first biotechnology-derived drug made from mammalian cells. Up to that point in time, everything was done in bacteria, starting in the seventies with somatostatin and insulin and growth hormone. All of the technology around Genentech was associated with expressing proteins in bacteria, fairly simple proteins. With tPA, we ended up with kind of a different level problem. The background there was, Diane Pennica was a molecular biologist—I think she still is—at Genentech.

Hughes: Yes, she is. I talked with her.

Young: She ran into Désiré Collen in a meeting. He was a Belgian researcher who had discovered tPA and had to work very hard making it by conventional methods, either extracting it, or he would work for months and months and months to make a milligram or half a milligram, and then treat a rabbit, and then he would have to work again. They ran into each other, and Diane had the good sense to invite Désiré over to Genentech, and I think Swanson signed him up on the spot. Désiré would say, "Yes, I am talking to the pharma[ceutical] companies, but they are very slow," and Genentech was able to move a lot faster than that. So they signed him up with all the rights to tPA. Then the question was Diane cloning it, and she was successful in doing that, and then, how in the world are we going to make this stuff? TPA is a much more complicated molecule than had been made up to that point. It is glycosolated, so in other words, sugar groups are added to the molecule. We first tried expressing it in *E.coli* and worked for months and months and months but couldn't. We could get protein expressed, but it was kind of an inactive gemisch since the glycosolation was necessary for solubility and activity. Of course, the analytical methods were pretty poor in those days but we did cabbage on to a mammalian expression system that Art Levinson had worked on

for another project and decided to see if we could express tPA in CHO [Chinese Hamster Ovary] cells, which were the system that Art was working with for a hepatitis vaccine. We got expression of tPA at very low levels, and it looked like it was active, and we couldn't do anything with *E.coli*. The way I remember it, Genentech always worked to not *lose* money every quarter, and the way we did it was; we would have these benchmarks in the contracts we did with other companies on various things. And we would have to achieve the benchmark to get money that then would pay the bills for that quarter. I think the company was remarkable in that it almost always broke even or made a slight amount of money.

Hughes: Yes, that is its reputation.

Young: Yes, for all the years [except for] maybe one quarter or something. There was a lot of internal discipline to do that. I remember we had this benchmark where we had to certify for the Japanese partner for tPA, that we had a cell line capable of manufacturing tPA. It [the benchmark] was like $1,000,000 or $2,000,000 or something. We said, "Gee, we can't really get this to work in *E.coli*; we got it to work over here in this mammalian cell line. We have no idea how to make a manufacturing process out of it though. We don't have the right people. We are all *E.coli* experts. We need the million dollars, so we are going to certify the mammalian cell system and try to figure out how to do it." I think we worked for a good year after that trying to get *E.coli* to work and we never could.

In the meantime, we had this mammalian-cell expression system and had to think about all of the issues associated with trying to make a manufacturing process because nobody to that point had. People made things in mammalian cells, but they were normal cell lines, very hard to work with. This was a cell line that was immortal and continuous. There were potential safety issues; there were scale-up issues; there were all kind of things associated with trying to make a product. The first thing we thought about doing is maybe hire some people that know what they are doing here, because this is going to be hard without people who know more about cell biology and making mammalian cell products [than we do]. The conventional technology for making them was not fermentation, but it was really roller bottles, where you would grow cells on the inside of this bottle, and it would turn very slowly, at a half a rpm or rpm, and there would be medium in there, and it would kind of slosh around. That was the way a lot of people would brew cell-culture-based-products. So we had Tony Lubenecci—I am not sure where he came from exactly—but he had cell biology experience. He and I went to the UK, and we hired three Wellcome scientists and manufacturing people. At that point, Burroughs Wellcome did have people that knew how to do large-scale cell culture for animal vaccines, among other things.

Hughes: Wasn't Wellcome working on tPA?

Young: That was later. It was a different group of people. So we didn't get people who were involved in the program. I can't remember this for sure, I think they ended up licensing it from another biotech company. But anyway—

Hughes: There was a lawsuit later.

Young: There was a lawsuit and Wellcome was one of the—

Hughes: One of the litigants.

Young: Yes. But at any rate, we hired a few of these Wellcome guys. I remember sitting in a hotel in London and interviewing these people. So we got them, and so we now had a nucleus of an organization of science and some manufacturing people that knew something about cell culture. But even though we had those people, we still didn't know much about scaling this up. I remember that we made a product by roller bottle, and we had a process for purifying it, and then we started treating patients in the clinical trials. The first calculations that we did, were that the dose was one or five milligrams. So then you could sort of figure out how you could buy enough roller bottles to make that much product. That was the system. As the clinical trials work progresses—it was Elliot Grossbart who was the clinician—the dose kept going up. So did the market, thinking about how many patients we would be treating. So pretty soon we were looking at a 100, a 150 milligram dose instead of ten, and it was almost impossible to make enough product by roller bottle. You can imagine them taking off over the entire building with these roller bottles. It was sort of the Rube Goldberg approach to biotech manufacturing. We just had to keep adding more and more of these things, which you then have to handle and empty, and so there is the whole manual process of it.

Hughes: Well, isn't there a world of difference between culturing mammalian cells as opposed to *E.coli?*

Young: Oh sure, because the mammalian cells grow a lot slower; they are a lot more fragile; they need more expensive media; they need it often. In those days, we didn't know how to develop media that didn't have serum and serum components, so there were all kinds of complications. These media that were used were very poorly characterized, so you had a lot of issues around changes of lots where some of the things were really dependent on growth factors and that kind of thing, and they weren't very well controlled. So there is a lot more variability and a lot more art associated with it.

Hughes: Was big pharma using mammalian cells at all?

Young: Not much. In fact, people were a little bit concerned about safety because these cells had certain viral particles in them that hadn't been fully characterized. It was kind of a theoretical issue about, Could you contaminate these cells with a

virus, which could then not get purified out, which would end up in a product? They weren't *real* safety issues so much as theoretical safety issues that we had to prove weren't issues. Trying to prove something isn't a problem is a lot harder than proving that it is.

Hughes: And you must have had to deal with this when you came to the point of dealing with the FDA.

Young: Oh, yes. So all of that was kind of layered in those early processes. And then there was a matter of yield: How are you ever going to make enough of this product at a dose of 100-150 milligrams per patient to really economically deliver a product that is going to make the company money? While we were thinking about this dilemma and watching the dose go up from the clinical experience, it was actually Jim Swartz, who was a Ph.D. chemical engineer working in the process development group who had come from Lilly—in fact, I had known him when I was at Lilly and had helped get him to Genentech. He is now off at Stanford as a professor in the chemical engineering school. But in those days he was there in the process development group. I think I mentioned him actually in [our discussion of] growth hormone. He was one of the key people that came up with technology to secrete growth hormone into the periplasm rather than have it intracellular. Well, anyway, every five years Jim would come up with an interesting breakthrough. So he said, kind of nonchalantly, "You know, why don't we try growing these cells in a fermenter? We've got a 10,000-liter fermenter that we bought for bacterial work and don't use. We have a pilot scale. How do we know that the cells won't grow in the fermenter? Or that we can't get a cell line that is adapted to growing in suspension? Other companies grow them in suspension." So he was the one really pushing us to try the experiments to see. I think some of the cell biology people were reluctant, saying "Well, they are too fragile, I don't know if it will work." But at any rate, we did the experiment, both a small and ultimately a 10,000 liter-scale. It worked great. So we were able to culture a lot of cells. [The cells] were very happy, they grew and made tPA, and so all of a sudden we went from an almost impossible kind of Rube Goldberg situation to having to buy enough roller bottles and handle them, and all the things you have to do. We went from that situation to "Hey, we have got the makings of a real process here that ultimately will make enough of this product to deliver to the market what we need to deliver."

So we did put the product into suspension and developed a purification process together. The key scientist involved in that was Stewart Builder. He and his group developed all of the purification processes that we have used, and also had to incorporate in the purification processes steps to remove the theoretical viruses that might be in there and validate all that. So between Stew and Jim and the cell culture people, there was just a horrendous effort to get the process scaled up and make it work on a theoretical basis and make product for the clinic. We actually discovered that the product made in suspension culture was a

little different than the product made in roller bottles. We ended up having to cycle back to the clinic and readjust the dose again. They had gotten up to 150 milligrams as a dose for the roller bottle material, then we found out that the cell culture material made in suspension was actually much more potent, or it had a different clearance in vivo that we never discovered exactly why. But it was slightly different chemically and we ended up having to adjust the dose back down to 100 milligrams.

Hughes: Were there any drugs on the market that had been produced by—

Young: No. This was the first CHO continuous cell line product that anyone had ever made.

Hughes: Really?

Young: Yes. So we had all of the issues that we would normally have as a pioneer—the FDA issues, proving safety, making enough, making it consistently, making it high quality. As we were establishing the process and supplying the clinic, we had the issue of, well, how are we going to make this for the market? We have no plant to produce it. I remember going to Swanson and saying, "Hey, Bob, we are going to need to build a plant here. There is no sense developing this product without the manufacturing, because you are going to spend some hundreds of millions of dollars to develop it, and then you can't wait until you get the clinical work before you start thinking about manufacturing. You have to do all that in parallel, and we don't have a plant to do it. So we need to build one. I need $25,000,000."

Hughes: [laughs]

Young: Which I thought it was going to cost.

Hughes: How did you know how to figure that?

Young: Well, by then we knew the size fermenters we needed, and we knew the general kind of process. Nobody had ever built a plant like this before, including us. So, we had an estimate of, I think, $25,000,000, and I think that was the best estimate I had. It turned out, I think, that that was Genentech's last $25,000,000, because cash was getting down there. So we had to delay the promised research expansion, and we needed to go ahead and spend the money for the plant.

Hughes: Is this the beginning of putting all eggs in the tPA basket?

Young: The tPA basket. Yes, it was.

Hughes: *If* you were going to develop it, you didn't have much choice.

Young: Right. We went back to the board several times saying, "Hey, we have to build this plant." I remember we had David Packard on the board. He was a great guy. He was always very profound, and people obviously were very respectful. He was getting up in age by then. So we would say, "Look, we need to build this plant," and he would say, "You know, maybe it is better if we really see if we have a product before we build a plant." Well, you know, in computers or in HP's [Hewlett Packard's] business, putting a bunch of tables in a room is the plant; it is not the long lead time that we have where it takes several years to get it built, validated, FDA approved. So I didn't have much time. But you know, the board cycled back and forth. I think when Kirk Raab came in like '85, he said, "Look, this is the business that we are in [pharmaceutical production]." He became a supporter to get the money to do that.

Hughes: Did Swanson gulp at the $25,000,000?

Young: Since no one knew how to do this, there was a whole effort in the days where we were considering the plant for considering other technologies that wouldn't require capital investment. I think a lot of people in those days, this was the mid-eighties, were thinking about how to make cell culture products, so there were a number of more bizarre efforts to do this that people were engaged in—not just suspension culture. There was a company in Vermont that had a kind of continuous fermentation system. There was a company in Minneapolis that had another bioreactor kind of system that they had developed for small bioreactors. The most bizarre was a guy up in the city here who had the idea that he would hook up the lymph system of the cow to circle into a fermenter to provide the growth nutrients. There were actually companies started on all those ideas. And of course, since we were reluctant to spend this much money, and people were very helpful in looking at alternate technology, we were running around evaluating all of these things. All of these companies failed, basically; none of these things worked. If we had picked one of them, we probably would have, too. But luckily we had good sense that these were all early. But a lot of them became public companies and were hot for a while. I think the cow guys were out in Hayward; it was called BioReliance, or something like that. There was another Monsanto spin-off that had special fermenters; they had bioreactors that they had designed. So anyway, there were a whole set of these [companies] that we evaluated in those days. As you can imagine, there was also a fair amount of—wouldn't call it controversy, but there were people taking various positions supporting these various technologies. I think what was driving most of it was to not have to spend the $25,000,000.

Hughes: Right [laughs].

Young: To be able to partner with somebody. "Surely somebody besides us knows how to do this!" So we dutifully evaluated all this and ended up building our own plant, which wasn't necessarily an easy thing to do, since it was also new technology. We were a little company then and had a few hundred people. Now

we were managing a $25,000,000 project, which grew to $45,000,000 or $50,000,000 by the time we were done, to add on to the side of the manufacturing building where we made the tPA. That was the project. Since we were constrained by capital, we ended up building what was a very crowded, cramped facility with lots and lots of pipes in it. We ultimately got it to work, but it was probably not the best project we have ever done, because we were in a hurry. Whenever you combine an aggressive schedule with new technology, and you are trying to do it in a new building where you are just starting, then you have got the recipe for delays and cost overruns. So we went through quite a few cost overruns and things that we had to go back and fix later. But ultimately we got it done.

Hughes: And were those primarily your headaches?

Young: Yes. Solely my headaches.

Hughes: Getting that plant up and running was your baby.

Young: Well, I had the process development group, and all the process development scientists, and the manufacturing people.

Hughes: The way you tell it, or the way I receive it, is that Genentech's very future was dependent upon the success of tPA. If you had diverted funds *away* from other research projects into tPA, and tPA failed, where would the company be?

Young: Well, the company would be in terrible shape. On the other side of it, we had a lot of confidence in tPA as a product, and the sales forecast that the marketing people were developing was instant billion-dollar product. I mean, they were *incredibly* aggressive. I think that there were a couple things we overlooked, which I will get into in a second. But it is easy to look at the number of heart attacks and the number of those that would get treated and come up with some pretty big numbers. I think it was kind of an unsophisticated look at what was going to happen in the market place. We didn't really underestimate the issues of making the product, because I think we knew that we had a tough challenge, but we *grossly* overestimated the market for the product. So we were visibly expanding the plant before we even had it built, and we were working on new processes for tPA, thinking that we were going to have to continue to increase productivity, etc.

We had another great scientist, Jennie Mather, who now has her company over here at Raven, who we also hired as a cell biologist in the mid-eighties time period and gave her the job of figuring out what the cell needed in order to—She did all the media development—what are the right media components, let's get rid of the components that were harder to characterize and control. Insulin. It was one the things we had to give the mammalian cells to keep them growing. So she actually cloned the insulin gene into the cell so it would make its own.

There were a lot of innovative things that we did in those days, and I guess the thing that I remember about them is that even though a lot of them never got adopted in tPA, they were the basis of most of the products that Genentech is now making that came along later. The next one was Pulmozyme, which was also a mammalian cell product. But all the productivity enhancement things that we learned how to do in tPA got immediately applied to Pulmozyme. They got applied to Herceptin. They got applied to Rituxan. They got applied to all of the mammalian cell products, which were basically everything—the antibodies that came along later. So all that technology in the plants eventually got used. Then, of course, with the tPA plant, we got delayed in [FDA] approval, so we thought we were going to be sitting there with this plant with nothing to produce. The plant was obviously bigger than what we needed for the market that ultimately developed, but all of that capacity eventually got used for other products, and then the technology and everything else. So really, the urgent nature of the project and all the things that drove it are things that Genentech is still using, and that became really the basis of the whole company from that point on.

Hughes: Were the media, et cetera, that had been developed patentable?

Young: A lot were. Some were patented. Some were kept as trade secrets. But it started a way of thinking and a fairly aggressive program in process improvement that I think Genentech still follows and makes their technology more productive than probably anyone else's. Since leaving Genentech, I have gotten on the board of a couple of other mid-size biotech companies, even some that were competitors of Genentech in those days. What you see is that their process technology is not nearly as developed as Genentech's. So they are much less able to compete and Genentech still has the best all around know-how.

Hughes: And would you say that that is at least some of the explanation for Genentech's recent productivity?

Young: Sure.

Hughes: It just seems, one after another, the drugs come out.

Young: Well, it was partly that. It was also partly—we haven't got into this—but it was also the result of the Roche deal, which we could get into discussing in a second—at least my perspective of it. But particularly 1995, when we had a change in CEO, with Kirk [Raab] leaving for Art [Levinson], and the decisions that were made there. Having all the process technology and manufacturing helped to accelerate a lot of products. But it was really the decision in '95 to spend much more on R&D in the next two or three years that is what you see coming out of the pipeline now. And that is strictly a result of being protected by Roche's put-and-call option of the '95, '96, '97 timeframe.

Hughes: Well, I really want to hear about that whole Roche deal, but let's finish with streptokinase.

Young: Or tPA.

Hughes: I mean tPA. [laughs]

Young: Streptokinase was the other stuff. [laughs]

Hughes: I know it! And that was going to be my question. I am wondering how much, if at all, that overestimate of the market for tPA was because streptokinase was not counted into the picture.

Young: I think that wasn't the major factor. I think the major issue was really— in my mind, probably two or three factors. The most significant factor was the side effects of tPA. So if you have a drug that you can give when somebody has a heart attack or when you think they have a heart attack, and it is benign other than dissolving the clot, then I think we probably would have sold the billion-dollars-worth of tPA. By the way, the pricing on tPA and everything else was pretty innovative. It was the highest price— There was a lot of criticism of Genentech when it set the price at $1,000 or—

Hughes: No, it was more than that.

Young: $2,000 or—

Hughes: It was $2,200.

Young: $2,200, yes. How can you charge that if streptokinase is only 100 bucks? But the issue was really one more of safety where there were more strokes as a result of getting tPA than—So you had a good risk for reward balance. But physicians I think—If you have one in a hundred patients that has a stroke and then dies or is debilitated completely, that sticks in your mind. I think cardiologists were less aggressive about giving [tPA] to everyone who just might have a heart attack, and made sure that they did before they administered it. The result of that was the penetration in utility was much less than we thought. Yes, streptokinase was there, too, and a lot of people used it. Urokinase was out there, also as a thrombolytic agent. But I think the major factor was the side effects. You could argue with cardiologists about statistics and about, well, that's a very low rate. You already have a half of a percent or 0.05 percent [for streptokinase]; this [tPA] is only 0.1 percent. But I think if you have one, the cardiologists didn't like it, and you know, strokes are debilitating; you get people living that are going to be paralyzed, or partially paralyzed, the rest of their life. I think that people were just much more reluctant to use it than we thought. Probably the third factor was angioplasty was beginning to be used a lot more. The side effects from that were perceived to be a lot less, and institutions where you had a

very experienced cath[eter] team and you get the patient to the cath lab quickly, that became a better alternative. So I think even now tPA is used a lot more in areas where there is no organized or effective cath lab. In bigger institutions, they just automatically stick a catheter in the patient. I think those were the factors. But we just didn't think about the effect on the cardiologists of the side effects, and also how you get these guys to change what they are doing and how hard that might be. I think we ended up with probably fives times overestimate of what the market would be, which I think basically was the main thing that put us in the clutches of Roche after that. Because not only did we mis-estimate the market, but we were acting during the period prior to approval as if it was going to a billion-dollar product, in the rate of hiring and building the companies up to the point where we went from 400 to 700. We had a lot of people, obviously we were spending the capital. We were getting ready for the next increment of capacity. We were hiring people in all parts of the organization. I think that if you build a cost structure up that it was difficult to sustain $250,000,000, which I think is the most that it had ever been in any one year. So, that was really the issue.

[End Tape 3 Side A] ##
[Begin Tape 3 side B]

Young: And then we also had streptokinase and GUSTO [Global Utilization of Streptokinase and tPA in Occluded Coronary Arteries] and the need to prove that tPA was better. That was more justifying its price than increasing market share.

Hughes: Yeah. How was the price determined? Are there some principles about how drugs are priced?

Young: Well, yes. I think in drugs you try to price based on the value you are delivering. It is almost never based on the cost of the product. It is usually based on what value you are trying to deliver, and of course most of the cost of developing the drug is in the development—the clinical work and all the science that you have to do to get there. Then it is also in all the [drug] failures that never make it to the market. So, you do surveys, and you ask physicians and payers what they are willing to pay, and you try to see how much elasticity there is. You look at competitors' products and what their pricing is, and what advantage you think you have. But it is largely an art as opposed to a science.

Hughes: And I would think you also the internal context. In Genentech's case, here was a drug that the company was either going to live or die on to a certain degree.

Young: Oh, yes.

Hughes: So you had to get a certain return, did you not?

Young: Oh, yes. The pricing policies of most drug companies tend to be quite aggressive these days, and they were then. But I think it was largely judgement. You did these surveys, and you see at what point people start gagging, and then you back off a little bit, and that's where you price it..

Hughes: Who was dealing with the FDA, and did you have any direct—

Young: I am only on the manufacturing side. I think there was an FDA advisory committee, and that was primarily Elliot Grossbart. I can't remember this exactly: I think Ralph Snyderman—he wasn't in charge of regulatory, but that was in his group—was dealing with them. Of course, the [FDA] advisory committee rejected it the first time. Then there was a campaign, with editorials in the *New York Times* and the *Wall Street Journal* and lots of pressure on FDA to go ahead and approve it anyway. Which they did six month later.

Hughes: What was the basis for the initial rejection?

Young: I think not enough data and not enough patients.

Hughes: How would you characterize Genentech's relationship with FDA?

Young: It was pretty aggressive and arrogant.

Hughes: Yes?

Young: Yes. I think we learned after that, because we got lots of approvals that happened after that. But on both growth hormone and tPA, I think we were much more in-your-face with FDA, and I think we learned that that is probably not the best way [laughs] to get them to do something. So I think that after that there was more ability to work with them.

Hughes: Was there quite a bit of educating of the FDA that had to be done?

Young: Yes, sure.

Hughes: I mean, they weren't used to dealing with this sort of product.

Young: No, there were lot of sessions in the early days just educating the FDA on the technology and how it worked and all that. Sure, we did a lot of that. But in the end it is just a medical decision. Is there enough safety data? The trials we did were probably not enough patients. I can't even remember what their specific reasons were for rejecting it the first time. But it probably had to do with the ratio between stokes and efficacy. Then the other issue we had even after approval where sales weren't really materialized— I remember that we got it approved I think at the end of the year. Which year would that have been? Would it have been '86?

Hughes: ‘87?

Young: ‘86 or ‘87, I can’t remember. But I remember the next spring everybody was watching sales, and the stock, of course, just started to sink. Then we started thinking about, what are we going to do because we are not going to have the revenue. There were lots of discussions about alternatives, and do we do layoffs? I remember in the late eighties all of us had lists of people we were going to lay off. That was done all right before we finally signed the agreement with Roche, and that was the thing that kept us from having to do that. I think that was largely Bob and Kirk [Raab] who said, “Let’s see if we can find a partner for this company.” And got Fred Frank involved, who is still the senior banker at Lehman Brothers, to help cook up a deal. I remember they went around and talked to all the U.S. companies. In those days, nobody was willing to make an investment like that in Genentech, primarily because you would have all this good will that you would have to write off—which now everybody ignores, which is kind of ironic. But then the concern was the dilution of earnings and that sort of thing, since Genentech didn’t have any back then. But at any rate, there was a lot of reluctance from the U.S. companies, and we finally got Roche interested. And Roche saw it as their interest, too, and put a deal together and agreed to a deal that I think was in both companies’ best interests. They ended up with a percentage of the company but no control, and a couple of people on the board, but no ability to control any of Genentech’s decisions. So it was really interesting.

Hughes: How did Genentech manage to negotiate that?

Young: I don’t know [laughs], that was Kirk and Bob. They did it. And they negotiated a good deal with potential product rights. But Roche had actually very little control legally. In fact, I remember when the deal was first signed—this was in 1990—you used to have to get approval from both the Genentech and the Roche CEO [for Roche employees] to even *visit* Genentech, which I think protected us a lot because there were probably 50,000 Roche employees, and every one of them had a job of coordinating something. So you could imagine that you would be visited by the quality [control] people and the environmental people and the safety people, and you would end up everybody wanted to come to San Francisco. It was a great way to keep the culture unique at Genentech and reduce the amount of interference with we had from Roche.

Hughes: When you get down to it, what was Roche actually buying?

Young: They were buying rights to the products.

Hughes: Well, yes. But what were the products?

Young: Well, there was a lot in the pipeline even then.

Hughes: Was there?

Young: Even then, sure. So they were buying that, and buying a very aggressive, talented research organization. What Roche would probably say if we asked them today is that in 1990 they were buying research, and they were buying innovative, biotech-oriented research which they didn't have. It think that is the part they valued absolutely the most. Now, there was manufacturing that went along with that which fit the biotech products that research was developing. They valued that, but probably figured they could figure out how to do that on their own; they probably figured out that they could sell on their own. But I think what they really valued was the Genentech research organization.

Hughes: Now, Roche had an agreement with Genentech on interferon, right?

Young: Right. Dating back to the mid-seventies.

Hughes: Which didn't go where it was supposed to go initially. Was that a deterrent in any way?

Young: No, not really. That was alpha-interferon which was licensed to Roche in the late seventies. They then developed it in competition with Schering, which was a Biogen licensee. So those were the two competing alpha-interferons, and Schering basically cleaned Roche's clock! Roche had all kinds of problems, and did get it approved for hairy-cell leukemia, I think, but was very late figuring out that it could be used for hepatitis. Schering was early in figuring that out, and basically had most of the market. It is actually reversed now, where Roche has become much better. They have gotten approvals now for hepatitis and have actually gotten a long-acting form developed which is really, I think, taking market share away from Schering. But, then it was the other way, and they were not that competent in developing it back in the late seventies, early eighties. I remember they closed their plant once for renovations, and FDA wouldn't let them re-open it, and so they lost a bunch in the market that way. So they had a whole series of horror stories.

Hughes: You mentioned Raab arrived early 1985. How much did his presence influence the Roche acquisition, or putting it even more simplistically: Do you think that if Raab had not come, that the Roche acquisition would have occurred? I guess it is the difference between what Swanson thought about it and what Raab thought about it.

Young: I think it is likely that there would not have been a Roche deal without Kirk. He was the driver. Bob was extremely entrepreneurial, very focused, very specific in his ideas and attitudes, and I am not sure that he would have been ever able to get himself to sell the company, or sell a big piece of it. Now, you know, desperation can lead you to a lot of things. But I think it was Kirk that was mainly the driver, saying, "Look, if we lay people off here, the stock will go into

a tail spin, and we are going to end up losing a lot of the value that we built, and a lot of culture that we built, and we need to do something more innovative." I think between Kirk and Fred Frank, who I think was the idea generator for how to put that deal together, which had this unique call-put option in it plus a big investment from Roche. I think they were the drivers and convinced Bob that he needed to do it. So Bob probably came along and said, "Okay, this is a way to preserve what is here and to potentially allow the company to go forward semi-independently. But I think that Kirk was the driver, so I don't know—if he hadn't had been there, it may be that there wouldn't have been a deal.

Hughes: Do you think that one of the main reasons that Raab was brought in *was* to drive the Roche deal?

Young: Oh, no, no, not at all. No, no, he was brought in to help get ready for the commercialization of tPA and get it approved and all the things associated with that. We had a very small sales force up to that point, and tPA was going to require hundred of sales people selling to hospital-based cardiologists. By '83, '84, we were looking for a pharmaceutical executive to help Bob, where we were starting to get out of his comfort zone with commercialization of products. So we actually interviewed and offered the job to at least one other [phone rings] pharmaceutical executive who didn't take it—Jim Vincent, who eventually went to Biogen. Kirk was another Abbott guy, who came kind of out of the same mold, that they talked to after that. But it was really basically the board saying, "Bob, you really need to get a second-in-command that knows something about the industry that you are in." I think Bob was a little reluctant; like most entrepreneurial CEOs, they don't want to give it up. But he did. They didn't really have the greatest relationship, so that was a little bit hard on all the rest of us.

Hughes: Was that just a matter of different personalities, or was it a difference in philosophy about what direction the company should take. [interruption]

Young: No, I think they largely came at things partly because of different experience, backgrounds, and started clashing almost from the very beginning. The first five years where Kirk was president and Bob was CEO, I think Larry Setren, who was the head of HR [human resources] at the time basically was managing the relationship between them, or trying to. They clashed on a lot of things. To give them the benefit of a doubt, I think they both were wired very differently, and they both came at things very differently. I think they had a hard time between the two of them after the first week on all kinds of things—about the culture of the place, about who should do what, about various roles, about strategic directions, and all kinds of things; they basically had a hard time agreeing on. So I think they ended up clashing from that period, and about '95 Bob gave up, and the board made him chairman, but he was out of any active involvement with the company from about '90 to '95. Then I think the CEO switched [to Art Levinson] and then Bob had already been out for a few years.

Hughes: Is it too simplistic to summarize the philosophical differences as big pharma versus biotech?

Young: That was probably part of it, but I think also Bob is an incredibly driven—stubborn is probably the wrong word— He was a person who had extremely strong convictions about things, and it was very difficult to change his course once he set on a course. Then Kirk was coming from an experience base of, hey, that is not the way it is in this business. I think they just clashed. And it wasn't necessarily that there was anything wrong with either one of them; often, an entrepreneurial personality is incredibly strong. Bob was probably trying to create something new and different and not another pharma company. I don't know if Kirk ever really bought off on the unique things in the culture that Genentech had, which I think was a problem for him—the informality, the lack of perks, the things that biotech companies do to more cherish their relationships in the science that is going on and that kind of thing. I don't know that he ever truly bought off on that.

Hughes: Why do you think he came in the first place?

Young: Ah—well, this was '85; the company had a pretty good reputation then. I guess I don't know the answer totally. I do know that Abbott at that time was run by a guy named Shellhorn who was chairman. Shellhorn was notorious for kicking out his presidents. So everyone that kind of got up into a position of second command and started—

Hughes: I see—they were gone.

Young: So Kirk was in a whole series of ex-Abbott executives, and I think he actually left at the point where he came to Genentech.

Hughes: He said something in his oral history to the effect that he wanted to be in charge of a speedboat.

Young: Yes, probably.

Hughes: You are saying, then, that he didn't necessarily buy into the culture that made the speedboat.

Young: Yes. I think he said he did, but I don't know in his heart that he really did.

Hughes: He had been a big-company man—

Young: Yes, for his whole career. He worked for a bunch of big pharma companies.

Hughes: What about this put—what is the term? [laughs] You can tell I am not a financial wizard.

Young: The put and the call in the Roche deal?

Hughes: Yes

Young: Oh, you are talking about beating the put.

Hughes: Beating the put! *That* is the term!

Young: Well, that is very important. The way the Roche deal was set up was that they had a certain percentage of the company; they gave us a significant amount of cash. Then there was a put that was to be exercised. That was a right that the shareholders all had. I think the [stock] price was like $60 or $62—I can't remember, it has been a while. So, at a certain date—I have to go back and look at the deal to remember when the dates were—but there was a date at which the shareholders had the right to give their shares to Roche and get $60 for them. So that was the put. That is a right that all the shareholders had, and Roche had to buy the shares. It was not their option. Then there was a call that Roche had a right to do that was at $82.50, I think, where they at their option could buy the rest of the company if the shareholders didn't put the shares. If the company was doing great, then they could buy the company at $82 or whatever the price was. If the company was doing poorly, they still got stuck with the company for $60. This was really more of a focus from '95 to the put date, which was like '97 or '98 or '99— something in there. I can't remember. But the idea was, hey, we don't want to be owned by Roche; we want to be independent. We want to build so much value in the company that we will be way over the price, and no one in their right mind would ever give them their shares—that was the whole idea. So it became kind of a simple rallying cry and a slogan and everything else, to add value.

This is kind of where the '95 change of CEO comes in. So, Art [Levinson] became CEO, and a few us then said, "We think we could beat the put, and the way to do it would be— the stock price is protected because you have the put price, and everybody knows they are going to get at least that much. So the stock kind of trades at a discount to the put. So, no matter what happens to company, how much money we spend, or whatever happens, it is not going to change that equation, so why don't we spend a bunch of money on R&D [research and development]? Let's increase our R&D spending. We have a lot of great ideas in research, we haven't had the money to bring them forward, so let's increase by 50 percent the amount we are spending on R&D, bring all of these products forward, get them into the clinic, and we are protected now. The stock price isn't going to—Wall Street won't care how much we are losing, and this is the time to do that." That basically became the strategy. So in '95, '96, '97—in there—we increased significantly the amount of R&D we were doing. A lot of the things that you see coming out now—Avastin, Herceptin, Raptiva—were in research, but we hadn't started developing. I think Genentech has been living off of that

for at least through this last year. Now they are going to have to come up with some things.

Hughes: So that was rather a good strategy, wasn't it?

Young: Yes. That was a great strategy. So the end result was that the company had so much success that people saw that, and the stock prices went way over the $60, and nobody put. In fact, it was even over the call price for a while there, right before Roche ended up buying the rest of the shares and refloating part of the company, back in '99.

Hughes: Interesting.

Young: So it actually worked out great. But it was all because—I mean obviously we had to have the products and we had to execute, but a lot of it was because we were able to have that period of kind of protected stock price, even through a CEO change and all that. That really was a kind of post-Kirk rallying cry. We had a lot of executives at the point where Art became CEO that didn't believe we could ever do it. They had done the math. The stock was down about $35 or $40, and they didn't think that we could generate enough value to do that. But, as it turned out, we could do that.

Hughes: Did you ever have doubts?

Young: Oh, well, you always have doubts, but it was worth a good shot, because you could see the logic of doing it. So, yes, the drug development business, biotech or otherwise, is an incredibly—it is worse than Las Vegas.

Hughes: [laughs]

Young: The average biotech product from research to commercialization, the success rate is only 25 percent, or was. So 75 percent of the things you work on are never going to make it, and you don't know which. You can use all the best science to try to figure out what the best candidates are, and that is what you try to put in, and even then you have got that kind of success rate.

Hughes: Now that you have your own company [ViroLogic], does it keep you awake at night?

Young: Oh, sure. But it is a great business, anyway.

In '95, we renegotiated the Roche deal anyway, gave them additional rights, extended it. And that is actually how Kirk got in trouble. As a part of that re-negotiation, he ended up requesting a personal loan—

Hughes: Why, when the company was doing so well, did you decide to give Roche more rights?

Young: [sighs] Well, we wanted to push out the date and maybe get the terms a little bit better. So that was the reason. We were ready, but not quite ready, so we needed a little bit more time.

Hughes: I read that there was a debate over whether tPA should be produced as one or two chains. I got this from the Raab oral history.

Young: Yes, there were two manufacturing methods. Production in roller bottles, used for early clinical trials, resulted in the two-chain form. Production in large scale suspension culture, used for late-stage clinical trials and the market, yielded primarily single chain. But we could not use the roller bottle method for the market. It would have made the product too expensive. The other thing on tPA was the GUSTO trial, of course, and so that was like a $50,000,000 bet that we could demonstrate clinically that tPA was better than streptokinase.

Streptokinase was [pesky?]. And that was really over, is the $2,000 difference justified, and there was no real good data. GUSTO 1 I think was an Italian trial. Remember that these trials started to come out when people were doing this and showing no difference. I think that we became concerned that we weren't going to be able to maintain the price, so we ended up designing a *huge* clinical trial. Dave Stump was actually the clinician that was most responsible for that. He is now at HGS [Human Genome Science]. It was designed to show a 1 percent difference in efficacy between streptokinase and tPA, and that's what it showed. The thing that I remember about it was that we had this great celebration when we got the results. We set up a tent in the parking lot and had the whole company in there. Then Kirk and Dick [Brewer] who was head of sales and marketing then, and I think Barry Sherman who was the head of clinical, were all in Washington, wherever they were doing the FDA press release conference or whatever. And I was the only guy there [at Genentech]. So I was the live person in San Francisco, and I got to announce the results to everybody. Everybody was cheering, and it was really terrific. They were on TV, but I was there for sure. I was the only executive that was still in San Francisco.

Hughes: Still on the job.

Young: But that was great. So we did win that trial. That would have been late eighties, I guess. Early nineties maybe. It might have even been after the Roche deal. I can't remember when.

Hughes: I think it was before, but I can find out.[1]

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1. FDA approval of tPA occurred in 1996; Genentech's merger with Roche occurred in 1990.

Young: You have to do your timeline stuff because it all runs together after a while.

Hughes: Okay. I understand that there was a development committee, and there were also product development teams?

Young: Oh, sure.

Hughes: And how does that all work?

Young: Well, we had project teams almost from the beginning of the company, working on various aspects of development. We had several rounds of, "What is the right formula here for product development?" I think the most intense work to get that right was actually undertaken about '95. We decided that we wanted to redo the structure and the way that we were doing it and get the most knowledgeable people involved and figure out how to set up the leadership, etc. So we did a major revision of our project teams and the product development committee that supervised them, and we did all that in about the mid-nineties. I remember I recruited Ted Love, who was a cardiologist in the clinical group, to be the leader of the product development group. Ted is one of these guys who is just a wonderful natural leader, and people will always follow him. He has a lot of charisma, etc. So he became the center of that. We hired some consultants to redo the way the teams were structured. We put in Ted's group an analytical group that could help analyze the portfolio and then re-organized the product development committee, which was the body in charge of monitoring all the various development projects that we had going. That was probably our most effective product development group, and it also coincided with the time we were increasing the amount of development work we were doing, and we needed it. Before then, I think, everything kind of focused on one project. So everyone worked on tPA; everyone worked on Pulmozyme. But now we had a lot of things going on, so we needed a more structured way of approaching it. We had a twin leadership system and decided to do it this way, where we had a scientific leader who was the project leader, and then we had a professional project manager who would assist them and do a lot of the leg work and the coordination, and write the minutes, and make sure things stayed on track with the budgets and timelines. So all of that got developed in the mid-nineties, around Ted. And then also Sue Hellman, who was by then elevated to head of development—well, first head of clinical and then head of development.

Hughes: Were there models for this organization?

Young: Well, there were some, and I think we used some outside consultants, but I think we taught them more then they taught us. But with a lot of it, we talked.

[End Tape 3 Side B] ##
[Begin Tape 4 side A]

Young: —various modified forms.

Hughes: And you say that model came in sometime in the nineties?

Young: Well, we did a major revision of it in ‘95, so yes, right in the mid-nineties. Before then it was a little easier to have project teams because everybody worked on one thing. So the whole company worked on tPA, the whole company worked on Pulmozyne. I think it was right after Pulmozyme was approved, that was ‘93, that we realized that, no, we’ve got to do more than one thing at a time. We have to figure out how to manage a broader array of projects at different stages and then maybe several at the same stage. So that is when we kind of retread the way that we went about managing.

Hughes: Now, when you say the whole company, do you really mean that? Even the molecular biologists?

Young: Well, no, the research people had their projects.

Hughes: So there was always this branched system at the base, that then narrowed down—

Young: It was sort of the post-research. A few of the research people, and then everyone else would be focusing on one thing.

Hughes: What about the transition from the research people into the development phase? How well did that go?

Young: It went very well—at least I remember that it went pretty well. I think they were always attached to their projects, and they would participate as they went forward. Maybe I was immune to any issues there.

Hughes: Oh, I think you probably would have been aware if they were there.

Young: There are always hierarchies within technical organizations, so at various times, various science groups were the king of the hill. And then as the technology changed or the emphasis changed, then people would maybe not feel quite as good. When I first started at Genentech—I think I maybe told you this—the organic chemists were the kings of the hill because they were the guys synthesizing the DNA, and nobody [else] knew how to do that right then. Later you didn’t need them, you could buy a machine to do it.

Hughes: And the molecular biologists have that connotation, too.

Young: Well, they were kings in the late seventies. I think it tended to be whatever the hot area was that was in scarce supply, and that moved according to how the technology developed.

Hughes: Yes, and moved, I would think, more towards a balance with the development group as the company is maturing.

Young: Yes.

Hughes: Let's see [looking through notes]. Do you think that when you arrived in 1980 that Swanson and the board had any concept of what kind of difficulties they might face in getting a drug to market.

Young: I think they didn't. You know, it was all new and it was a pioneering effort and still is to some degree today, so I think they had no idea what problems that they would face. Boyer often will say, "Well, if I knew that it was going to be this hard, I would have done something else." It was a lot harder, it took a lot longer, obviously it cost a lot more money, but I think that that nobody thought that at the time.

Hughes: I was thinking that when you were talking about the development of the CHO system and the mammalian system. Was it not the belief in the early days, that all these products were going to be produced in *E.coli*?

Young: Oh, yes. Of course. We had no idea what was going to be required in more sophisticated products downstream. They basically let Art in his lab work on his mammalian cell expression systems, but we had no idea that we would ever use them. One product he did work on was actually turned down by marketing, which even to this day if you talk to people at Genentech they are upset about it. We had in the late seventies, we had a technology in mammalian cells that Art had invented for making hepatitis vaccine. And the marketing people then—I didn't know any difference either; I was there too—basically said, "Wow, that is a bad market. Vaccines are cheap and there are liability issues."

Hughes: [laughs] Why do we want to get into vaccines?

Young: Yes. They didn't support it, and so we never did anything with it, and then Merck (bless their heart) developed a recombinant hepatitis vaccine. They said, "Yes, [vaccines] are cheap, so we are going to charge $100, not ten cents," and Merck had a few-billion-dollar market.

Hughes: But they were making it in yeast, weren't they?

Young: They did make it in yeast, but this [Genentech's] was as good or a better process. Now we would have had to go through the safety issues, but with a vaccine the amount of protein you need is very small, so it would have been a different order of magnitude manufacturing problem than we had with tPA.

Hughes: Was it basically Swanson's decision that you were not going to be a vaccine producer?

Young: I think that it was the management's, but you know, it was the marketing people at the time who, I think, would have been Jim Gower or Bob Byrnes. And Bob was very innovative. He was always good at bringing the right skills in. It wasn't that he didn't know because he [brought] in people who he thought had experience at the part that he didn't know. Bob Byrnes was an early hire who was a sales and marketing executive, and then Jim Gower after that. It is just nobody knew. We were all in a new environment, inventing a new history. Marketing people have to have something to compare it to, and if it is a new pioneering thought or effort or product, they have a much harder time (I think anybody would) at pegging what this ought to be worth and how to do it. If they can say, "Okay, I am bringing out another beta blocker, if I know what the other ten do, and how they are marketed and all that, it is a lot easier. So I think anytime you have an innovative product, it is a lot more hit and miss where you are going to act and what is going to happen. So they were just basically comparing this vaccine to something that was already known in the business, and vaccines at that time were kind of known as a shitty business. Once I asked Roy Vagelos, who was CEO of Merck, at the time they developed their hepatitis vaccine. I said, "Well, why did you do that, and why did you price it like you did?" He said, "I don't know, we just thought we were going to have an innovative technology; we needed to make money on it, and we couldn't sell it for ten cents, so we made it $100." So they basically were looking at the same problem and coming up with a different answer, saying, "This is a good business, and we are going to change the way that people think about this." I think their market was health-care workers, people that were exposed, that could afford to pay. They were not treating the general population of people. They ended up with a couple-million-dollar market. So, to me it was a lesson in innovative products. You really have to think carefully about how you evaluate those, because you can't use the conventional marketing comparisons; people just don't know what to anchor it in.

Hughes: Well, it sounds, looking at it in my simplistic way as, "What do you think the market will bear?"

Young: Well, that is often the way things are priced, which I guess is a surrogate for what the value is.

Hughes: Tom Kiley suggested that I ask you about Walter Cronkite's visit.

Young: Oh, right. We were getting a lot of publicity in the post-IPO days. This would have been in the early eighties, and we were still in the original building over there [South San Francisco] in Building 1. We had a kind of pilot plant just down from Swanson's office, and it had one big fermenter that we bought from Lilly but never got to run, and then we had a bunch of ten-liter fermenters, little guys, little glass fermenters. They were sitting outside of this thing, and that is where we did the experiments. So the process people would do those, not to make clinical material, but to develop all of the conditions that we needed. So

Cronkite visited, and they were giving him a tour. So they came in and wanted to photograph him in the pilot plant and take pictures in there. So, what I remember is that his cameramen all came in mass; they are in this place where no one ever goes, where we have all these little fermenters bubbling, and they were busily unplugging the fermenters to plug their cameras in, and you know the whole place was going down while they were in there setting up. But they eventually set up, filmed Bob and Cronkite in there. I do remember there was a Herb Caen article the next day in the *Chronicle*. The article basically said, "Walter Cronkite visited Genentech, Swanson entertained him, but had to leave early for a softball game." [laughter] So the implication was that Bob kind of stood up Walter and said, "I have to get to my corporate softball game." Which was the Genentech team and someone else. So that was the Walter Cronkite visit.

Hughes: How organized was Genentech when you arrived? Was there, for example, such a thing as an organization chart and formal business plans?

Young: Well, there was some of that, but it was pretty disorganized. It was growing very quickly, people were brought into the organization not necessarily a lot of discipline with what they were supposed to do. So there was a fair amount of conflict over roles and responsibility and things that kind of had to settle in. Every time we brought a new person in, we would go through accommodation of what that person wanted to do. Bob was, I think, fond of throwing people into the pot and seeing what happened. We looked for a long time for a head of research, this was a difficult job to fill, in the early eighties. We just couldn't find anybody. Bob was basically having everybody report to him, and Herb Boyer was filling in, and he said, "Hey, we need a head of research here." So we interviewed a number of people. We interviewed David Botstein from MIT, who eventually came for a different job. We interviewed, I think it was the head of the NIH, [Donald S.] Fredrickson, right. That was another model. Then we eventually hired David Martin, who I think came also in the early eighties- '82, '83, '84.

Hughes: '83, I think.

Young: Yes. So when Dave came in there was this immense accommodation to his views of things—he is a very strong personality. I remember that it was actually very beneficial for me because he decided—this is probably a little simplistic—that he had too many basic scientists, molecular biologists, biochemists. He needed more biologists, because he wanted to study drug effects and that kind of thing and he didn't have any of those kind of people. So he said, "Hey, Bill, why don't you take all of my biochemists?" I said, "Well, this is great, because I am going to have to hire these kind of people anyway to do process work, so that I can have all of these guys for purification scientists," and basically took the best of what the company had at that point in biochemistry and moved it over to process development, so it was great for me.

Hughes: But what about the biochemists, were they happy enough to be transferred?

Young: They were very happy, and a lot of them had great careers and did very, very well in that environment. But Dave was very, very quick to do those things. So everyone had to accommodate. Then I remember a few years later Bob decided to hire Botstein, and we had already had at least four heads of research by then. We had David Martin, Mike Ross, Ralph Snyderman, and Tom Glenn. So these were all high-ego executives running various parts of science. Bob said, "Well, I just thought he [Botstein] could shake things up." [laughter] So then we had five. But that was kind of more his style. It was less controlled, so you had to kind of fight for your territory and get in the combination of your people. I don't know whether that makes you better or worse. It probably makes you better because you have to defend what you are doing, and that is the environment that makes you stronger.

Hughes: How do you pronounce his name—Setren?

Young: Larry Setren?

Hughes: Yes, that's it.

Young: He was the head of HR [Human Resources].

Hughes: And he wrote the introduction to the [G. Kirk] Raab oral history, and in it he says something to the effect that in the very early in the days, I guess he is talking about the 1980s, that Genentech had a reputation as a prolific research organization, but was not particularly good at targeting candidates for actual product development. Do you agree?

Young: Well, no, I think that the early research days were not about discovering new molecules and new action. The whole strategy was about, let's make insulin because it is a molecule that already exists that is in short supply, or is going to be; let's make identical human ones. Same thing for growth hormone. So these were picked because they were known molecules. But later, after growth hormone, then you are faced with the issue of inventing something new, because you kind of run through the protein drugs that are out there. So I think that that was also part of the idea of hiring someone like Dave for the head of research, to start thinking about, Hey, we can't just copy things that are out there; now we have to invent some new things. So we have tPA; we have Pulmozyme, and how do you really get a research organization to do that? It was a big change, because up to then they were technologists. They were cloning interferon, but interferon was known from natural sources, etc. So then it is kind of a different format. And we probably stumbled around for a while before we figured out the best way of doing that. But that is really the transition that the company was trying to make. So I think that is probably a fair criticism, but I think that it is understandable given what the initial products actually were. And now they said,

"Now we have got to create a research organization that can be innovative and develop new approaches to disease," which is a whole different thing than copying some product that nature has already there. Setren was one of our many heads of HR; we seemed to go through quite a few of them. He was about third from the start of the company. He probably had the most to do with helping Kirk and Bob kind of relate during that five years or whatever where they were working together most closely.

Hughes: I still don't have a picture of how intimately or not the board was interacting with the company. When you became COO [chief operating officer]—when was that?

Young: '97.

Hughes: You must have—

Young: Oh, I interacted with them very closely. Sure, sure.

Hughes: Well, that is what I want to know. How directly was it?

Young: There was not a huge interaction between board meetings, but we had four or five board meetings a year. There were all these capital requests and manufacturing things that I ended up going for. So management did interact with them quite a bit. Bob was very good and way ahead of his time, compared with what is happening nowadays, at picking board members who could provide different perspectives on the company, because of their different experience background. So he was very resistant to letting insiders on the board. Basically it was he alone, and then it was he and Kirk. His view was, employees shouldn't be on the board. We should reserve the board seats for independent directors who can bring something. So that is the way he built it, and I think he did a great job of it. We had some wonderful people at various times who weren't always perfect, sometimes we screwed up, but by in large if you think about the board members, they were all incredible people. Tom Perkins is the chairman.

Hughes: Right!

Young: We had Herb [Boyer] who was always on the board. We had [Dave] Packard for a while, who was wonderful in his insights about early development. That is why Bob got him, if you remember back to when they first started.

Hughes: Do you think that some of Genentech's famous culture came through Packard?

Young: Not really. No, I think it was already there. But I think that the most influential culture person besides Bob was probably Boyer. I think that the things that he did, particularly not so much on the rest of the company but certainly on the science side by emphasizing that scientists should be allowed to publish what

they do in a pretty aggressive way, and that the credit for the innovative work that is done should be the scientist, not necessarily the partner, chairman, or the director or whatever. And just creating an environment of academic life were the greatest gifts to the company that [Boyer] gave. Basically it allowed the company to attract the absolute best people and allow them when they were very young to make their reputations. If you put them in an industrial environment—at the time the prevalent one was the pharma companies—they couldn't develop their reputation because they were suppressed from publishing, they weren't allowed to go to meetings and talk. The authorship of what they [the scientists] did was usurped by the department heads and leaders. Herb was incredibly strong in saying, "No, we have to let them develop their careers and their reputations and publish in *Nature*," and all of this innovative stuff. He probably had the most to do with that culture than anybody. So that was his biggest gift to us.

Hughes: All this, though, had to be balanced against the need for intellectual property protection.

Young: Yes, sure.

Hughes: Which would have been new to Boyer, in the beginning anyway.

Young: Yes, well, it was. So Bob probably bought that, and they made absolutely sure that patents got filed. So what would happen was that the lawyers were the ones that ended up working through the night to get something written up. Rather than saying to the scientists, "No, you have to wait till the next meeting to do that [talk about a scientific finding]." So they really worked hard to make sure that, yes, intellectual property got protected. In fact, we had to put a system in place because it was <u>such</u> an academic culture that stuff did start getting out, and people were starting to send in abstracts, and we had to put in a process to get legal sign-off before you did, and all that. We then had to threaten people that we were going to fire them if they kept violating it. That did get put in place, but the patent department was the one that had the burden of making sure they got stuff filed. Tom Kiley himself, I am sure, spent a lot of nights writing something up and getting it ready. Yes, you have to protect the company, but I think that when in doubt we published it, rather than doing it the other way around. I think that everyone there appreciated it, and that is the reason that you have Genentech science cited so frequently in such major publications. We even started using that for PR [public relations]. We can figure out how many citations they got and what publications, and [Genentech] was by far the number-one industrial organization. We even beat out the government. I think that Herb was the main architect for that. Absolutely.

But the board itself, I think, didn't really get involved in the culture of the company or in—my perspective was that they didn't. I think they were all busy business people that came there four or five times a year. And certainly every

meeting was fascinating for them, and they loved the company, most of them. They would all say, "What you guys are doing is tremendous. It is all pioneering stuff." But I think they were not really managing the company, which is good.

Hughes: Talk a little bit more about the transition from Raab to Levinson. I have heard so little about Art, particularly.

Young: So this was '95, and we had just completed the negotiation with Roche, or it was going on. I think that it had been completed by then. Probably for some months before that, the board had been concerned about Kirk for various reasons and had been interviewing a lot of us. The result was that he ended up resigning in '95. The board had a meeting that we had actually in New York, made Art the CEO. Art actually went out of his way to make sure that I was willing to stay and that I was happy with him.

Hughes: Because you were in the running as well.

Young: Yes, and I was disappointed of course. But I think that Art and I made a really good team, and he went out of his way to make sure that I would stay. I ended up a year or so later being COO, so it was great for me because I got to do some new things that I hadn't done before. I think the transition was very popular inside the company. My guess is that the Roche people had a lot to do with this selection. I think it goes back to what they value about Genentech, and I think a lot of it is the research. Art was clearly the one in the company that could continue to get the loyalty of the research people, having been in charge of research. Inside it was very popular.

Hughes: But couldn't he have been faulted for lack of business acumen?

Young: Well, he was, but he turned out to be a lot smarter than people thought. So, yes, I think that was the rub, but I think he has proven them all wrong, and I think he is a smart business guy, and he works well with the organization that he has. He has actually probably done much better than the Roche people probably thought he would, I guess. Not necessarily that we thought he would, but I think that they thought he would.

Hughes: I would think that one of his first problem must have been to correct the damage that had been done by the Raab episode.

Young: Well, the damage that we were suffering then was primarily around our sales and marketing practices. We had gotten a bunch of warning letters from FDA; we were being criticized for overly aggressive marketing practices. There were several legal cases going on with the Justice Department, looking into the marketing of things like growth hormone, including one executive that had been—I guess he got indicted. So he was in court. And all of this revolves around what Kirk was leading, because if nothing else, he was the commercial

head of the company and really responsible for that, because he knew more about that than anyone else. I think also there was a feeling on the part of most of the management then, and I put myself and Art certainly in that category, that we had almost nothing to do with the commercial side of the company. So, when we are reading about all the trouble we are in, we are saying, "Hey, how come we weren't talking about that in the management committee and dealing with it, and why are we finding out this way?" And it makes you really feel kind of bad that you are thought of as not being the most ethical of organizations, because that is not the way the company sees itself. I think that all of that was in there. Art—and I have to put myself in there because I went to a lot of the meetings also—we worked hard to get back on the right track with FDA and fire people who were violating the internal sales and marketing guidelines and got really aggressive. So I think that got straightened out pretty quickly. And then eventually the various legal actions got settled. But yes, that was sort of put on Kirk and I think that was generally what he was directing. But that was the internal split in the company. We in management felt like we were busy working on our science stuff, in development and manufacturing stuff, and we were all surprised and not really involved in what was happening on the sales and marketing side.

In Kirk's defense, the whole system was also changing then. Communism was gone; the FBI was discovering health care. I think that there were a lot of laws and regulations on the FDA's part and the government's part that started getting enforced in Medicare abuse and that kind of thing, and practices that were normal in the seventies and eighties became illegal in the nineties. In a way, we didn't change fast enough to kind of fix what we were doing, but in a way it was carried over from the way most companies were operating. If you look, a lot of companies got into the same kind of trouble with FDA about how they advertised and dealt with information and all that. But we were probably a little more aggressive than we should have been even then. But you know, it is a little company and under a lot of pressure to get sales and grow.

Hughes: And it is a bunch of aggressive people [laughs].

Young: Yes, a bunch of people who, that is their personality. You probably didn't hire the most laid-back sales and marketing people. But I think internally that got straightened out really fast. The company got those things resolved, got focused very quickly on new R&D and increasing R&D and figured out how to do development better, and I think that all of that went in the right direction, and I don't think that there was a very long residual effect from that. So I think that Art did a great job.

Hughes: He did indeed; I mean, he is still there.

Young: Yes.

Hughes: You were COO for two years.

Young: Yes, almost three [1997-1999].

Hughes: What do you care to say about that period?

Young: Well, for me it was great because I had all that I ever wanted to run at Genentech. I had all the development activities, product development, etc., all the manufacturing operation activities that I had had before, and sales and marketing and business development, which were new areas for me. I actually got a kick about interacting with the sales people and seeing what they did and learning a bit more about it. I am not sure I contributed a lot to it, but I made some personnel changes and hopefully got some of that on the right road. I had a great business development group which did a number of very innovative deals in that period. I give Nick Simon credit for this, who was running business development. We had money for increasing our R&D budget, but not indefinitely, so we basically farmed out a couple of products that we thought were good and innovative, but couldn't afford the P&L expense for us to develop. So Nick came up with a pretty innovative arrangement with Xoma on Raptiva, which is a psoriasis drug that was approved, and basically put that in their hands to develop. They did it, got it improved, Genentech took it back, and now they are selling it. It was a great way to expand the number of things that we could do. So that was a good time for me.

[End Tape 4 Side A] ##
[Begin Tape 4 side B]

Young: I thought, well maybe this is a good time to think about what I want to do next. Rightly or wrongly, I thought Roche would probably exercise more control post-IPO; the board was changing; all the independent board members that were on there were gone or leaving. So I thought, maybe this is at least a good time to at least think about other things. So I went to Art and said, "Art, how long are you going to stay?" [laughs] He said, "Well, I like being CEO, I will probably stay here a while." I said, "Well, okay, Maybe I will look at some other options; I might decide to stay." He said, "Well, that would be great. If you stay we can give you more responsibilities." I said, "Well, I don't really want any more. I like the job I am doing, but maybe it is a time to be a CEO or try some slightly different business." Anyway, to make a long story short, I ended up coming to ViroLogic, primarily because I believe from Herceptin work that we did, that therapy where you guide the therapy based on a diagnostic that was paired with a therapeutic was going to be extremely important, and medicine going forward, more and more important. I kind of wanted to learn that side of the business a little bit and see if I could develop another major trend in medicine after biotechnology. So that landed me here where there was a working model in HIV that we have gotten almost to the point of profitability. Now we are taking on some technology for cancer; I think that disease is prime for this kind of

technology. But that was basically the rationale. There was nothing against Genentech or anything about it. In fact, I probably left a lot of money there that I am still looking to recoup. But you know, at some point you have to do what is fun and interesting and not necessarily do it based on how much money you make.

Hughes: How much has Genentech been a model or an anti-model for what you do at ViroLogic?

Young: Well, it is an incredible model. Just speaking for myself, a lot of the science emphasis, the culture, the informality, these are all things we learned there—building a board with independent views that can help you. There are so many examples that come from the Genentech experience, including a bunch of Genentech people that work here. You almost get too much of it; you don't want to be Genentech. In fact, the HR [Human Resources] head here would fine me five bucks every time I said Genentech for the first year, and I lost a lot of money because it is so ingrained in you, and you don't want *everything* to be a copy of Genentech. You want to kind of invent your own. I think we have done that, but there are a lot of good things that we brought here that I think are just wonderful things from that company. So maybe we are more Genentech-like than they are.

Hughes: [laughs] Could be.

Young: Could be, there are 6,000 of them, and there are only 200 of us.

Hughes: Well, I am at the end of my questions, but have we left out any stories?

Young: Oh, I am sure, but probably ones that I don't want to put in a book.

Hughes: [laughs]

Young: We certainly covered the essence of it.

Hughes: Well, good. I certainly thank you.

[End Tape 4 Side B] ##
[End of Interview]

SALLY SMITH HUGHES

Sally Smith Hughes is a historian of science at ROHO whose research focuses on the recent history of bioscience. She began work in oral history at the Bancroft Library in 1978 and joined ROHO in 1980. She has conducted interviews for over 100 oral histories, whose subjects range from the AIDS epidemic to medical physics. Her focus for the past decade has been on the biotechnology industry in northern California. She is the author of *The Virus: A History of the Concept* and an article in *Isis*, the journal of the History of Science Society, on the commercialization of molecular biology.