CHEMICAL HERITAGE FOUNDATION

CHARLES COONEY

Life Sciences Foundation

Transcript of an Interview
Conducted by

Brian Dick

Boston, Massachusetts

on

14 August 2013

(With Subsequent Corrections and Additions)

CHEMICAL HERITAGE FOUNDATION
Center for Oral History
FINAL RELEASE FORM

This document contains my understanding and agreement with the Chemical Heritage Foundation with respect to my participation in the audio- and/or video-recorded interview conducted by Brian Dick on 14 August 2013.

1. The recordings, transcripts, photographs, research materials, and memorabilia (collectively called the "Work") will be maintained by the Chemical Heritage Foundation and made available in accordance with general policies for research and other scholarly purposes.

2. I hereby grant, assign, and transfer to the Chemical Heritage Foundation all right, title, and interest in the Work, including the literary rights and the copyright, except that I shall retain the right to copy, use, and publish the Work in part or in full until my death.

3. The manuscript may be read and the recording(s) heard/viewed by scholars approved by the Chemical Heritage Foundation unless restrictions are placed on the transcript as listed below.

This constitutes my entire and complete understanding.

Signed release form is on file at the Science History Institute

(Signature) _____
Charles Cooney

(Date) Aug 7, 2017

OPTIONAL: I wish to place the following restrictions on the use of this interview:

_____

_____

I understand that regardless of any restrictions that may be placed on the transcript of the interview, the Chemical Heritage Foundation retains the rights to all materials generated about my oral history interview and will make the title page, abstract, table of contents, chronology, index, et cetera (collectively called the "Front Matter and Index") available on the Chemical Heritage Foundation's website. Should the Chemical Heritage Foundation wish to post to the Internet the content of the oral history interview, that is, direct quotations, audio clips, video clips, or other material from the oral history recordings or the transcription of the recordings, the Chemical Heritage Foundation will be bound by the restrictions for use placed on the Work as detailed above. Should the Chemical Heritage Foundation wish to post to the Internet the entire oral history interview during my lifetime, I will have the opportunity to permit or deny this posting.

I understand that the Chemical Heritage Foundation will enforce my wishes until the time of my death, when any restrictions will be removed.

This oral history is designated **Free Access**.

***Please note*:** Users citing this interview for purposes of publication are obliged under the terms of the Chemical Heritage Foundation (CHF) Center for Oral History to credit CHF using the format below:

> Charles Cooney, interview by Brian Dick, 14 August 2013 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0993).

Chemical Heritage Foundation
Center for Oral History
315 Chestnut Street
Philadelphia, Pennsylvania 19106

The Chemical Heritage Foundation (CHF) serves the community of the chemical and molecular sciences, and the wider public, by treasuring the past, educating the present, and inspiring the future. CHF maintains a world-class collection of materials that document the history and heritage of the chemical and molecular sciences, technologies, and industries; encourages research in CHF collections; and carries out a program of outreach and interpretation in order to advance an understanding of the role of the chemical and molecular sciences, technologies, and industries in shaping society.

INTERVIEWEE

Charles Cooney was born in Philadelphia, Pennsylvania, and attended Upper Darby High School. Growing up, he would often play with electronics, inspired by his father who was a systems analyst for General Electric. After graduating high school in 1962, he attended the University of Pennsylvania, where he majored in chemical engineering. There, he entered a National Science Foundation undergraduate research program, where he designed a reactor to study the continuous growth of microorganisms. After receiving his undergraduate degree, Cooney attended the Massachusetts Institute of Technology [MIT] for his graduate degrees. At MIT, Cooney's research focused on heat production during the fermentation process, with a thesis in oxygen consumption and CO2 production in microorganisms. He received his master's degree in 1967 and his PhD in 1970. Cooney then attended the Bristol Myers Squibb Institute for Medical Research for his postdoctoral fellowship, specifically working in penicillin manufacturing. He joined the faculty at MIT and continued working with his thesis advisor, Dr. Daniel Wang. While teaching at MIT, Cooney became interested in the burgeoning biotechnology field and joined Genentech in January of 1980. Cooney's work at Genentech involved the fermentation of single-cell proteins, recovery of biological products during the manufacturing process, and the planning and design of new plants. He continued his consulting work, helping to form Bioinformation Associates, which worked with the company Genzyme. Cooney joined Genzyme's board and was active with the company when it went public in 1986. Outside of his work, Cooney is a high-altitude mountaineer, having climbed Ama Dablam, Mt. Blanc, and Kilimanjaro.

INTERVIEWER

Brian Dick received his PhD in sociology from the University of California, Davis. Before coming to the Institute he was a research associate at the Life Sciences Foundation. His research interests include the history of agricultural biotechnology, the emergence of the biotech industry, and the Human Genome Project.

ABOUT THIS TRANSCRIPT

Staff of the Life Sciences Foundation conducted this interview, which became a part of our collections upon the merger of the Chemical Heritage Foundation and the Life Sciences Foundation into the Science History Institute in 2018. The Center for Oral History at the Science History Institute edited and formatted this transcript to match our style guide, but, as noted, Science History Institute staff members did not conduct the interview. The Center for Oral History, Science History Institute, is committed both to preserving the recording of each oral history interview in our collection and to enhancing research use of the interviews by preparing carefully edited transcripts of those recordings. The preparation of interview transcripts begins with the creation of a verbatim typescript of the recording and proceeds through review and editing by staff of the Center; interviewees may also review the typescript

and can request additions, deletions, or that sections be sealed for specified periods of time. The Center keeps track of all changes that staff, interviewers, and interviewees make to the original typescript. Please contact us if you would like additional information about these materials. We have established guidelines to help us maintain fidelity to the language and meaning of each recorded interview while making minor editorial adjustments for clarity and readability. The transcript also includes time stamps at five-minute intervals. We omit without noting most instances of verbal crutches and all instances of nonlexical utterances. We also make small grammatical corrections where necessary to communicate interview participants' meaning. Finally, staff of the Center create the abstract, chronology, and table of contents. With the availability of online full-text searching of our transcripts, the Center for Oral History opted to discontinue the practice of preparing a back-of-the-book index for each oral history transcript in 2020. **The Science History Institute is committed to the responsible presentation of the history of science by addressing evidence of inequality and oppression as well as the subsequent silences in our collections. To that end, we recognize there may be language in our oral history collection that is outdated, offensive, or harmful, such as, but not limited to, the following: racist, sexist, Eurocentric, ableist, and/or homophobic language or depictions.**

INTERVIEWEE: **Charles Cooney**

INTERVIEWER: **Brian Dick**

LOCATION: **Boston, Massachusetts**

DATE: **14 August 2012**

DICK: So today is August 14, and we're sitting in the office of Charles Cooney. So just to start off, if we could maybe just get some back—general background on, where you were born, grew up, maybe some just general information about your mother, father, siblings, that type of stuff?

COONEY: Sure. I was born in Philadelphia, Pennsylvania. I grew up in—outside of Philadelphia. I went to high school at Upper Darby High School, graduated in 1962 from high school. I think that's—I think I've got that right. And after that, went to the University of Pennsylvania as a undergraduate chemical engineer.

My career—I was a very—It began in a very simple one. I grew up in a simple household. My mother had never been to college. My father had been to an associate's program, interestingly at Penn many years—many years before, and he was a systems analyst. And my first introduction to computer programming was within bits and bytes, 1's and 0's that he taught me when I was—I guess in grade school. 'Cause he was one of the very early programmers and systems analysts and programmers for General Electric. In fact, was involved in GE's first computer payroll system at their plant in Philadelphia.

So I was inspired early by my father to think about new technology, although he was not particularly technology-savvy. But he was also very good with tools, so I learned how to do carpentry and plumbing, and handle all kinds of tools—things that students don't get to do today very much. And that was an important part of my career, doing things with my own hands, using screwdrivers, wrenches, saws, whatever was needed to repair whatever was broken around the house. And we did that. And I took things apart, and occasionally got them back together again. Had a chemistry set that had been—that had belonged to a neighbor, so it was a second-hand set, and enjoyed doing chemistry as a—you know, in grade school and junior high school.

Became interested in electronics when I was in—when I was in junior high school. Again, used to take things apart and even build them, and go to Radio Shack and buy kids and get them to work. And had a little workshop that—I, again, was instilled by my father's fascination with doing things with tools and building and repairing, repairing things.

So that was actually an important early part of my own thinking and upbringing. Experimenting with science. Doing practical things. Playing with electronics and mechanics. I rebuilt a couple of cars with a buddy of mine when I was in high school, and both of them ran.

DICK: Hey!

COONEY: With—With some false starts. [Laughter] One 1949 Studebaker we seized up the engine in the first time we cranked it over, so we had to rebuild it again, but it worked after that. So those were important lessons.

DICK: What type of, say, you know, experiments or electronic devices were you tinkering with during those days?

COONEY: Well, we built radios. We built amplifiers. We tried to incorporate telephones into—into intercom systems, old telephones. We had a—and amplifiers for hi-fi. So this other buddy of mine, he and I used to, again, take things apart, salvage the parts, and then learn how to reuse the parts. This is the time we were buying resistors and capacitors and figuring out how to put them together. Did a little experimental circuit design <**T: 05 min**>, simple circuits.

But probably the biggest thing was building my own hi-fi system that is used certainly through my high school career. Radio Shack, so it was sort of following the directions, not a lot of improvisation, but becoming familiar with the basic skills, and simple circuitry, and understanding what it was about. So when I went into high school, all—the other thing I did, I played sports, primarily things like running cross-country, track and field. And as I went into high school, for instance, it was sports—I couldn't make up my mind. Did I wanna run? Did I wanna go to track and field? What, you know, what was I interested in? And, sort of, one of those, you know, adolescent debates.

A safe one, if you will. So I chose hurdles. So I had a bit of both. And that actually is a pattern that I have followed throughout my career, where I've had multiple things that I've wanted to do, and I've always tried to create optionality. Then of course you have to make a decision, because you can't do everything.

And I would find these compromises. So I realized much later in life that choosing hurdles was a compromise between track and field events. And then I got into high school, and I had thought I would probably go down the route of electrical engineering, because I like circuitry. I did a little programming that I had learned from my father, and was beginning to think about computer science in its most elementary form—I wouldn't call it science, but it is computers. And then I got into high school science, and of course high school biology circa 1960, science teachers were certainly talking about DNA, had something about genetics, to do with genetics, but that wasn't so clear at the time when you go back and look at that timeline. And biology was interesting, but I really was fascinated with chemistry, probably coming from my simple experiments with chemistry. Textbook kind of stuff, nothing of—exotic. But a familiarity and an excitement about what chemistry would do. And so then—but at the same time, I was in one—my high school was just beginning to teach calculus, so I took calculus

before I graduated. So here I was, you know, electrical engineering, mechanical stuff. I really was an engineer at heart.

Chemistry I was absolutely fascinated with. I was pleased as a senior to get the chemistry prize in high school. A fairly large high school.

DICK: What was the chemistry prize? How had that—?

COONEY: Well, the chemistry was just excellence and doing well in the chemistry class, both the laboratory and in the classroom. And the prize I got was actually a book on chemical engineering. Somehow my chemistry teacher, Mr. Thorpe, recognized that I had this dilemma between chemistry, mathematics, science, engineering. So then I was thinking about college at that point, and finances were tight. I would—wherever I went, I would have to go on scholarship. I wasn't going to—even though tuitions of course were a lot lower in 1966 than they are now. [Laughter]

And I only applied—well, actually I applied to three schools. I aspired at one point to go to the naval academy, and with—it was an engineering education, and I was attracted to aviation, or thought I was. Although I had no reason to be. And then I applied to Penn and Cornell, so they were the only places I applied. That is not a strategy you would use today to apply to college. [Laughter] I was accepted at Cornell. I had a scholarship at Penn. I did not have a scholarship at Cornell, so Penn it was. And I had an alternate appointment at the naval academy, rather than a—I was a second alternate, so <**T: 10 min**> it was unlikely that I was going to get in.

DICK: I see.

COONEY: That was a really good—I was very fortunate, because I would've been in the naval academy, graduating in the class of ’66, in naval aviation—not a good place to be.

DICK: Yeah. [Laughter]

COONEY: It was not a good time to be there. But I was, you know, it was an aspiration of mine. So I went to—I looked at Cornell, looked at Penn, and, you know, there are those events that happen in your—at various points in your life that are pivotal, and one of them was going to Penn.

So I went down—this was, you know, the five miles into the city, or the seven miles into the city from where we lived, which was just west of Philadelphia. And the then-department

head was Arthur Humphrey, who's very much of a luminary in biochemical engineering, one of the fathers of biochemical engineering as we know it today. And Art was the department head, and I said I wanted to—he looked at my grades and board scores, which were—okay. And he personally toured me around the department.

DICK: Wow.

COONEY: And around campus. You know, and how often—as a high school senior does a department head of a significant department do that? [Laughter]

DICK: Yeah.

COONEY: That was one of those "wow" moments. And the combination of that, plus having a scholarship at Penn, that's where I went. So at the age of seventeen—oh, and at that point I was, you know, deciding what it was I wanted to do. I decided chemical engineering. It was one of those chemistry, mathematics, electrical engineering—how do I bring them all together? Chemical engineering was the logical choice. And I, frankly, had little real understanding of what chemical engineering was. I just knew that it was a combination of things that I liked to do.

So that's what I did. And I had—I was accepted into that department. So I went off at the age of seventeen, and moved onto campus, and basically never looked back. I was at Penn four years. And then I had another pivotal moment. I wouldn't say that I was a stellar student, and had one really bad sophomore year. But Art Humphrey gave me some advice, and he kind of pulled me back in. And then, my next pivotal moment was through a national science foundation program. It's the NSF undergraduate research program, NSURP.

And I think that was in the early days of that program. Penn had a grant to support a few undergraduates doing research in the summer in chemical engineering. Somehow when I was in early chemical engineering, I had taken biology, and I really, really was fascinated with biology. And microbiology and chemistry. And I had the opportunity as an undergraduate to do one of these summer NSFURP programs, and I did. It was a chance to work in the laboratory, hands on, which I liked.

It was engineering things that I liked to do, as well. I had a chance to continue that research into the semester. And I became really fascinated with this interface between chemical engineering and biology, particularly microbiology and biochemistry.

DICK: What was the research that you were—?

COONEY: Well, it was continuous microbial culture, so continuous growth of microorganisms, a theme that I continued for many years in my subsequent research in graduate school. And specifically, it was to design a reactor that would allow you to cause bacillus to continuously sporulate. So it was a two-stage, or a multi-stage bioreactor. <**T: 15 min**> Grow up the cells in one stage and have them sporulate in a second stage. And I designed a novel multi-stage second piece of this reactor that was a series of multiple progressive stages that would allow—give the cells time to sporulate. I got started on the project with a student doing his master's thesis with Art Humphrey at the time, and so I had mentors of a PhD student, of a master's student, of a postdoc—not a postdoc, but a visiting faculty member from Hungary.

And all those individuals were really kind of important people, because they created the culture that I worked in. They stimulated me to think innovatively about what I would do. Art gave me a lot of supervision but no constraints. He really, you know—and that was actually was really a very important part of my learning. He gave me an opportunity to fail, to do things that were—you know, might not work.

And certainly, some of—many things, it didn't work very well. But I was able to do things. I learned microbiology. I learned a lot about the mechanics of running reactors, and building equipment and keeping it sterile, and all kinds of useful techniques. [Laughter] And that led to my first paper, which was a—in 1966, when I was still an undergraduate.

Which I co-authored with others, others in the laboratory, but had a very active role in. And so that was a very important part in my life, because it allowed me to make the transition from not doing well in academics to graduating and doing well. Having the opportunity to do research in the lab, and find that I liked that. And to again make one of those decisions, bringing chemistry, biology, engineering together into what be—what was a career in biochemical engineering. When I went into undergraduate school, I had no aspirations to go beyond a bachelor's degree.

I figured I would go to industry, work as an engineer doing whatever a chemical engineer would do in industry. No thoughts of going beyond a BS degree. By the time I was halfway through, and I was in the research lab, I realized, “This is cool stuff!” And I enjoyed undergraduate school. I was in a fraternity. That was almost my downfall, but I look back favorably on it. [Laughter] I did have a good time. I wrote. Again, crew was one of those sports that allowed you to work as a team, and yet you were—you know, it was very focused on individual skill, but individual skill manifested in a team. And I liked being outside. I liked outdoor life. That probably came from my scouting career, which also had some interesting influences later in life. So the combination of crew, for sure—fraternity, learning what chemical engineering was about, bringing chemical engineering and biology together to biochemical engineering, and being inspired to go on and do something with—something that was different.

So that actually began a lifelong partnership with Art Humphrey, because he said he would've taken me as a graduated student, but he said, “You shouldn't stay here. You should go someplace else.” And I only applied two places, which kind of–

DICK: Oh, really? So again, very—[Laughter].

COONEY: Very narrow, yeah. Again, a strategy that I would never give my undergraduate classes today. But I only applied two places, University of Wisconsin and MIT. Both, you know, outstanding schools. And at Wisconsin, I would've had the opportunity to work for Ed Lightfoot, again, another very important person in biochemical engineering, and he wrote one of the seminal texts <**T: 20 min**> in fluid mechanics. Just a terrific person. Or come to MIT, and work for Dan Wang, who was a former student of Art Humphrey's, but he and I hadn't overlapped. Actually just missed each other when I was an undergraduate, and Dan was finishing his graduate work.

DICK: I see.

COONEY: But Dan was just starting at MIT, so I was one of his first students. So I did come to MIT, and I came here because the research that I would have a chance to do was kind of more to my liking than I would've had at Wisconsin. Those are always important decisions, but you make them on simple reasons of the time not because it's any great foresight of—or vision that one has.

DICK: Well, was Art helping you, in terms of saying, "Hey, you know, here are the places, and—"?

COONEY: He said, "These are two good places. These are two good people. It's really up to you to decide." And the fellowship that I had here at MIT was an NIH fellowship, which was a—I forget what I was offered at Wisconsin, but it was a prestigious trainee-ship that I was offered. And I just kind of liked the work, and I came up, and I took the bus up. You know, at that time, I had only flown once in my life, and that was for a crew race that I had flown up—against Harvard, and so I rowed on the Charles—on Mohawk Airlines, which was a—it was like the—you would never have heard of it. It merged, I think, into Eastern, which most people have never heard of that one either, so… [Laughter]

So I flew up to Penn—I flew up to Boston when I was an undergraduate. Then I took the bus up to tour MIT, and explore whether I would come here. Liked Boston, and so decided to come here as a graduate student. And I did, with the expectation that I'd get a master's degree. No thought that I'd go on for a PhD.

And had a chance to—actually, I did my first—well, I did my master's thesis with Dan Wang. Fascinating project. It was to measure the heat produced during fermentation. And to see if there was a way that we could predict the amount of heat that was being produced. So, again, it fit my skills—experimental. I had to build equipment. I had to build what was then—basically

making a calorimeter out of a fermenter. So I operated the fermenter, bench scale, fourteen meters, as a calorimeter so I could measure the heat produced not just by the organisms; I could measure the power consumed by the motor, operating the system at steady state. I mean, so there's a bit of electronics, so I used my electronics circuitry building. I built my own circuits for doing this, doing this work. I was—I pushed through misters to the kind of state of the art of the misters at the time, for measuring small [inaudible] temperatures. I measured oxygen evolution, CO_2 production, heat production, and within a calendar year finished my courses and finished my thesis.

DICK: Oh, real—one year?

COONEY: One year. And I had my second paper, which was on—which was actually an important paper at the time, correlating oxygen consumption with heat production. I essentially showed, for microorganisms, what people had showed for coal, that combustion in—by microorganisms, whether it's combustion by a microorganism or combustion of coal; you had the same correlation for rate of reaction, growth or combustion measured and correlated with oxygen production and CO_2 —oxygen consumption and CO_2 production. So it was a really cool thesis. It was fun. It worked. It was simple. It was a good master thesis. It was not a PhD topic. We got a paper, and—that was well received, <**T: 25 min**> and actually quite useful for—it's still useful today, actually.

DICK: Were you a—I mean, you know, going through coursework, your—master's project all in one year, I imagine—well, did you have time where you—? Did you have any extracurricular activities at the time? Or was it pretty much just…

COONEY: No, at that time, I just—I did do a little bit of rowing on the Charles. Not a lot. I liked hiking. I liked the outdoor stuff, which I continued to do a little bit of, not a lot. I really—I really pretty much hunkered down that first year as a graduate student, getting to know Boston. I had just gotten married, and so my wife and I were—you know, I was a student and she was a nurse. I had a chance to see biomedical engineering in action. I got to know the surgeons over at MGH. I would—they would invite me into the operating theater. Again, you wouldn't have that happen today.

But I used to bring them pizza. I'd sit up in the gallery and watch, and they'd come up on a break and eat pizza that I brought in. And this was during the night. And they said, "Well, why don't you come down. And you're an engineer—why don't you come down and take a look?" So I saw brain surgery, open-heart surgery. You know, stand you right over the patient, right in there. Those are experiences that, you know—seeing things in real time, you—it, again, was an important lesson. I always liked—I didn't do anything with the patients; I kept my hands off. [Laughter]

So I liked doing things hands on, but I didn't with any of the patients. That was a good thing. But you're there; you see it; you feel it; you hear it; you smell it. You're just sort of part of it. And that was a lifelong lesson, to always want to be there. If it's in a manufacturing plant—to this day, as a board member of companies, I've traveled around. Like, I go to the companies. I go in the lab. If it's a public company, with locations around the world, I stop and then I visit them. And if there's a manufacturing plant, I go there. I wanna see it. I wanna see things in action. I wanna know what it really is about.

So to this day, I do it all the time. And I've been in fermentation plants on every continent, and, you know, it's been a lifelong thrill to see manufacturing in action. And that's my passion, how to make stuff. It was when I was a high school student; it was when I was in college; it was when I was in graduate school; and it still is today. I like to take engineering and see it manifest itself in terms of products, services. Do useful stuff. I get turned on by steel and concrete. [Laughter]

But as a master's student, I had no aspiration to go on for a PhD. And when I did begin to think about a PhD, I was really at that time really excited about biology. Two other—no, three other people, important in my life academically. One was Sal Luria, who won the Nobel Prize in biology. And I took my introductory microbiology course with him.

DICK: Oh, wow.

COONEY: Boris Magasanik, who was one of the really key people in microbial physiology. I took microbial physiology with him. And even throughout my career here, I was on—he and I have been on PhD theses—committees together. And Gene Brown, who was later dean of science but taught biochemistry. The three of them taught me to really deeply understand microorganisms, microbial physiology, and biochemistry. And at one point I was looking at applying for a PhD into a biology department.

DICK: What led to this? You know, because you were going into the master's sort of thinking, "This is it." Maybe going to industry afterwards, or—what led to the shift in, say, <**T: 30 min**> thinking, you know, "I wanna go to a PhD program"?

COONEY: I liked being in the lab. I liked research. I liked—much more than I ever would've guessed. In retrospect, it's be—I think it's because I'm still an experimentalist. But, in retrospect, because I just like—I like doing stuff. I like learning. I don't mind making mistakes. I've certainly made my share of them. [Laughter] Learned from them. That thrill of going to a new place, and physically doing something different. That's also probably the reason I became very actively, later in life, engaged in high-altitude mountaineering. You know, going to new places, actively doing things, seeing things you just wouldn't have seen you know, in an armchair, or at low altitude.

So it was that sheer enjoyment. And working at interfaces. That's a theme that has been endemic to my career from high school forward—from grade school forward. I just like bringing different things together. And to me, that was a real experimentation. Biochemical engineering was that. So I took this intellectual excursion into—I was just really turned on by biology. And you can see from the people that I had teach me. Harvey Lodish was another –

DICK: That's right.

COONEY: I took his course in molecular biology the first time he taught a course at MIT. We later became good friends in founding Genzyme and I can share some stories about—nice stories about Harvey. But those were the people that I learned biology from. But then, as I went—I did that intellectual excursion, to really trying to think about doing the PhD in biology, I fell back to, "But I really like engineering." So I decided to stay in biochemical engineering. At that time, at MIT, it was within the Department of Nutrition and Food Science. Not within the chem-E department.

DICK: Interesting.

COONEY: And it wasn't until 1980-ish that biochemical engineering moved into chemical engineering. So here we are, on to graduate school, 1966. Got my master's in '67. Was going to do a different piece of research for my PhD. My thesis advisor was Dick Matelas, a colleague of Dan Wang's. And as I am embarking on my PhD thesis, which was on continuous microbial culture, Dick decided he would go on sabbatical, and then took a leave of absence in Israel. And I was left—but he was still my advisor in name. [Laughter] This is 1968, '69. There were no faxes. There was no internet. So we actually wrote letters.

DICK: Interesting.

COONEY: So, "Tell me about your progress, and what are your problems?" And I would send a letter off to Israel. By the time I would get a reply, I had long since solved the problem. [Laughter] And while Dan Wang was not officially my PhD advisor at that time, he really was the one who supervised my thesis. And I was—in the end, I was his first PhD student, in 1970. So I finished my—I finished my PhD pretty quickly, so I was—I did my master's and PhD in three and a half years.

DICK: Wow.

COONEY: Which was kind of fast, and so there I was, 1970.

DICK: Were you still doing, like, crew, and, you know, some other—? I mean, you're going really…

COONEY: No. Yeah, again, I didn't do a lot. I did the occasional hiking, outdoor stuff. Occasionally I would go on the river, but not very much. I ran, but I wasn't doing a lot outside. I was really—I was really focused on my—getting my degree. And<**T: 35 min**> then still not thinking, you know—still thinking I would go to industry, and interviewed at a couple of universities, and—but this is 1970, so we're in the height of the Vietnam war. And my draft number was a pretty low number. So I didn't have a lot of options. But one of them was to go to the public health service, so to do my military duty, I was active in the war protests and marched in the many things going on around Cambridge, and that was the thing to do. I mean, none of us believed in the war at that time. But I did believe that it was my responsibility to do military service. So I was going to go into the—and I had an appointment at the public health service. So I would've gone to NIH.

And then, finishing up my PhD—this is late ’69, and at that point, Dick Matelas decided to resign from MIT and stay in Israel. And so a position opened up, faculty position, which was the furthest thing from my mind, in—sort of in terms of staying at MIT. And so I said, “Yeah, it's an interesting idea.” And the way that—one thing led to another in conversation, and they offered me a position.

And I finished my thesis in January of ’70. I said, “Well, look. Let me do a short postdoc. Or let me do a postdoc,” which I did in industry. I went to Squibb, Squibb Institute for Medical Research, but really it was in Squibb Pharmaceutical Company. This is 1970, before they merged with Bristol Myers. And I worked in the—I worked in penicillin manufacturing. So I did research in manufacturing. I was working with forty cubic meter fermenters.

DICK: Wow.

COONEY: And doing—I mean, I was doing experimental design at scale, beginning to apply computer control at a very early stage. You know, computers were pretty rare at that time in industry. But we were doing monitoring and simple control. And I was working in the pilot plant, and doing—getting my data from these large reactors. And I had another pivotal moment in that experience. One, it was a terrific experience, because it was real hands on. I was really in the plant. And I was standing one day and went on a pillar in the bottom mixer, installing a probe, because we had to build and install our own mixer. So I built, physically built the probes that we put into the reactors. And you couldn't buy them at that time.

You had to build them if you wanted to do it. And we were measuring dissolved oxygen. So I'm standing in the reactor, forty cubic meter reactor, much bigger than the room that we're in, and—with the key to the motor in my pocket, on a—in a harness, on a rope with somebody at the top. [Laughter] It's kind of dangerous—

DICK: Yeah.

COONEY: —inside these things. But it's also a very hot day, but it's very cool inside the reactor. And I'm looking around, and I say, "Gee, this is what it's like to be a microorganism, standing here in this environment." And to this day, when I teach, I have a slide that says, "Think like a microorganism." Put yourself in the position of the organism and think about the environment around you at the micro scale.

And this has held me in good stead as a paradigm for doing research. You know, putting yourself in the place of the organism or the molecule, if you're a catalyst. Or wherever you are in—I've also done a lot of work in developing countries, and it helps there as well. And so I learned that. I developed this passion for manufacturing. And that's when I really <**T: 40 min**> fell in love with steel and concrete, you know, making stuff at scale. That's what I really liked doing.

And so then I had an opportunity, as I knew I was going to join the faculty in September of '70, which I did. To this day, a lot of my teaching revolves around, "Well, how do you convert technology to making something?" So at that time, biochemical engineering was about antibiotics; it was about foods. It was making—converting petroleum or methanol or methane to protein for use in animal feed. It was about making amino acids for uses—from supplements. Making enzymes for—eventually, for use as catalysts. And that's what we did research on. That's what we learned to do.

I would describe my early career—describe my late career, too—as really about the manufacturing science, process science. How do you bring together biology, chemistry, physics of engineering to make stuff? How do you operate a plant? How do you build a plant? How do you design a plant? And in those days, we were interested in single-cell protein. One of my early consulting jobs was with Dan Wang with a very large single-cell protein plant in Italy. And they—I mean, these reactors were four hundred cubic meters. They were big.

DICK: Wow.

COONEY: And I think there were ten of them. Eight or ten of them. And they were continuous. And I knew how to do continuous culture. And there were yeast fermentations. I had done a lot of early research on cultivation of yeast, particularly on methanol and hydrocarbons, but mostly on methanol. And it was like a kid in a candy store. These big

reactors, big centrifuges, big motors, you know, really making stuff to scale. The lesson I learned there was that in order to get a manufacturing plant to work, you also have to understand the politics as well as the business. And in order for that plant to operate, it simultaneously needed approval by the ministry of finance, ministry of in—no, ministry of health, ministry of industry, and ministry of environment. And the plant could never get all three to provide permission at the same time. [Laughter] At any time, they had two.

And they could never get the third. There was always wrangling back and forth. And this was Italian politics. And we can only speculate what the issues were. I won't—I won't. For the record, I'll spare the speculation. [Laughter] But, you know, mid-1970s Italian politics, in the south of Italy, in Calabria. There were a lot of interesting dynamics. But it was a great experience. Plant never operated, but—at least not commercially.

DICK: [Laughter] Where were you? Were you involved at all, in terms of getting in the politics, or was it just something that became clear that's something that needs to be accounted for, that—?

COONEY: I was not involved in the politics. I was only involved as a consultant to help them start up and get the plant running. But you couldn't help but become a witness to the political dynamics. And it's a—in Calabria, it was a—the Mafia was a big player in that particular region of southern Italy at the time. Maybe they still are, I don't know, but they certainly were at the time. So the politics were complex. And business was complex. I guess somebody made money in the process, but—no idea who it was. [Laughter]

But it was a great consulting gig. I learned a lot about large-scale equipment. And it also was—I did a lot of consulting from my very early career. See, business engagement in the 1970s, by an academic engineer <**T: 45 min**> was socially acceptable. It was not acceptable at that time for scientists, necessarily. Particularly biologists.

That becomes very important. So you jump forward to late ’70s, and the beginnings of biotechnology, and to the increasing interest for the biologists becoming involved, and scientists in general, in industry. As engineers, we worked with industry all the time. It was accepted as part of what you did. It gave you unique knowledge, which you could never use confidential information in the lab.

But you had that knowledge. You knew what was important. And it began to put me again at another interface, an interface between business and engineering, and business and science. So this goes into the early to mid-70s that I began to accrue that insight, that experience.

DICK: I know that, you know, Asilomar takes place in ’73. There's the, later on, the Cambridge ordinances. There's Boston Biotech begins to—Biogen starts up, and others. Were you, sort of, keeping up with what was going on in those areas?

COONEY: Oh, more than keeping up with it. So here we are, late 1970s, early 1980s. Cetus had been formed for a couple of years. But Cetus was—had an ambivalence about commitment to what we know now as biotechnology. But they had some really cool technology to take advantage of natural screening. It was largely robotics, but a good vision.

DICK: Did you ever interact with the—Cetus there?

COONEY: Oh, yeah.

DICK: Did you consult?

COONEY: Yeah, I—so in late 1970s, I had three opportunities emerge. Cetus, Genex, and Genentech. Dan had just joined Biogen as a founding scientific advisory board member. And so he wasn't available as a consultant, because you normally consult for one of these companies at a time. Okay. And there were only a few people who knew anything about manufacturing. So here you have now companies that want to take biotechnology and make stuff.

DICK: And they gotta scale it up.

COONEY: And they gotta scale it up. So you hire people from the pharmaceutical industry. But from a scientific advisory perspective, there were only a few of us available at the time. I mean, this is pretty exciting stuff. So late 1970s, I visited Genex in Maryland. I visited Cetus, and they went as far—they took me into the inner sanctum, introduced me to their core technology.

DICK: Who was meeting you at Cetus, and showing you around?

COONEY: Pete Farley and Ron Cape, and the guy I went diving with…Oh, the third founder. I'm drawing a blank on his name.

DICK: I think it—was it Moshe Alafi?

COONEY: No.

DICK: Or Donald Glaser?

COONEY: No, they were coming from the finance and the advising side. It was a triumvirate. It was Ron Cape, Pete Farley, and—the guy's name will come to me in a moment, but he had—this guy had taken probably about seventy—1978—see, Dan and I also taught a course to industry that we'd been teaching, or he'd been teaching, since about '67. I started teaching in 1970 in fermentation technology. So one of the founders of Cetus came and took this course about 1978, '78 or '79; '78 I think. And he was a diver. I'm also a scuba diver. And we started talking about diving, and he said, "Well, come out to California, and visit Cetus, but let's go diving." So shortly before that he had been bitten by—in fact, the way this Cetus got its name was that this guy—Cal Ward.

DICK: Cal, that's it.

COONEY: Cal—Cal Ward. So Cal had—he was a diver and a surfer. And he was out surfing with friends off the coast of California, <**T: 50 min**> and he got bit by a fish, big fish. And managed to—in the calf—managed to come in. He got in safely, but badly bit, and they thought initially it was a great white. And the constellation for the whale is Cetus. And they were looking for a name for the company, so they called it Cetus. So a couple years later, I went diving with him, and—which was great fun. We were diving in the kelp fields off of northern California, north of San Francisco. And diving in a kelp field, if you've never done it—

DICK: No, yeah.

COONEY: —I highly recommend it. It's like a forest. It's an underwater forest with these huge kelp in about thirty feet of water. And we're swimming in and out of the kelp, and I can—I'm following him. And it's easy to follow, because you look at the back of his leg, and you know it was a great white, because you can see the triangular teeth marks embedded in his leg.

Along with the other—where the other eighty or a hundred twenty stitches were that put his leg back together. So all of a sudden we're—we come out of the kelp, and we're in open water. Open water is shark territory. Cal's out of there. He's back into the kelp. [Laughter] And I go, "Where the hell is he?" So I figured out where he was, and anyway, we had great diving in the kelp, and then we went abalone fishing, which you can't do scuba; it's all free dive.

And I learned to dive for abalone with Cal. So you free dive with a tire iron. And the abalone sit like it's a big suction cup on a rock, and they're off the rock breathing and filtering the water to eat. So you got to free dive down, about twenty feet of water, and then you sneak up on the abalone with a tire iron, and flip it. So you take it off the rock. And of course, if it senses you there, it just clamps down to the rock. So the first time you do this—second time, you—so there's a technique. [Laughter]. Cal could get two at a time. I'd flip it, and you get it, and then you take your abalone, and—at which point, you've used up all the air in your lungs, and you wished you were up top. And you get back up, just sucking the last little bit of air out of your lungs, and you got this abalone. And so, if you're really skilled, you put them inside your wet suit. But you don't put the suction cup against your chest, or you get one big hickey. [Laughter] So you learn to put the suction cup to the—

DICK: To the opposite side.

COONEY: —to the, yeah, other side. So we got the abalone, anyway, we—and went back to his house, and had the freshest abalone that—if you've never had fresh abalone, it's just marvelous, got out of the shell and pounded it, and we grill it on the grill, and it was outstanding.

So that's how I met—that's how I met Cal, and I got to know Cetus, and I got to know Ron and Pete. So I went to Genex. I went to Cetus. And I knew Bob Swanson; I had met him a couple of years before, and Bob invited me out to Genentech. So I went; I did these trips. And I had the opportunity to become a scientific advisor to one of the three. And another pivotal moment: I was in—this was January of 1980, and I was with Bob Swanson and a couple of other people at the company. There must've been thirty, about—in fact, there were thirty employees at Genentech at the time. Building Three was their—just inside this warehouse. They had a small [inaudible] plant at the time. Bill Young, who was—had just joined the company from Lilly as the vice president for manufacturing.

And I'm in the conference room, thinking what a—you know, which of these three options—they were very different, each of which was very interesting. I was actually leaning towards Cetus. But Bob came in the conference room, and he sets this big bottle, probably about three inches in diameter, six inches high, sets it in the middle of the table. It was a little conference room right outside his office. And he said, "This is what we wanna make." This bottle was filled with a white powder, which in those days in California, you're—you're <**T: 55 min**> suspicious of what the white powder might be. [Laughter]

DICK: Yeah. [Laughter]

COONEY: But it was human growth hormone. Nowhere in the world at that time had that much human growth hormone existed in one place at one time. It was a big bottle of frothy,

white powder, of human growth hormone. And, you know, I'd talked to all the people, Dave Goddell and Arch Levinson, and that whole team, where—they were there at the time. And Bob just—I had known him for a couple of years. And I said, yes. You know? They made me an offer. My basis price of my stock was five cents. There was some nominal cash compensation as a consultant for so many days. And that began a decade of my commuting from Boston to south San Francisco.

Probably at least and probably eight times a year. Got the TWA flight at 6:00 [p.m.] out of Boston. Got up to my hotel room, which then was the hotel right adjacent to the airport. There's no hotel there anymore. It was a Hilton. I got up at 8:00 [a.m.] the next morning, and we'd work till 8:00 [p.m.] at night at Genentech, went out for dinner. It was my introduction to California wines.

DICK: Yeah?

COONEY: You know, we explored different wines each night. I worked two days like that, caught the 10:00 flight back to Boston, and I—it was my love affair with Genentech. And here you are. You've got recombinant biotechnology. They had done the deal with Lilly, and transferred that to Lilly. They were making human growth hormone, and this was their first product. The first product they made was human insulin, for—

DICK: It—for the—Lilly.

COONEY: Which was very important for the development of the company. Lilly had shown the faith, put their money on the table, to both validate the technology as well it gives—as well as give them the cash. Lilly and Genentech both got terrific deals. I mean, Lilly got it at a bargain, and they were there from the beginning, and they were quite good to work with. And Genentech got a start, and Lilly was important for that happening. So I came on board January of 1980, and being asked to, you know, "Help us build the technology to make this stuff." Nobody had done it before.

Nobody had scaled recombinant proteins. Nobody knew how to recover them at scale. It was just new territory. I was going onto a new mountain, although this was before my high-altitude mountaineering, but it was going onto a new mountain. It was going to a new place. Nobody had been there before. And here I had a chance to be a part of designing those processes. Their first manufacturing plant we designed in Bill Young's office, which was half the size of my office, on a blackboard.

Bill Young, Jim Schwartz, myself. We said, "Well, what would the plant look like?" And we started to sketch it out on the blackboard. And several iterations, and eventually, around that time, Genentech had also done a deal, an equity deal, with the engineering

company…Fluor. Yeah. It became Fluor-Daniel. It was Fluor at the time. And Fluor invested in—Fluor made more money, I think, on Genentech stock than any of the businesses that they were in. But they decided they wanted to become *the* place to go for an industry that didn't exist. They took the risk, and they wanted to design Genentech's first plant. Which, by the way, I was going through my attic. Those are the original drawings of Genentech's first plant.

DICK: Oh, really? Would it be possible if afterwards I took, like, maybe a photo of those, then?

COONEY: Sure.

DICK: Wonderful.

COONEY: Yeah, yeah.

DICK: Great.

COONEY: They're all marked up. I spent hours and hours over at the—these are PIDs—you know, marking them up and getting them right, and—<**T: 60 min**> You know, it hadn't been done before. And Fluor said, "I wanna do it," and they put money into the company. I guess they charged Genentech something to do the engineering work, but not much. And they learned how to design it, and it began with this blackboard in Bill Young's office.

And that was their first sketch. And then they got the lab notebooks from the people in the lab, and began to build the first plant at Genentech. And it just was, sort of—just kept on rolling from there. So for a biochemical engineer to be, you know, "Yeah, I'm doing my research here—" At that time I was not doing recombinant DNA work, although I started shortly thereafter. But I was doing work on enzyme catalysis. I was—fermentation for single-cell protein, fermentation for antibiotics, fermentation for beer—computer control the beer. Developing methods for computer control of bounds for processes, particularly fermentation. That's what my students were doing, and really learning how to apply engineering principles and biological concepts to make stuff. Make enzymes; use the enzymes to catalyze reactions; make the reactors.

I realized that there were very few people doing research in downstream processing, recovery of biological products, and I managed to convince Alfa Laval to provide us with a very large grant to build a small pilot plant, which we operated here at MIT, and had to begin a whole new program on recovery of biological products. So we began to do that as well as

fermentation. And that was yet another place for me to go off and get my hands dirty and [do] something different.

So I did downstream and upstream. Then we began to teach a course in downstream processing—an industrial course, like the fermentation course. And I just gave it for the twenty-eighth time a couple weeks ago.

DICK: Oh, wow. Yeah, I was there.

COONEY: [Inaudible] a couple weeks ago, last week. And that all came out of involvement with Genentech, involvement with other companies, understanding the industry. And, you know, I feel so privileged that even when I was a young student, I had the opportunity to know the people who had founded the fermentation industry—who had become part of it. And then to become, you know, before biotechnology was biotechnology, to really be in a position to be there from the beginning. Design the first manufacturing plants. So then, at the same time—so 1980-ish, '80 –

DICK: You mentioned Genex. Did you go down and visit Genex, and—?

COONEY: Yeah. Yeah, I went down to Maryland. [Yes].

DICK: Did you, like, meet with Leslie Glick?

COONEY: Les Glick, [yes]. Yeah, Les was the person who invited me down, who I was talking with. And who had invited me to be on their scientific advisory board. So it was—yeah, so it was the people who had founded the companies that I was working with at that time, and I knew personally.

DICK: *Hm*. Well, let's—yeah, let's go ahead and go—I apologize for interrupting there, and—

COONEY: It was—these were pretty neat people. They were really, really fine individuals, both on a personal basis as well as a visionary and professional basis. Hard hitters, also. Pretty assertive and aggressive in a business sense.

Which is what you needed to be to raise the money. So at that time, a group of us at MIT—George Whitesides, Chris Walsh, Harvey Lodish, Tony Sinskey, myself, Graham Walker, Phil Rousch, ChoKyun Rha—there should've been eight names in there. The eight

founders of BIA. A number of us had been approached in the late ’70s, early ’80s by venture capitalists as our colleagues had been. “Why don't you help us form a company? Here's some money.” And we quickly realized that there <**T: 65 min**> was plenty of money, but most of the people didn't know what to do, “So why don't we form a consulting group and advise them on what to do?”

So we had chemists, chemical engineers, microbiologists, geneticists, molecular biologists, material scientists, all with different disciplines, and we came together. We formed BIA, Bioinformation Associates. And we did a number of—a number of things. We did some multi-client studies. We decided that we could bring the literature and the field together into a single repository of information, critical analysis, better than anybody else, because we were looking at it from multiple lenses, very different perspectives.

DICK: How did you guys, sort of—were you even meet—? I mean, all these different disciplines, and—I know that you're, you know, were in contact with Lodish and others, but how did you all, sort of, just come together at—?

COONEY: We knew each other personally from MIT. We, in some cases, taught together. And we just thought it was a—we had created—there was this little network of people that we came together and over some beers and food. Probably Chinese food. Spent some time thinking about, “Well, what might we do? Who else should be involved?” And we didn't know what to do, that we really felt passionately about. We didn't have a particular technology to spin out of MIT, necessarily. And we became good friends. We had a lot of mutual both personal and professional respect, because we were all different lenses. We weren't competing with each other. We were looking at things through a different lens. And because we enjoyed working with each other, we had a real good time. And we made some money doing it.

So one of the projects was a consulting project. Genzyme was just being formed by Sherry Snyder and Henry Blair. And they—I forget how we first met them, but Henry came to us and said—well, no; Henry Blair was at Tufts, and Sherry was an entrepreneur, and we knew the venture group that was backing them both, Oak Management. Well, it was NTA Associates, Joe Littlechild, and NTA, and Ginger Moore at Oak. And they were looking at doing a deal with a microbiology depart—a group of faculty all in the same microbiology department. And we were asked would we take a look at this package, and they were thinking of bringing them all on as scientific advisors this way almost the whole department, or some subset of the department.

DICK: Where is this? It was the New England Enzyme Center, or—?

COONEY: Yeah, and I think I'm not going to quote which department it was. Because we rejected it.

DICK: Oh, okay. Yeah, yeah, yeah. [Laughter]

COONEY: At the time they said, "Well, rather than that, why don't we, BIA, work with you in the founding of Genzyme?" And that's what happened. The creation of Genzyme became, over a period of about a year, I think it was, a consolidation of four assets. There was the Tufts—the Cerezyme—NIH-sponsored Cerezyme project, or Ceredase project, at that time, extracting glucocerebrosidase from placenta. That was Henry Blair's work. And then two physical assets in the UK; one was Koch-Lite Reagents Company, which basically was in the UK equivalent of Chapter 11. And the other was the diagnostic enzymes division of Whatman Biochemicals down in Maidstone, and they were making a bunch of enzymes for using clinical diagnostics. And then BIA as <**T: 70 min**> the scientific—the eight of us as essentially de facto scientific advisory board.

And in doing that, BIA was—at that time, we were given a meaningful equity share in the company and a seat on the board, which I ended up as an—I was representing—I was a BIA individual, so I joined the Genzyme board. They hadn't yet hired Henri Termeer. And one of our first tasks was to help them recruit a CEO. Sherry Snyder is as good of a—listen, he's a real entrepreneur, but he's not a technically—he's not technically savvy. He would say that, and I would agree with it. [Laughter] And wanted to bring in some professional management, so one of our first tasks as BIA, working with Genzyme, as part of Genzyme, was to attract Henri. Or talk to the CEO to attract Henri.

DICK: Who? Was Henri, sort of, already in your sights, or was it looking around at other places that—and then—?

COONEY: There was a recruiter involved, and I forget who the recruiter was, who identified a number of people. Henri very quickly surfaced to, "This is a guy we would really like to bring on board." He was young, enthusiastic. He was then, and of course is today, a terrific people person. Willing to take risks. Really good at industry experience, though not in biotech, because nobody was—[inaudible] in those days. [Laughter] But they came from Baxter, and good— this is—his good pedigree, good chemistry, good personality, vision, a doer. And so I officially joined the board at the meeting previous to the one at which we hired Henri. And so at the time we sold the company, I was the longest-standing board member. The other of the original board had left. So I worked with Henri, very—as a board member, and as a member of BIA, very closely for almost thirty years. Again, you know, what a phenomenal experience. Genzyme was in a sector of the biotech industry that was discretely different than what Genentech was in, so I could—

DICK: You could do both, yeah.

COONEY: I could do both. Those days I was also a consultant to DuPont from the—this was DuPont's very early entry into—actually, I've been consulting for DuPont since the late ’70s, when they were just beginning to consider biological processing. Long, long before any of the current people in DuPont were engaged in the company, I was a consultant to the company.

In fact, I remember one of my consulting—one of my first visits to Cetus was as a DuPont consultant. And Cetus was trying to convince—that was when Cetus—this was late ’70s—that's when Cetus was just beginning to get themselves into the recombinant DNA, DNA business. And Josh Lederberg—it was the first time I had met Josh—did the presentation on behalf of Cetus to introduce—so that was one of my early teachers, if you will, in recombinant DNA technology. [Laughter] So that was quite fun. I was also involved in that time with Cowen and Sons. They're investment bankers. They did some early investing in the biotech—late stage investing, too. And actually, through Cowen I had a chance—I was an early investor in Amgen. So I bought—

DICK: That's a good—

COONEY: Before it was public I bought a few shares of Amgen at about four dollars a share.

DICK: Did you meet with anybody at Amgen?

COONEY: Yeah, I knew the early people. Dennis Fenton—I'd been a consultant at Pfizer. I consulted for Pfizer for seventeen years, <**T: 75 min**> from about 1974, maybe, through, yeah, through—’74 through 1990, I guess. So I consulted for Pfizer, and there we worked with antibiotics, a lot of penicillin work, citric acid. We had a lot of—again, process technology, large scale. So I worked very closely with companies, again learning how to make stuff. Tried to get Pfizer into the biotech area; I just could never. They just couldn't grasp the risk in the early days of biotech.

DICK: Yeah, well, how were they perceiving it? Or what—was it just some, “This isn't gonna go anywhere?”

COONEY: “Wait and see. Wasn't gonna—it might go somewhere; if it does, we'll eventually get into it.” But they just could never, never get their hands around. And I knew—I worked with senior management there; they just couldn't get it. But I had a good time doing it. Real, large-scale, process engineering at Pfizer. So I was happy. Big tanks, and all that kind of stuff. And I worked with DuPont in their—as I say, in their early days of getting into the business. And I was a consultant to Cowen and Company, who were early analysts and investors. I would work

with them on some of the due diligence that I had a chance to co-invest a couple of times with some of their investments.

So I get to know Dennis Fenton. I knew Dennis; in fact, I helped recruit him to Pfizer as a research scientist out of Rutgers when I was a consultant to Pfizer. And then I remember getting a call from Dennis one day about this opportunity he had at Amgen. And while I was conflicted—I was a consultant to Pfizer—I really encouraged him to take it. I couldn't say, take it, but I could get real enthusiastic about Amgen—Amgen's technology. [Laughter] And that was the best move he ever made.

And it was good for—it was good for Amgen, too. A loss for Pfizer, but—and Dennis was very pivotal. So I knew the early people and also the early management, or even some of the later management at Amgen, and followed them. Fun time, and to be part of it! At the level of working on the PIDs for Genentech, or help create Genzyme, and at the board level, I had done—I had been fairly early in my career, I got involved in corporate governance. And, again, it's an interface. It's the business-technology interface. And my first directorship was with Paul Corporation.

DICK: And what—?

COONEY: The Paul is one of the premier filter manufacturers, an important vendor for the biotech industry. In fact, the person who replace me on the board of Paul, when I came off the Paul board, then I got involved in another startup membrane company. But when I came off the Paul board, they liked the idea of having a scientist on the board, or engineer. So Jim Watson joined the—he followed me on the Paul board. And then, I've been involved in a bunch of large companies at public companies, as well as startup companies, from a governance perspective.

So then Genzyme was my second—well, it wasn't a public entity at the time, but eventually we did the IPO. You know, again, Genzyme was one of those privileges in one's career, and as Genentech was, to be part of something like that, and see it go from this disparate group of assets—fortunately we—BIA—agreed to do the Genzyme deal, to come together with them to create this company before I visited the Koch-Lite facilities in the UK.

Because that was an environmental hazard with an accident waiting to happen. <**T: 80 min**> Fortunately, it never did. [Laughter] And we cleaned it up, and it is now an absolutely first-class pharmaceutical site. Expanded many times over, using—they have one of the world's largest continuous manufacturing plants for pharmaceuticals at the Haverhill site.

DICK: What were they producing initially when they were—when Genzyme acquired—?

COONEY: Reagents.

DICK: Reagents, okay.

COONEY: Reagents. We liked it because they were making stuff. They had sales. One of the key things in the founding, the start of Genzyme was—exciting things about it— Unlike the other biotech companies, it had products and revenues from the get-go. Not very much; biological production of diagnostic enzymes. Chemical production of chemical reagents. Some custom synthesis. But we were making stuff, and we built the company around the paradigm of taking science to make things. So you can see why it was so attractive to me. Because it was about making stuff. And we just—we built it out from there.

DICK: So, you know, one of the—I'll certainly want to discuss more of the products, but the Ceredase of course is one of the early products. How was that thought in terms of a market? Sort of before the Orphan Drug Act was passed?

COONEY: Well, the Orphan Drug Act had—would've been passed before or passed like—So not—it was around that time.

DICK: I think it was eight—1983, I believe.

COONEY: Yeah. So it was being passed at about the same time that it was being developed. So you're asking how was the—what was the thinking about it before that? It was very simple. That there was an unmet need for get—and for children with Gaucher's disease. It was driven by NIH funding, because one of the early patients diagnosed with Gaucher's disease was a child of a scientist at NIH. And she was quite influential in getting NIH to work in this direction. The discovery was made that glucocerebrosidase was the missing enzyme. And Tufts, under the direction of Henry Blair, was under contract to extract this enzyme from human placenta and provide—and they provided the initial enzyme that was used in clinical trials, of which the son of the scientist was one participant. The first patient.

DICK: So was it Brian Berman that—?

COONEY: [Yes]. Yeah. And it worked. And it worked real well. I mean, it's an amazing drug. So then the challenge became, how do you scale it up? And so when Genzyme was formed, it took over the research project, the NIH-sponsored search project from Tufts, so embraced that, and then began to look at how you would scale it up from collection of a lot of placenta.

Originally the Boston area; eventually through an agreement with Institut Merieux in France, in Lyon, to gather and process placenta on a larger scale, and begin to manufacture and sell and provide, for a limited number of patients—first in clinical trials and then commercially—this product. So there wasn't a need at that time for the Orphan Drug Act to be in business. Of course, when that happened, it's, "That's great." Because the intellectual property protection for some of these products was not well defined.

It did become well defined for this product, because using technology that originated—the original idea was—Harvey Lodish in one of our BIA meetings with Genzyme staff—Henry and others [had] the idea to do glycoprotein remodeling. So that turned out to be very important for targeting of the Ceredase. <**T: 85 min**> So they incorporated the glycoprotein remodeling as part of the final purification process for making Ceredase, and we learned how to scale up. Now, scale up turned out to be as much about supply chain. How can you get enough placenta and process them appropriately with enough viral reduction? You know, placenta, human blood, hep C, AIDS, that's all emerging, and understanding of it, at the same time. We were fortunately able to put in a good viral reduction step early in the process, so that it wasn't a real problem, but it's always there as an overlay.

And we knew long term, placenta wasn't going to satisfy the market, although in the early days we had no idea how big it was. Well, we had an idea; it was just, it was wrong. We thought it was much smaller than it turned out to be.

DICK: I believe that Henry was sort of skeptical that it could be scaled up. That, you know, there wouldn't be enough placenta and whatnot to—

COONEY: Oh, from the very beginning he was skeptical that it could be. But he also recognized from the very beginning that it was a product that met an unmet need, and we had a very strong position to bring it to the market. So he drove that process, and he was an ardent supporter of Ceredase as a product. And we had to be innovative around supply chain. We had to be innovative around physically how you did the manufacturing. We had to be innovative about how you got paid for it. And the real business was—with these kinds of products, is the reimbursement strategy. People didn't realize that in the beginning. It's all about reimbursement strategy. How do you get someone to pay for these very high-priced drugs?

And the way you do is, recognize the value. So it's value pricing. And the value is: patients live, or they die. If they live, their quality of life is pretty bad. And as well as for their families. And if you treat them, the cost is exceedingly high, and the quality of life is very low. So we realized very early it was about value pricing, understanding how to work with patients and their providers, and every patient was a one-off. We knew every patient, because it was an unmet need, and the patients are globally distributed. And you also have to commit yourself to providing product for patients who—for whom you can't get reimbursement.

You can't leave them hanging out to dry. You've got to treat them, too. And that was fundamental to life at Genzyme. It was about the patient, and where you could get reimbursement at a price that was frankly a good deal for the governments and the providers, because it was value pricing, and it was an exceedingly good deal for the patients, because they lived. And they lived productive, healthy lives. With what turned out to be a family of drugs that are incredibly safe and efficacious. The adverse reactions to these products were essentially nonexistent.

DICK: How did—I know that, for example, there was an ODA report criticizing the high price. Were you involved in terms of, you know, those discussions, those debates over…

COONEY: Well, I was not involved in that ODA report. I couldn't be, because I was involved with the company. But I had been involved in a bunch of ODA reports, so I—we knew all the people. In fact, BIA had done a couple of ODA reports in other areas. What that ODA report did was to establish a dialogue around not just pricing but providing therapy for rare diseases. And this is even—these well <**T: 90 min**> fall under the Orphan Drug Act because the number of patients is miniscule, even compared to the Orphan Drug Act. It's in the thousands. And these are true unmet medical needs. And the science of biotechnology and all of its different pieces, not just recombinant DNA but all of the things that are embraced by biotechnology –

Enabled the industry to treat these patients—and produce the product, and treat these patients. Is a high price reasonable? Well, if you don't pay the high price, who's going—how are you going to—how are you going to drive the research for this whole class of drugs? And there was a very attractive margin, a very large margin, on Ceredase. And what happened to that money? It didn't get back to shareholders. It didn't get into any of our pockets. It one hundred percent went back into building the company, and multiple there—therapies for more and more patients. I think the model—I have no remorse or concerns or, you know negative feelings about the pricing.

It was what it needed to be to drive the industry and the development of new drugs. And that's where the money went. All of it. All that profit. Right back into more products. And, of course, the shareholders didn't see the cash flow, and the price of the stock goes up, so, yes, of course, employees made money on the stock; investors made money on the stock; banks made money on the stock. It's true for all the biotech companies, because they were creating value. But in all cases—Genentech, Amgen, Biogen—the money goes right back into the company and developing new drugs.

DICK: Well, [inaudible].

COONEY: Yeah. That's the model. And the US has paid a disproportionate share of developing new drugs for the world. I don't feel bad about that either. We can afford to.

So why shouldn't we, as a prosperous nation, be subsidizing global health? I think it's a good thing. And so I never complain about the price of medicine. I do think our system for reimbursement and the overhead that you pay for multiple insurance companies sucks.

DICK: Yeah.

COONEY: And is a waste of—a waste of money, but that's not—

DICK: That's a side issue that—

COONEY: —that's not something—I can't—if I could change it, I would. [Laughter] It's not where I have any influence, so it's—my opinion is my opinion.

DICK: Now, were you the…I know that in '84 there was enough Ceredase to treat Brian Berman with the first patient. Were you able to be there to see the results? I don't know if there's a reason why, but I'm just—

COONEY: No, I never met—personally I never met Brian or any of the members of his family, but of course felt like I knew them. We as a company knew all the patients. And I—later on I did meet patients as a part of my walkabout at a company. And I think I probably visited—I certainly visited more parts of the company than any other board member, and probably most employees as well. But, you know, in thirty years, you get a chance to do more than people who are there a shorter time.

DICK: Yeah, yeah. And being on the board that entire time. Some of the other products. I know there was early work on hyaluronic acid?

COONEY: Hyaluronic acid.

DICK: And how did that—I know that the facility for that was not built until the later '80s, but when did that begin? When did Genzyme begin, sort of, looking at that as a product?

COONEY: Well, it began with BIA. That, as a product, that came out of BIA. One of our members, Cho Rha, who is a material science person, had been working with hyaluronic acid. <**T: 95 min**> And she and Tony Sinskey, her husband, who's a microbiologist, also had been

involved in that work. And we started talking about it, and looked at the opportunity for biopolymers in medicine, and thought it would be—really be an interesting product to go after. And Genzyme began to work on it. So that was from the very early—started very early.

And the initial route was to make it microbially. Very interesting process. I was very actively involved in the scale of the technology. Built a facility and did some work here, but built a facility in the UK in Haverhill, outside of Cambridge, where Koch-Lite was. Developed quite good microbial production of the technology. Quite good technology for microbial production. And the challenge in HA was to get, initially to get very high molecular weight to get the viscous properties that gave it its value and it's function.

DICK: That's like post adhesion surgery, yeah.

COONEY: Yeah. And then we eventually acquired a company that made it from rooster combs. And while we were skeptical that rooster combs would ever be a viable way to make it, it's the dominant way of manufacturing today. And we have a—"we"—Genzyme. It's not "we," anymore. [Laughter] Has a plant in New Jersey that processes rooster combs. And the roosters are bred specifically. They have big—these big combs, and it has a very high content of HA.

DICK: Interesting.

COONEY: And so they built—but they did build a plant to make microbial HA, which was used for a while, but then the rooster comb material here turned out to be better.

DICK: Did you go visit? I know you like to be hands-on. Did you go and see the rooster farm, and…

COONEY: I didn't go that far. I didn't go to the rooster farm. [Laughter] I have spent time in the plant, and I've seen the combs coming in. [Laughter] But that's as close as I got to it.

DICK: Okay. Now, the other thing—so there's the Ceredase, which is from the human placentas, but when did, sort of, the idea to begin developing a recombinant version of Ceredase—

COONEY: Pretty early. Because exactly as you mentioned a moment ago, that Henry was concerned about being able to supply the market, both in volume and quality, because it was human-derived material. We collectively realized that there's—we were going to have to use recombinant DNA. So very early in the process, before it was scaled and commercialized, there

was beginning work on developing recombinant method. And the development time cycle, timeline, is lengthy from clone to market, it's a slow process.

So it was recognized that we should get a recombinant product on the market as soon as possible. It's sourced from—it's a very different source. It's a very different process. It was going to require its own clinical trials. It's not a biosimilar. This was before biosimilar was a concept.

DICK: [Inaudible] [Laughter]

COONEY: But it is a biosimilar. So we developed the product. It was [inaudible].

DICK: What was the difference? You know, moving from Ceredase to what became Cerezyme? In terms of—

COONEY: From the patient's perspective, none. From the production and marketing, supply chain is totally different process. Being there was knowledge from the placenta material <**T: 100 min**> about what the carbohydrate structure needed to be, so you could target it properly. And its behavior during purification. But it was a totally new process that needed to be developed. So new technology, new process. And the trick was to understand and learn how to manage the transition, because you don't say, "Okay, it's Tuesday, August 14. Let's switch today from one product to another." First of all, the original product was working successfully in patients, so you don't take a patient off of it if you're working successfully. So clearly, the new entry would be for new patients as a starting point.

DICK: So people who were not already taking Ceredase. And that would be—raise ethical issues in clinical trials if you're—

COONEY: Yeah. But, you know, you're going into clinical trials. You're going into manufacturing knowing a lot about how to design the clinical trial, and how to design the specs for your manufactured product. What it would have to look like. So a lot of uncertainty was off the table. We knew the market was there. We knew how to assay it. We knew how to characterize it, and we knew what it should look like. We had a good—we knew how to dose it. So a lot of uncertainty was technical uncertainty, and market uncertainty was—more market than technical. And then the product is in multiple markets, multiple countries.

Each country has its own regulatory. And this is a surprisingly poorly understood concept. And I think the FDA is beaten up too badly, or gets beaten up badly as a consequence. A regulatory problem—FDA doesn't—isn't doing it right. And that's wrong. The FDA is very good, and I served on an FDA advisory panel. In fact, I chaired one for a couple of years. So I

got to know the FDA quite well, and I've tremendous respect for the FDA and the challenges they work under.

But it's all the other regulatory markets. Every country has its own regulatory apparatus. So if you were in a product—if you have a product in five countries, how many regulatory approvals do you have to go through? Five.

DICK: Yeah. [Laughter]

COONEY: If you're in eighty countries, how many do you have to go through? [Laughter] So transition and switchover is non-trivial. And that was—that had to be managed. And we knew how to manage it. We'd learned because of the nature of the product that it was a rare disease. You were on a named-patient basis. A named-patient basis is actually a very specific term in Europe and other countries, where we knew all the patients.

We're also on a named-patient basis, but we knew all the patients. We knew who needed it. We dealt with the regulatory environment in a very direct and one-on-one basis. I mean, we took the product through. And you're only dealing with a few patients in each market, so you got to know the regulators. You got to know the reimbursement. You got to know the patient. So could manage—I think we, you know, we understood how to manage that market better than anybody, at a time when major pharma is saying, "All this isn't—rare diseases, that's not a real business." Now look at the model they're adapting.

Genzyme is very innovative, not just in its products, its processes, but everything about bringing a product to market, and bringing it to the patient. There was a reason that there was a strong patient focus.

DICK: Yeah, and I'll have to come back, especially to some of the sort of financial structures that were implemented at Genzyme. The various tracking stocks, which would later on—but the IPO is in June of 1986. You wanna just talk about the process of deciding to go public, and, you know, did you go on the roadshows, that type of thing?

COONEY: No, I didn't. <**T: 105 min**> The roadshows were done by Henri Termeer and Henry Blair, which is very typical. And I went with the investment bankers. We on the board, of course, were actively—obviously, you're involved in that and what is the right timing, and pretty exciting to do that throughout. Because at the time, we went—this time we did the IPO, biotech was very attractive to investors. And here we have products. We had cash flow.

Although what most companies don't realize is that one of the worst things that can happen to you early in your life is to have cash flow. Because then you have a basis on which to financially evaluate the company. If you don't have products or you don't have cash flow, then

you can—you're valued on promise. [Laughter] But we had cash flow, and we had a business, and—

DICK: And so it was good, because I know, you know, but you have the Genentech IPO, [inaudible] IPO, but then there's, sort of, the ups and downs of the market where—

COONEY: Yeah. Oh, yeah.

DICK: —you know, it can be very finicky. And was that, sort of taking into consideration in terms of timing the IPO that is…

COONEY: Oh, you like to think that you can strategically pick the best time. I think it's luck. Because of the—what drives a market up and down are things that are often beyond your control. So you do your best to time it when you think—in a window that you think is going to be attractive. So did we try to be strategic in that regard? Sure. Did we do it at the optimal time? I doubt it. [Laughter] But that wasn't because we didn't do it right. We did it as best we could, and took the market at whatever it was at the time. I forget what—I even forget what it was [inaudible] at. Well, it was so long ago. That's long history, long past history.

DICK: [Laughter] Let's see. So we've discussed some of the constructed new facilities for HA, the—was the HA facility, was that in Haverville also?

COONEY: Haverhill, yeah.

DICK: Haverhill.

COONEY: That was in—it was. And that's the site we bought outside of Cambridge. And then significantly expanded it. We kept expanding the footprint that—whatever land we'd come on available, we would expand. And we grew into it as quickly as we could buy the land. It's quite a large site. Very nice site. Nothing like the early days. [Laughter]

COONEY: When we [inaudible]. But, yeah. That's where we built the plant.

DICK: And then what—and there's a number of acquisitions being made; well, two early on, and then in 1989 Integrated Genetics comes in. And how did—I know that Henri Termeer and

David Housman, or Bob Carpenter at least, were in talks with one another. What were your thoughts, in terms of—

COONEY: Well, prior to that, we didn't have much in the way of recombinant biotech experience. We were a company making biological products and chemical products. We were making—we had a line of business in the diagnostics. And that was going quite well, although—is it, you know, you're selling into a fairly competitive environment. We knew we needed to bring recombinant DNA capability and capacity into the company. And you either bring it in organically—you begin to hire the people and pull it together, or you acquire. And Henri and David and Bob were—had talked about IG. IG was having trouble.

They were about to go under. So we started to take a look at it. And I remember my first visit to IG was on a Sunday morning, to out and visit the labs when there was nobody around. <**T: 110 min**> [Laughter] So we went out to—toured the facilities and visited the labs to physically see something that we might make an offer for, early Sunday morning. It was quite cool. And we liked what we saw. We were doing this without management, but people in the company didn't know that we were going to—whether we were interested in doing this. And then that led to the offer to buy the company. And that saved IG as a company, and it gave us capability that we didn't have and we knew we needed, because certainly then, we certainly knew we needed to do a recombinant glucocerebrosidase.

And IG not only came with the technology, they had some products. They had a couple of interesting assets. One was the transgenic goats, and we had no idea how to value the transgenic goats.

DICK: And what is that? Producing TPA in their, in the milk at—

COONEY: Yeah. And we looked at it and said, "You know, that was not in the value calculation." [Laughter] And we didn't know what do—we would do with it, except that we would keep it, and nurture it, and to try to understand it. Which we then later spun it out as Genzyme Transgenics. And then there was also another set of hormones, animal hormones, that we didn't see as being where Genzyme wanted to go, and we found so—as a buyer someone who wanted to—was very interested in these products. So we sold that off, and I forget what the net purchase price was, but at the time we sold off that asset and then looked at the purchase price, it became a very attractive financial deal.

Of course was an extremely good acquisition with really good people, and a new facility. And, again, a place where we could buy land around it and expand it. So the campus out in Framingham, [Massachusetts,] which embraces the original building that we bought with IG, is quite a large campus. There's sort of a modus operandi there. [Laughter]

COONEY: Once we get a footprint, we—

DICK: Expand there at the—

COONEY: I learned a lot about buying real estate, too.

DICK: [Laughter] Yeah, because that would be part of scaling up, is learning all these things that you don't necessarily consider that are involved. Did you—just, you know, a quick side—is that something that you bring up in your courses, in terms of, you know, these things that you don't necessarily think about, involved in scaling up, but…

COONEY: Oh, yeah, yeah. I mean, the lessons that I've learned from—going back to when I did my postdoc at Squibb, to seventeen years as a consultant for Pfizer, to Genentech, Genzyme. I then became involved in the whole—in Astra, before it became AstraZeneca. I was on the Astra board when we merged with Zeneca. So another—I voted myself out of a job there, also. [Laughter]

But I got—through that connection I got to know India, so I became involved, an investor in and involved as a board member at Biocon in India. And I'm still a board member, for twelve years now. So I was a board member at Biocon before we did the IPO in India. And there we sold off an—later sold off an enzyme business to Novozymes. So we now have a—what is India's largest biotech company. But again, in different areas of the business, so I could do that simultaneously with Genzyme.

DICK: Yeah, I think Biocon, I mean, it's kind of an interesting story with, I'm pretty—

COONEY: Kiran, Kiran Mazumdar.

DICK: Yeah, yeah. Her role. And did you go out and view the facility and everything? Or…

COONEY: Oh, yeah. I first got involved in India in 1989, I guess. A friend of mine who just became the CEO of Astra, when it was still just Astra, called me up, and said, "As I'm taking on this new position as CEO," he said, "I realized we had this asset in India, a research lab that'd been set up a couple years before." He said, "I don't know what to do with it." And he said, "Would you go and do an assessment for me? Take a look at it and come back and give me an opinion?" Sure. So I did.

I ended up recommending that if they did *A, B* and *C*, that this would be a good investment for them, for a research laboratory. The biggest part of *A, B*, and *C* was to actively engage not just leave it as off by itself to grow in isolation, but to really become part of the company. And they—he accepted the recommendations, and then they asked to be on the board of their subsidiary company, because they've had to have an Indian board and a Swedish board. And I sat on the board—I was part of the Swedish board, even though I'm not Swedish. Cooney is not a Swedish name. [Laughter]

And India's a very social place. And one of my former PhD students ended up going back to India and joining Biocon. And so I got to know, though my contacts in India, in Bangalore, I got to know Kiran socially. And then, since Arun Chandavarkar, who is now the COO—whenever I was in India, I'd just drive down and visit Biocon. Well, then it was just in enzymes, food and industrial enzyme company. So I just got to know him socially for a few—over a few years. And then one night in the early ’80s, early ’90s—when was it? Yeah, early ’90s. We were having dinner. There were about six or seven of us having dinner. Kiran, myself, and people from Astra and—we were talking about Mphasis and Wipro, which were just beginning, these companies, in the—and they're doing contract research in the IT space.

And as dinner went on, I'm sure it was helped by a little local wine. Why couldn't we do this in the chemical and biology space? And by the end of dinner, we all thought that was a pretty good idea. And Kiran was willing to take that on. So, to a person, we got out our checkbooks, and we wrote checks to Kiran. No contracts. Just said, “This is a good idea. Just get on with it.” And this was at a time before you could easily do foreign direct investment.

So we said to Kiran, “Here's the money. Take these checks. Cash them. Go start up this company,” which became called Syngene. It is now a hundred-million-dollar company. So we just gave her the checks, and said, “When you can figure out how to issue shares, issue some shares.” And a year later I got a certificate in the mail of some shares.

But in the meantime, Kiran just went along, and she started this little operation, Syngene, for contract research. And then later, she wanted to consolidate, so I did it once again, too. I invested in another small business with Kiran. And then she wanted to consolidate a number of small little companies that she had founded into a single company, and prepare to do an IPO a year or two later. So asked me to join the board as an independent director. Non-exec independent, which I agreed to do, since I was going to India regularly.

And then—that was twelve years ago. We did that, and I became a director of the company, and then began to go four times a year instead of once a year for Astra. And eventually I came off the Astra board, after it was—after they merged with Zeneca. And I'd already been on the main board. So I came off that board, too, when they merged. And we then, at the same time that we consolidated the different pieces of the company, decided to move to become a pharmaceutical company.

So we kept the enzyme business, but decided to go into making—using fermentation technology to make generic products, statins primarily And some immunosuppressants, but

primarily the statins. Not in the antibiotic space. A lot of people already in that space, but nobody was really in the statin space at that point. So we did that, and built it out as a pharmaceutical company, did the IPO. A couple of years after that <**T: 120 min**> decided, okay, Kiran was able and willing to bite the bullet and get out of the enzyme business that she had founded originally twenty-five years before that. So we sold that to Novozymes, a hundred million [dollars]. And at that point we were doing really well in the pharmaceutical space, and also beginning to drive the company to become an innovator company and not just a generic. And so they had a group of innovator products as well as doing quite a bit of business in the generic space. And they had the lot—they had the first and largest biologics manufacturing facility in India, and just launched last weekend the first commercial product, biologics—a novel, first-in-class molecule in India for psoriasis.

That's another, again, fascinating story. It's all about making stuff. It's about being willing to go to interfaces: biology, chemistry, engineering, biology, business, engineering. That's where the action is. That's where the fun is. And you don't have to stick to one thing. You can bring them together, and that can take you to a new place. And that's been the single mantra in my life, just by bringing things together, people together, technologies together. Go to someplace other people haven't been.

And then one of my kids wanted to do rock climbing, and that led to high-altitude mountaineering. We started doing big mountains. Which took me to new places and new experiences.

DICK: Were there any big mountains in particular that you really enjoyed?

COONEY: Well, yeah, that one on the wall. That's Ama Dablam. It's just south of Everest.

DICK: Oh, okay.

COONEY: Seven thousand meters— twenty-three thousand feet. That one, with my two sons and one of our guides, Huascarán in the Andes. That picture's taken at about twenty-thousand feet on the mountain. And you can tell it's nothing but snow—

DICK: Yeah.

COONEY: —given the background. Mt. Blanc, which is up there above the door, 16,500 [feet]. Denali, in Alaska.

DICK: So, serious—

COONEY: Yeah. And Kilimanjaro in—which is not a technical climb; that's a nice hike—in Africa. So [inaudible] mobile for continents. Some big mountains, and, you know, it's terrific times. And I learned a very important lesson in mountaineering. A very important lesson. It's about goals. That you need to have clarity of your goal, because you make decisions based upon your goal. And when you're up on a big mountain, what is your goal? And if you choose the summit as your goal, that's a death wish. Because if you start making decisions on the basis of that goal, you're going to take yourself into nasty weather, or on a route that isn't safe. And the result was deadly. Not liter—I mean, literally, not figuratively. So your goal is to all get back down. And then you realize that seventy-five percent of the accidents happen on the way down.

So getting down is more difficult than getting up. So, clarity of goal. And it's not necessarily the—it's not necessarily the most obvious. So, you—you know, whether it's manufacturing, whether it's drug discovery, whether it's out of the high mountains, clarity of your goal, and then making decisions consciously around that, is really important. So that was a life—that is a life lesson that obviously I've learned successfully, because I'm here talking to you. [Laughter]

COONEY: And you see death in the mountains. It's very humbling. It's a great environment. And my climbing partners are my two sons.

DICK: Oh, that's really nice.

COONEY: Yeah.

DICK: Well, one thing— Let's see. We're at about 11:15. I know that you'll need some preparation work.

COONEY: I have a—I have to stop at 11:45, if—

DICK: Okay. Okay, great. Great. So we have still a little bit more time here. I guess just some of the—well, I guess one thing would be the <**T: 125 min**> tracking stocks as a financial structure, and I'm just curious how that came about, and the goal or strategy behind that.

COONEY: Very relative, very simple. Like, the growth of any business that requires a lot of cash, it takes cash. So how do you finance your growth and your development? An IPO is one

vehicle to finance. A secondary offering is yet another vehicle to finance. A specific project with a large company, where you can have a combination of project financing and maybe even equity financing, is yet another vehicle.

So we, like every other biotech company, we—Genzyme— we're always looking for ways that we could raise the cash to finance the science, the technology, the scale-out, the product development that we believed was important and likely to be successful. So we became fairly innovative financially, as well as technically. And the tracking stock, we weren't the first to— you don't want to be the first to use new financial vehicles. [Laughter]

There were a number of examples, but none within our industry of tracking stocks. So the idea, the goal was to raise money to support specific projects to drive them to success. So that's what we wanted to do. So the concept of tracking stock is that you carve out a specific area of technology, some projects, products, a number of ways to define it. And that you raise money against success in that project, and you do so with a vehicle that is a tracking stock.

So it's a derivative of your primary stock, the—in the simplest since, you have the same board for the primary stock and the tracking stocks, but the tracking stocks are linked to very specific directions. Surgical products is one, one example. And we felt that this would be—and was—an effective way to raise the kind of money that you needed to develop those areas into products, and to give investors an opportunity to benefit by doing it. If it was just a project buried within the larger portfolio of the company, then the ability for investors to realize value from it is highly diluted.

If you separate them [inaudible] a tracking stock, then it can be attractive for investors interested in that area to have visibility onto that product, process, technology. So that's what we set out to do. And we raised money several times through tracking stocks. Each with its own market, or market cap, and the stock was traded independently on the NASDAQ exchange.

DICK: And I guess it gave investors, sort of, an easier way to understand what's going on, rather than looking at, like, you're saying, the larger—

COONEY: Yeah. Yeah. If I wanna follow surgical products, which is a very different business than Ceredase and Cerezyme this gives me a way to do it. And to realize value from success in that area. And you only would do a tracking stock if you believe that you could have success in that area. In retrospect, it's a fairly hard way to manage—

DICK: Oh, really?

COONEY: —manage your different projects, because you are walled off. You know, if you all of a sudden, you want to do a major change, or you want to do things that are cutting across different technologies, it creates some barriers to—

DICK: I see.

COONEY: —to doing that.

DICK: Is that—as you just said, 2003 that the tracking stock structure was eliminated? Was that partly why, is that—those constraints there that…

COONEY: Yeah. Yeah. I think <**T: 130 min**> we absolutely did it for the right reasons at the right time, but eventually, times change, and technology and science change, and businesses change. And it was a difficult way to operate. So I think we got out of—we were able to remove the tracking stock structure, and I think that was a good decision also, at that time, under those circumstances. So, you know, I mean, things change. The world evolves.

DICK: [Yes]. Well, here—and just to look at some of the products here, there are a few that I definitely want to cover, and the—certainly if there's any particular ones that you think are particularly important, certainly let me know. But the Fabrezyme, so you're getting more, you know, other, sort of, orphan drugs. How did the decision to go after treatment for Fabry's disease…

COONEY: Well, you need—to be successful in these kind of products—and we learned this from Cerezyme—Ceredase and Cerezyme—you have to have a disease that is amenable to administering an active enzyme. Or it could be another molecule, but there's this whole class of liposomal storage diseases—there are many others, as well, hemophilia being probably the most well-known, and certainly dwarfism, with a lack of active human growth hormone is yet another. So you need a disease that is treatable by an agent that you can make. That's the fundamental science.

Okay? You have to be able to deliver it to the patient in a way that it is effective to the patient. And there has to be enough of—it has to be a really unmet medical need that is not being addressed by some other alternative, otherwise you're in competition. And if there's one—there's something that's already there, the market is already being satisfied. Now, if it wasn't being—if it was being satisfied by something that wasn't adequate—the whole strategy behind MS is an example of that—where you could come up with something better, that works, too.

But for Fabry's and for Gaucher's and Pompe—these were diseases that were amenable to administering replacement therapy and having it work. So you've got a market. It's an unmet need. You can expect that you can get reimbursement for the product. And you have also worked with the technology that's necessary to make it and deliver it. So it's not just making the product; it's making and delivering it to the patient.

So you have to know the whole supply chain. The physician, the community. How are the patients diagnosed? So you need to understand that. You need to understand how you get it into the supply chain, and can you deliver it to the patient? I mean, who delivers it? Is it lifelong? It's probably lifelong therapy. Can it be reimbursed? Are there enough patients to make a business? I mean, ideally, you would like to say, "Ha—One patient. I can save one life." But it has to be more than that to make it work. But it doesn't have to be a lot. I mean, these are small diseases.

And you could do real good. And so we—there have been a lot of learnings from Gaucher's, and how to manage that whole process. But it's a very holistic approach. It's not just, "Oh, let's make a product, and people will come to buy it." It's a much—It's a much more deterministic path that you have to follow.

DICK: And then there a number of other things I—and I don't want to go through all of them, but are there any other products that you think are, you know, particularly revealing in terms of how Genzyme works, or that posed particular problems that had to be resolved?

COONEY: Well, I think there's several. <**T: 135 min**> One of the things that we did as a company was to constantly look for unmet medical needs where innovation in technology—primarily biological science—could make a difference and deliver value to that patient. And that led us down a number of very interesting paths, some more successful than others.

The whole tissue engineering area. One of the things that we did early was to develop Carticel, for patients with these defects in their knees, where you would take autologous cells from the patient, grow them out, expand the cell population, and then reinject them in the patient. And you could deal with these knee defects. Other joints, too, but the knee was in particular. Very tough business. Product, very successful. We were going into a very new supply chain, a very different kind of business, autologous cell replacement therapy, and it was tough. I mean, the business is still there, but it's not big.

It never grew the way we expected, and nor did we necessarily understand how orthopedics would take to it and use it. And we developed some very innovative technology for autologous cell expansion, everything from how you ship it to the company; how you expand it; how you ship it back to the patient. I mean, even, you know, knowledge of shipping containers. And understanding FedEx. [Laughter]

Very interesting, you know, from my point of view, I learned a lot. Tough business. And so that whole cell replacement therapy—I think we were ahead of our time. A lot of the things we did were pioneering. They were businesses, but not—certainly not blockbusters. Gene therapy—very early players in gene therapy. Probably—Genzyme probably has the largest patent to [date] in gene therapy, both of a tome development as well as things that were patent—intellectual property that was acquired.

The scientific team—second to none with—in gene therapy, within the company. But it's just been a very slow process to come to a sufficient scientific understanding of all the implications of not just the safety and efficacy, but how you deliver, and what diseases are appropriate, and how you treat patients. It's beginning to become a real business. And certainly beginning to have some traction in the marketplace, because it's successful with some diseases. But we were very early players, put a lot of money into gene therapy, and learned how to manufacture, learned how to deliver, learned all the different parts of the business. Worked in multiple diseases. And it's just now becoming a business. It's been much, much slower than any of us would have thought when we made the decisions to embark down that path.

The Genzyme Genetics—the genetic testing business. Again, very innovative in terms of building out the business. Consolidated a number of companies in building Genzyme Genetics, which was eventually sold before Genzyme was sold as a very successful freestanding business. Genzyme Diagnostics, the roots of that are at the very beginnings of Genzyme, and with the inclusion of the Maidstone diagnostics business.

Very different markets. Genzyme consistently would be willing to take the risks, both with innovative technology, innovative markets, putting businesses together, and <**T: 140 min**> was very good at doing acquisitions and integrating the people as well as the technology from those acquisitions. That was a core competency that the company had. A lot of companies have very difficult times doing an acquisition and integrating people and technology. We were good at it. We were very good at it.

DICK: Yeah, I wanted to, you know, as we're beginning to get to our end of time here, if you could discuss the—in 2009, there's the manufacturing problems arose. And if you could just speak a—you know, how did that occur? What were—how was it dealt with?

COONEY: Well, it was dealt with very aggressively. The occurrence of viral infection in animal cell culture—large-scale animal cell culture—had been well known for a long time. When it happened it us, at that point in time I knew of nine or ten other companies that had had similar problems. A couple of those were known publicly. All of those companies came to us and said, “How can we help?”

There was a very appropriate sharing of—this was seen as an industry problem, and the industry came together to try to solve it. Everyone else who had had the problem with viral infection, it was nonmaterial to the company and was dealt with without any material impact to

the company. It got public exposure for us because it was material, and that's because we had an inventory shortage. I'll come back to that.

So we had the viral problem. Why did we have it? To this day, it's not clear what the source of it is. And for all the companies that had the problem, for most of them, they don't know where it came from, but it happens.

But what you do is clean up and change how you process. But here we had been in the business of manufacturing with animal cell culture products for a very long time, fifteen-plus years, and it had not been a problem before. So we made the assumption by how we operated that we knew what we were doing. We thought we were doing everything right. And the evidence for that is that we had not had a problem. So we thought—and so you don't go and change things; that has another implications if you're doing it right, and by all indications, we were. We knew that we had a capacity issue coming up, because three years before this we had started to build two new plants, expand Framingham and expand in Hale, that facility. So we made the commitment to build capacity, and it takes four to five years to bring new capacity online. So we knew where we were. We knew that we were going to need new capacity, and we were putting hundreds of millions in the ground to expand that capacity.

And we had a product, Myozyme, which turned out to have a much higher dose than originally we had thought. That puts constraints on capacity. And the drug was extremely effective, safe and efficacious. So it was a high dose, but it was very safe and efficacious. And it saved the lives of patients, particularly kids, young children.

So we knew we were going to have a period of capacity constraint. We could have said we're going to manage with a certain amount of inventory, so that if there were a problem, you didn't—there was no reason to believe there would be, but the industry tries to manage with a six-month inventory in general, or longer in some cases, just as a matter of course. Or, we could treat the population of patients that needed the enzyme. So it was a very simple decision. Do you manage your inventory, or do you treat the patients?

And the patients are alive. Okay? <**T: 145 min**> Kids are alive, or I manage my inventory? And that decision was obvious. Our whole culture, our whole life, was about treating the patients. So we took a risk, and we thought it was a reasonable risk because we had not had any manufacturing problems before. And then the proverbial shit hits the fan, and you have an infection. And you have to shut the plant down. And a viral infection is very difficult to get rid of. And you try and do an investigation, find out what the source is, but, you know, this just—it's very difficult to do. And most people never really identify what the real cause, the source of it was.

So it hit us. It hit us at that time when we had vulnerability on our inventory, because we had chosen to provide drug to patients. So it had material impact. And it took the air out of the stock price. And they didn't come back to us investors, and that is a public story that's been seen and told over and over again. And in response to the [inaudible] investors, then they want to drive the sale of the company. And Sanofi stepped forward and one thing led to another. In the

meantime they did a very heroic effort; amazing what was done to turn that plant around. Replace everything. Sterilize, I mean, the entire building. Not the entire building, but the production suites.

They were going after flies with sledgehammers, which is what you need to do. They pulled out—there were no stops, in order to turn the plant around. But it takes time. And that puts some patients on restrictive supply. Couldn't survive—couldn't address new patients, and we had to manage it. But because we knew every patient, we could manage every patient. Other companies did come in with products. It gave Shar [inaudible]—and Shar did a really good job of how they managed their entree to the business. And they dealt with it in a very responsible manner. So, fortunately for patients, there were some alternatives that emerged. You know, for us it's a competitive product. But what we really care about is the patient.

So, I mean, that was a good thing. That was the good news, that those patients could be treated.

DICK: Yeah. Well, I'm thinking we got about five minutes here. And I know you're involved at the—with other companies, and perhaps, you know, we could talk over the phone or meet up another time, if you'd be open. But, if you wouldn't mind, I would love to take some photos of the early Genentech plants. I think that would be very –

COONEY: Oh, yeah, yeah. [Inaudible]. I suspect that we have—

DICK: It's okay. Yeah, yeah. And any—

COONEY: [Inaudible].

DICK: If there's any issue, just let me know, and—

COONEY: The drawings that are sitting here on top of my still.

DICK: Yeah. [Laughter]

COONEY: So that—this is a still circa 1930s from backwoods of Vermont.

DICK: Oh, really?

COONEY: For moonshine. [Laughter] Yeah, these are—you know, things were done very differently back when I was [inaudible] because see, my notes were on the original drawings. What I was thinking of doing is framing them, framing one of these, anyway. I wouldn't frame them all, but—

DICK: Yeah, yeah. No, I think that's—

COONEY: But, you know, these—have you ever looked at PIDs, and… I mean—

DICK: No. Very—

COONEY: This is—you know, you're looking at every valve and tank and sensor. We spent hours and hours and days and days over this stuff. This is the continuous sterilizer. So that'll be fun.

DICK: Yeah, yeah, <**T: 150 min**> and—

COONEY: [Inaudible].

DICK: —it certainly—and it looks like we're also collecting items for archives. You know, oftentimes you have things that'll be in attics or in basements. And obviously, you know, certainly people are getting ready to sort of toss things out, "Well, wait—" What we—I know that we find those things very valuable.

COONEY: I will keep that in mind.

DICK: Great, great. Well, let's—

COONEY: Fine, yeah. Let's see, a video card, also.

DICK: Oh, great, great.

COONEY: One of the other things I do, I'm the faculty director of the Deshpande Center. Somebody—we founded it ten years ago to identify early-stage technologies at MIT that have potential to spin out to companies. And we've been very successful, spun out twenty-seven companies.

DICK: Wow!

COONEY: I've committed, at MIT, 12 million [dollars]. But those seventy-seven companies have raised over 450 million [dollars]–

DICK: Wow.

COONEY: —in venture financing. So it's been a terrific experiment, in terms of how you accelerate the commercialization of technology.

DICK: Yeah, yeah.

COONEY: Which is what I needed to talk about in just ten minutes.

DICK: Even then—well, thank you very much for sitting down and—

COONEY: Well, it was this—I hadn't reflected on some of those early days in a very long time, so I hope I didn't ramble too much. It was—

DICK: Oh, no, no, no. Not at all.

[END OF AUDIO, FILE 1.1]

[END OF INTERVIEW]