

Robert Vince Ph.D.
Narrator

Lauren Klaffke
Interviewer

ACADEMIC HEALTH CENTER
ORAL HISTORY PROJECT

UNIVERSITY OF MINNESOTA

ACADEMIC HEALTH CENTER ORAL HISTORY PROJECT

In 1970, the University of Minnesota's previously autonomous College of Pharmacy and School of Dentistry were reorganized, together with the Schools of Nursing, Medicine, and Public Health, and the University Hospitals, into a centrally organized and administered Academic Health Center (AHC). The university's College of Veterinary Medicine was also closely aligned with the AHC at this time, becoming formally incorporated into the AHC in 1985.

The development of the AHC made possible the coordination and integration of the education and training of the health care professions and was part of a national trend which saw academic health centers emerge as the dominant institution in American health care in the last third of the 20th century. AHCs became not only the primary sites of health care education, but also critical sites of health sciences research and health care delivery.

The University of Minnesota's Academic Health Center Oral History Project preserves the personal stories of key individuals who were involved with the formation of the university's Academic Health Center, served in leadership roles, or have specific insights into the institution's history. By bringing together a representative group of figures in the history of the University of Minnesota's AHC, this project provides compelling documentation of recent developments in the history of American health care education, practice, and policy.

Biographical Sketch

Robert Vince was born in Auburn, NY. He earned his bachelor's degree in pharmacy from the University of Buffalo in 1962. He then completed a Ph.D. in medicinal chemistry at State University of New York (SUNY) at Buffalo in 1966. After completing his doctorate, Dr. Vince became an assistant professor at the University of Mississippi, but then pursued a position at the University of Minnesota's College of Pharmacy, where he became an assistant professor in medicinal chemistry in 1967. Dr. Vince has contributed to and developed many drug interventions over the course of his career at the University. Most notably, Dr. Vince developed the HIV drug abacavir in 1987, which was commercialized by GlaxoSmithKline in 1999 as Ziagen and resulted in over \$600 million dollars in revenue for the University. Through his portion of the proceeds from the sale of Ziagen, Dr. Vince established the Center for Drug Design in 2002 as an independent entity within the Academic Health Center to support academic research and drug development. Dr. Vince continues to direct the Center and conduct research.

Interview Abstract

Dr. Robert Vince begins his interview by describing his interest in science and medicine generally, his graduate research, and how he came to be professor at the University of Minnesota in the College of Pharmacy. In relation to his research while in the College, Dr. Vince discusses the following: his research on antibiotics and drugs with anticancer activity; the transition between exploring natural compounds and the creation of synthetic compounds within medicinal chemistry; issues he encountered in research attribution; his work on anti-herpes drugs; patenting issues in academia and the passage of the Bayh-Dole Act; and compound testing for activity against the AIDS virus. He then reflects on the development of the Center for Drug Design and developments within the Center. Discussing the history of the School of Pharmacy and the AHC more broadly, Dr. Vince covers the following topics: Lawrence Weaver's tenure as dean; the clinical emphasis in the College of Pharmacy and the creation of the PharmD program; teaching and continuing education; the role of the PharmD in medicine; Gilbert Banker's tenure as dean; the growth of the College of Pharmacy; the position of the Center for Drug Design within the AHC; and the merging of the positions of vice president of the AHC with dean of the Medical School. Dr. Vince concludes his interview with his recollections of former President George W. Bush's visit to the University in July of 2002.

Interview with Doctor Robert Vince

Interviewed by Lauren Klaffke

**Interviewed for the Academic Health Center, University of Minnesota
Oral History Project**

**Interviewed in Weaver Densford Hall
on the University of Minnesota Campus**

Interviewed on August 6, 2013

Robert Vince - RV
Lauren Klaffke - LK

LK: This is Lauren Klaffke. It's August 6, 2013. I'm interviewing Doctor Robert Vince in his office in Weaver Densford Hall.

Thanks for meeting with me today, Doctor Vince.

RV: You're welcome. Thank you.

LK: I wanted to begin by asking you where you were born and raised and how you became interested in pharmacy and medicinal research.

RV: Medicinal chemistry.

Well, okay. I was born in Auburn, New York, which is right in the center of the Finger Lakes Region of New York State. I went to high school there.

I was always interested in science, chemistry, and physics. One of the things I was interested in was medicine, but I didn't want to go to medical school. I didn't want to be a physician. I wanted to be more of a scientist. At that time, I decided to go into pharmacy, because pharmacy then was a lot of basic science, a lot of chemistry. Then, there was the medical aspect of applying the chemistry and science to developing medicine.

So I went to pharmacy school. I worked in a pharmacy during the summer. Then, I decided in about my sophomore year that I didn't really want to be a pharmacist. I

wanted to do research. So when I went back to the State University of New York at Buffalo, College of Pharmacy, I asked one of the professors if I could work on a research project. He was new there. He was in the medicinal chemistry department. He was the chair of medicinal chemistry. At that time, all the medicinal chemists were doing chemistry, mostly trying to synthesize natural products. A lot of the courses, even in the pharmacy school, were geared toward the chemistry of natural products. So that's how I got started.

I started on a research project isolating materials from a plant, alkaloids. My job was to isolate these alkaloids and see if I could purify them. They were from a plant called *ceanothus americanus*. There were alkaloids in there that caused clotting of the blood. In fact, maybe back in the cowboy days, they used to pack extracted teeth to stop the bleeding. People carried it around.

LK: Ohhh.

RV: It's also called [New] Jersey Tea for some reason.

So I started doing that as an undergraduate. I isolated these alkaloids and, then, someone published a paper where they did the chemical structure of one of these alkaloids using x-ray crystallography. I thought, they're taking all the fun out of chemistry. I'd rather do something else now.

So I went back to my professor and asked him if I could work on another project. He gave me another chemical project. It was pure chemistry, rearrangements of molecular molecules. So I published two papers in the *Journal of Organic Chemistry* based on that research as an undergraduate.

Then, I decided to go into graduate school and work with a professor whose name was Howard [J.] Schaeffer. I told him, "Look, I want to work on something that's more biological." I was taking a course on DNA [deoxyribonucleic acid]. I went back and said, "Can I work on this project trying to take one of the enzymes that is involved in DNA production and break it down and, maybe, try to design molecules that will inhibit this enzyme?" So, then, we started to do that. That's what I did for my Ph.D. thesis.

LK: Okay.

RV: I don't know how much detail you want on that, but that's how I got into graduate school. I got a Ph.D. in medicinal chemistry.

I went to the University of Mississippi my first year as an assistant professor. I had a hard time getting things started in Mississippi. Things were kind of slow there.

I found out there was an opening here at [the University of] Minnesota. I applied for it. I came up here, and they hired me as an assistant professor.

LK: How was the environment at Minnesota different than the environment at Mississippi or the organization of the school?

RV: There were a lot of things at Mississippi that I wasn't used to. I was from the north and a big city, Buffalo, and a big university. There was a medical school there so they had all the medical journals and all the chemistry journals. When I went to Mississippi, I started doing research. I'd go to the library and start looking for journals, and they didn't have most of the journals. One day, I complained to the librarian. I said, "You know, you don't have any of the journals that I would expect."

She said, "Why don't you find out what journals we have and design your research around them?"

LK: Ohhh.

RV: It was that type of thing. I just couldn't get going. Things were really slow. When you ordered something for your research, it would take a long time for it to come in.

So I actually wrote back to Howard Schaeffer, and he said, "There's a position at Minnesota. They're looking for somebody with your background, somebody that does chemistry and also applies it to biological projects."

Actually, they told me that they had already selected someone. The chair of the department said, "I'm going to a meeting in Las Vegas. It's an American Pharmaceutical Association meeting. If you want to come down there, I'd be willing to talk to you." So I went to the meeting, and I talked to him. His name was Ty [Taito O.] Soine. I talked him into inviting me up here for a seminar and an interview. I came up and before I left, they told me they were going to make me the offer.

LK: Oh, wow.

RV: I said, "If you're going to make an offer, I have to know by July first, because it wouldn't be fair for me to let Mississippi know later that I'm not going to be there." So on July first, I got a call and a telegram from the dean here who was Dean Larry [Lawrence] Weaver offering me the position. He also sent me a letter. I have the letter up on my bulletin board.

LK: I saw that!

[laughter]

RV: That was, like, what, \$12,000 a year?

LK: Yes.

[laughter]

RV: That was a big salary then. It wasn't salary I was looking for. It was just some other place where I could get going. I knew Minnesota had a good reputation in medicinal chemistry. Medicinal Chemistry was the big department in this college for about seventy-five years. They had quite a reputation, so I was happy to come here.

LK: You said you published two papers while you were an undergraduate. Is that unusual?

RV: Well, I don't want to say, "Yes."

LK: [laughter]

RV: Back then, it was. I think it still is, yes. There might be more opportunities for undergraduates to work on a research project now than there were back then. I didn't know anybody else who had done it. At Buffalo, we had some other students who started some research projects but they didn't publish anything.

These two papers were called "Molecular Rearrangements of Cyclic Beta Diketones," so you can tell it was just chemistry. What happened was the professor told me to make this material in the lab, make this compound, and I went to make it, and you know from chemistry what you expect to get from a chemical reaction. Well, it didn't give that. It gave me something completely different. We couldn't figure out what happened. So my job was to find out, and we found out the molecule had rearranged into something else. In the process of finding what this product was that formed that we didn't expect, I ended up with two papers just on the molecular rearrangements that we discovered that were a new type of chemistry.

LK: You said you had gone into your undergraduate work wanting to do pharmacy. Did you switch your major from pharmacy to chemistry?

RV: No. Actually, I spent one year at a community college in my hometown and, then, I went to pharmacy school. Pharmacy school wouldn't accept a lot of the courses that I had taken. So I went to talk to the dean during the summer before I started school. I said, "I want to take twenty-one credits a semester so that I can finish in three years." It was a four-year program, and I had already taken one year. He said, "No, we've never had anybody take twenty-one credits. You can take seventeen." I started going to night school and day school. Then, I took courses during the summer and stayed and did research projects during the summer, too. That helped. So I was able to graduate in the three years, but it hurt my grades a lot.

[chuckles]

LK: You were busy.

RV: I became the lab instructor so that I could make some money, also.

LK: Oh, wow.

RV: My parents had only gone to the eighth grade.

LK: Oh, wow.

RV: We didn't have a lot of money. I had to get loans, just like people do now and, also, try to make some money so that I could pay for things.

Then, I went on to graduate school. When you become a graduate student, they start paying you as a research assistant. So I started getting a little more...\$2400 a year.

[laughter]

LK: Then, you made the big money, the \$12,000.

RV: Yes, that sounded great. Geez, \$12,000.

LK: When you came to Minnesota, you were very much looking for a strong research environment. Did you do a lot of work with the basic sciences, as well, or was there a lot of support...?

RV: When I came here, I had already applied for some grants while I was at Mississippi. Two of them got approved by the NIH [National Institutes of Health]. But before they even started giving me the money, I had accepted the job here. So that was all transferred here.

LK: Okay.

RV: I was interested in some antibiotics, and the idea was that we would study how they worked and try to make derivatives of them, make better antibiotics, etcetera. So I was doing chemistry. I would hire people like post docs and I had graduate students when I was able to attract some. I was kind of young at the time, so a lot of students didn't want to work with me at first. I was, I think, twenty-six when I came here.

LK: As an assistant professor?

RV: Yes.

LK: Wow.

[chuckles]

RV: I got some post docs, and they usually had a Ph.D. in chemistry. They would do the synthetic chemistry. Then, I hired a technician to do the biological work. The technician

would take the enzymes we were working with and take the materials that the chemists made and test them on the enzymes.

Then, we were interested in antitumor activities, so we were working with mice. The NIH used to do a lot of testing on anticancer agents, and they would use mice. So I went and spent a week there to learn how to do this mouse work. Then, I would teach my technician how to do that. So we started doing that.

When we tried to get more grants on the antibiotic area, the NIH said that there wasn't much interest in antibiotics at that time. One of the antibiotics I was working with also had anticancer activity, so I switched over to the anticancer part and sent the thing back in, and got it funded.

LK: I saw you had a lot of funding from the National Cancer Institute.

RV: Yes, and I did, right up until the time that I started getting royalty money from a drug that we designed here.

LK: Is that Ziagen?

RV: Yes, Ziagen. Then, I really didn't apply for grants anymore, because we had this Ziagen money. So I was able to use that.

LK: I read the book that [Yusuf] Abul-Hajj co-wrote on the history of medicinal chemistry here. There was some discussion in the book regarding a transition between natural compounds and the creation of synthetic compounds within medicinal chemistry. Do you have any comments on that transition?

RV: It was slow. When I first came here, we even had a department called Pharmacognosy, which was the study of plant materials. A lot of pharmacy was based on that type of thing. Most of the people were working on plant products—natural products, they called them—but, then, as they found out how these drugs work and that they inhibit certain enzymes and more and more information became available, instead of relying on trying to find some natural product that might do what you want it to do, if you knew what the target was, you'd figure, if I inhibit this enzyme that's going to stop DNA from being produced and, therefore, this might have antitumor activity, so then you could go back and start designing your own molecules. You didn't have to rely on the natural product. So people started designing molecules if you knew what your enzyme target was. You can think of an enzyme as being kind of like a jigsaw puzzle with one piece missing. That piece missing, that little hole there, is designed to recognize a molecule of a certain shape that would fit into that hole. If you know what that hole looks like, you can go back and design a molecule that will fit in there. While it's blocking, sitting in that hole, the thing that the enzyme is really looking for can't come in. So it blocks it. Most drugs now are based on blocking some enzyme or fitting into some site in a receptor that's already built into your cells, which are just like enzymes. So scientists also started taking these natural products and modifying the molecules so that they would

fit better into these sites. You find a natural product that maybe inhibits your enzyme but, then, you start modifying it a little bit, and it might fit even better. That's kind of where the transition started going from the natural products to more synthetic things.

There is still a lot of natural product work being done. We have a person in our Center, Christine Salomon, who isolates natural products from various sources. She goes down into that... What is that mine that goes down about a half a mile down into the ground? The Soudan Mine [Soudan Underground Laboratory]. She isolates bacteria that have been down there and have never seen the light of day, interesting things that she isolates. She gets samples from all over the world. She has also gone deep sea diving for sponges.

LK: Oh, wow.

RV: She hasn't been diving recently, but she used to. She has a degree in oceanography and also chemistry. We still have part of our Center that does a lot of that. It turns out to be very interesting.

LK: Yes. I'm always interested in how much diversity comes into the different health sciences, a lot of business knowledge and, then, oceanography coming into it and all these other fields.

RV: Yes, yes.

LK: It's really fascinating.

We were talking about enzyme inhibitors. What would you want to highlight surrounding your work on anticancer agents in the 1970s, or particular components of drugs that emerged?

RV: When I was a graduate student, we were working on an enzyme or a few enzymes, and we were making inhibitors. That's what I said I wanted to do, and I took this course on DNA. Later, I went to Howard Schaeffer, and we started working on an enzyme called adenosine deaminase. We were designing these molecules so they would fit into the site of the enzyme. I don't know how much background you have in that type of thing, but enzymes will take a material in the cell and convert it to a product.

LK: Yes.

RV: So we were publishing these papers on what the molecule has to look like to fit into this enzyme as an inhibitor. It bothered me that our compounds were inhibitors, but the enzyme didn't convert them to anything.

LK: Hmmm.

RV: I would argue with Howard and say, “Look, if they’re fitting in the active site, why aren’t they converted to a product just like the normal substrate?” He didn’t have an answer for that.

So, one day, I came up with an idea of how we could design a molecule that will do that and actually be converted to a product. I presented that to Howard and I said, “I’d like to work on this. Maybe it will be a substrate for adenosine deaminase. If it is, then these types of molecules can maybe have antitumor activity, antiviral, because they’ll be converted up the process to be a DNA component.

LK: Right.

RV: Well, he didn’t want me to work on it, because he felt that I already had a lot of projects going, and he didn’t seem to be that interested in it.

So I left there in 1966. I went to Mississippi. I couldn’t get started. I didn’t get anything going.

I got my grants, and I came up here. It was in 1967. I was working on this project. I had talked to my post doc about this idea I had. All of a sudden, I get this letter from Howard. He said, “You know, we made that compound that you suggested, and it works. It does what you said it was going to do.” Those weren’t his exact words in the letter. He said, “Here’s a paper that we’re going to publish.” He put my name on it.

LK: Right. Yes, I’ve read a little bit about that.

RV: Oh, yes?

LK: Yes.

RV: So I went to Ty Soine, and I said, “You know Howard put my name on this paper, but I never worked on it. But it was my idea. Should I take my name off?” He said, “No, you can use the publication. You’re an assistant professor.” I said, “But I was going to work on it.” “I would advise you not to work on that, because it will make it look like you’re following Howard’s lead. You have to establish your own identity.” In the same letter, which I still have, Howard told me that he was taking a job at Burroughs Wellcome as head of medicinal chemistry there. Well, a few years later, one of my people went down there to interview for a job. She came back and she said, “They’re all excited about this compound that Howard Schaeffer developed. I think you had something to do with it. They wouldn’t tell me what it was. They said, ‘When you talk to Howard, he’ll probably tell you.’ I did talk to him and he never said anything.” So, finally, I called Howard and I asked him. It was based on that molecule that I had proposed. I said, “Well…” What happened was he took that compound that they made that I had suggested. They tested it as an antiherpes agent. AIDS [Acquired Immune Deficiency Syndrome] wasn’t even known then. Herpes was the big problem. It was active. They couldn’t patent it, because we’d already published it.

LK: Ohhh!

RV: This was all without my knowledge, see? So they made a change in the molecule, which you normally do. There's four bases in DNA: adenine, guanine, cytosine, and thymine. This was the adenine, so they put guanine on there and that was active, too.

LK: Right.

RV: And it was a little more active, so they were able to make the argument that, well, the guanine compound was a little more active, and we didn't expect that. If you don't expect something, it's not obvious, and you can patent it. If it's something that is obvious from something else, then you can't. He said, "You didn't have anything to do with it. Your compound was the adenine. This was the guanine." Well, they're the same thing.

LK: Yes.

RV: I didn't think that much of it at the time. I figured I was just happy that one of my ideas did something. Well, later, they started making such a big deal out of this molecule and the Burroughs Wellcome people were going and giving talks. This one person at Burroughs Wellcome was actually getting all the credit for it, and she didn't even have anything to do with the design of a molecule. Then, I found out later from this person, my post doc who actually did get the job down there... She said, "You know what they did? This other person"—her name is Trudy [Gertrude E.] Elion—"had a compound that they were going to develop for herpes." When they discovered this one of Howard's, they decided to scrap hers and go with this one. She had been there for so many years and had such a history there, and they were grooming her for the Nobel Prize...all the credit was kind of put on her. She didn't work on it, but she did a lot of the follow-up metabolism studies.

So I wrote Howard a letter, and I said, "You know, you guys are going out and giving lectures on this, and I feel as though I had a lot to do with this. Even you're not getting credit for this." When he got my letter, he called me up and said, "Well, what do you want? We can't give any money." I said, "I don't want money. I just want some acknowledgement. It would be helpful for me."

It was ready to go on the market as acyclovir. So a few weeks later, it got on the market or a month later or something, and it was written up in *Newsweek*. It was the biggest breakthrough in a century of antivirals. One of the [Minnesota] *Daily* [University of Minnesota student-run newspaper] people came over to talk to me, because she heard that I did that type of work. I said, "I had something to do with this. You could call Burroughs Wellcome, because Howard told me he would acknowledge my involvement." She came back a couple hours later and said, "They denied any existence... They said you didn't have anything to do with it. It was different." So I figured, well, they're not going to give me credit. I found out later from people who worked at Burroughs

Wellcome, at the time, that they were afraid to acknowledge me, because then they felt that they'd have to acknowledge Buffalo, because the compound was made in Buffalo and all this stuff. I never did know how Howard felt about the fact that I didn't get any credit for it.

LK: Did you take any legal action against...?

RV: No, I didn't.

LK: Was the University or the department trying to support you in...

RV: This department?

LK: Yes.

RV: No, I didn't even... No, because that wasn't developed here. They wouldn't have anything to do with it.

In fact, Howard told me, "I'm going to be giving talks. I'll make sure that I talk about your involvement." He didn't. Trudy Elion got all the credit for it. She did win a Nobel Prize.

LK: Did she? Wow.

RV: Not just based on that, but she worked with another person, his name is George Hitchings, and they had been pioneers in this Burroughs Wellcome company for years. They made a few drugs and, then, of course, they then gave her credit for this drug. She did a lot of metabolism work on it, later. They also gave her credit for AZT [azathioprine]...

LK: Oh, wow.

RV: ...which she had nothing to do with because AZT was actually developed after she left there. She didn't leave; she retired. AZT was not designed as an AIDS drug. It was something made back in the 1960s.

Burroughs Wellcome got credit for that. Burroughs Wellcome doesn't exist anymore. It was bought by Glaxo [SmithKline].

I felt as though they could have at least acknowledged my contribution. I wasn't asking for anything, except this is how this drug came about. The history of that got lost because nobody knew that. Burroughs Wellcome just made this nice story for themselves about it. [chuckles]

LK: I don't know if this expresses my naivety, but I've never heard this idea of... What was the word you used? Not training but preparing someone to win the Nobel Prize.

RV: Grooming.

LK: Grooming, yes. [laughter] I hadn't thought about that.

RV: That's what I was told by other people, that they were grooming her for the Nobel Prize. Even my former post doc, who worked down there, told me. In fact, she was all upset about it. She called me up one day and said, "They've got this painting as you come into the building, and they've got all these molecules. They've got Trudy Elion and Hitchings in the background." And she said, "And acyclovir is there. Do you know what they do? They give certain people credit. They decide who gets credit for things. They gave her credit because..." I told you. The reason my former post doc—her name was Sue—was upset about this is that she was worried that her work wasn't going to be credited to her. She was working for some person who was kind of taking the credit for the idea that she was coming up with, and she was worried about that. That's why she was so upset about it.

LK: Is that some difference between working in academia and working within industry, that kind of losing credit for your work?

RV: Oh, yes. In industry, I'm sure that happens a lot. Sure. The people in industry, they're working for the company, and they have to do whatever the company tells them. If the company wants to give them credit, they could. They don't get to publish a lot of their stuff. It's a lot different from academia.

LK: Yes.

You, eventually, began working though on herpes, correct?

RV: Yes.

LK: Did you begin that research in the 1970s when you got here?

RV: Mid 1970s. During the early 1970s, no one was really working in antivirals. There was only one antiviral on the market. I had an offer to become the manager of the Medicinal Chemistry Department—this was in 1974—at 3M. They said, "What would you think are the new areas we should go into?" I said, "Antivirals." They practically kicked me out the back door. They thought that was a terrible idea. They said, "Antivirals are like anticancer agents." The FDA [Food and Drug Administration] would never approve them. It would be so hard to get them approved, because they have to be toxic. Mostly antivirals you would think of as something to inhibit DNA synthesis and that's going to inhibit cancer. All the companies felt that way. However, when acyclovir was discovered, it was found that it wasn't toxic as an anticancer agent, because the virus activated the drug itself. So if it went into a cell that didn't have the virus, it didn't do anything. If the virus committed suicide by activating the drug, then the drug killed the virus. Once that happened, then everybody, all these companies, started working in

antivirals. In fact, 3M even called me and wanted me to help them develop some... I said, “Hey, you guys, I told you once before, and you didn’t like that idea.”

I figured we’d do our own stuff. We did design a compound but this was like, I said, the mid 1970s. It was before I knew about acyclovir. We didn’t know enough to patent it, and because we didn’t patent it, none of the companies would develop it.

LK: Ohhh.

RV: We tested it against acyclovir, later when we found out about acyclovir, and we found it was much better than acyclovir. In fact, if you gave acyclovir to animals that were infected with a human virus, as soon as you stopped giving the drug, the virus comes back. With our drug, when we stopped giving it, the virus didn’t come back.

LK: Hmmm.

RV: We published a paper in *Science* showing the difference, but because we didn’t have a patent, the companies that we went to said, “We don’t want to spend all this money making a drug and, then, anybody else can just make it.”

LK: Yes.

RV: So it never got developed. We called it cyclaradine.

LK: That’s such a strange environment for drug development—that you have to have that patent to get it to market.

RC: Yes. That was how I learned my lesson.

What happened with that drug when we developed it is we made it to be an antiherpes agent. I told you there was one drug on the market. Well, the drug was only used for eye infections, because if it went into the body, these enzymes chewed it up so fast, it never got to the site of action. One of the enzymes that was chewing it up was the adenosine deaminase that I had done my Ph.D. thesis on. I figured, well, I know how to design a drug that will resist this adenosine deaminase but still have the anti-viral effect. We made it. Nobody was testing viruses at the time. We couldn’t. So I sent it to a friend of mine at the Southern Research Institute in Birmingham, Alabama. He gave it to their virologist. They were testing compounds for the government, at the time. We didn’t hear anything back for a long time. In the meantime, my post doc wanted to present the synthesis of it at an American Chemical Society meeting in San Francisco. We went to San Francisco. I was there. She was there. My family was there. I ran into John Montgomery, the guy I had sent it to. He said, “I just got some data back from Bill [William M.] Shannon. Your compound is really active. It’s more active than the one that’s on the market, Ara-A. Maybe you better not talk about it.” I didn’t want to disappoint my post doc, so we went ahead and talked about it. It was part of the program, but we didn’t mention any of the antiviral work. John said, “Maybe you should patent

it.” So when I got back to Minnesota, I told them, and they said, “Since you presented it, we can’t...” You can get a U.S. patent, but you can’t get any foreign patent.

LK: Ohhh.

RV: But because we couldn’t get a foreign patent, that was a major thing for the companies. They just wouldn’t take the chance in putting all the money into it.

LK: When would you say this big push to patent discoveries...? For you, it came with the acyclovir. This must have been a larger trend in academia.

RV: No. In academia, most people didn’t patent. Everybody did research for just publishing. We didn’t even think about that. Companies weren’t interested in anything that was developed at a university, because most of it was supported by NIH money. The NIH had such restrictions on some company buying the rights, that the companies just weren’t interested.

LK: Right.

RV: The government wanted march-in rights where they could come in and just take the thing away and start making it for their own purposes. They would only allow a five-year license with a company.

Then, about 1980 or around that time, there was what was called the Bayh-Dole Act. That changed the whole thing. They said, “Look, anything that the NIH funds, the inventors have a right to patent, and they have the right to even get something out of it. They get part of the royalties, and the universities have the right to license it.”

So, all of a sudden, companies became interested. That was just a few years before we discovered our AIDS virus drug. Then, the universities all started building up their licensing departments and everything and looking for things to patent. Before that, professors kind of looked down their nose at patenting. Even some of the professors in my department kind of looked at me like, well, you’re patenting stuff. We don’t do that. We’re not trying to make any money. Well, what I found out with this cyclaradine was if you do not patent something, then nobody will use it. It would have been better if we didn’t discover that drug, the cyclaradine. If somebody in industry had discovered it, it would be on the market now.

LK: Right.

RV: The fact that we did it, and we didn’t know enough to patent it... We put it out into the public domain. Now, nobody will touch it. I felt it’s our obligation. We’re spending this money, taxpayers’ money, in this case, and we’re making these things, and, then, wasting them by not patenting them. We should have the obligation so they will be developed. Because if you patent something, and it’s a good idea, a company will come in and if they think it’s going to be worth their effort, they will, then, put up all the money

it will take for clinical studies. It takes a billion dollars, over a billion now, to put a drug on the market.

LK: Right.

RV: So they don't want to spend all that money and then find out that they can't even get their money back from it. I feel as though we have an obligation to do that.

LK: There's so much controversy, I think, surrounding drug patenting. If you can't get it to market, it's not going to help anyone.

RV: Actually, that's what happened when we discovered our AIDS drug.

LK: With Ziagen?

RV: We made this on our own. I didn't even have a grant for this. I had some extra money. I had a person that came here from China as a visiting scientist, and I had to come up with a project for her. I wasn't expecting her since she originally came to work in another lab.

LK: [chuckles]

RV: I said, "I've got these ideas about AIDS." AIDS had just been discovered. There was only one drug, AZT, but that was something that was made in the 1960s that they just kind of found by screening. It only took her six months to make about fifteen compounds. We sent them to testing. The NIH tested them for us. They called me up at home on a Saturday and said, "Wow. These compounds are the best ones we've found since AZT. We want you to patent those. We will put up all the money until some company takes over, but we don't want to get caught holding the bag. If you don't patent it, nobody is going to take it." So we, immediately, patented these things, because I had learned my lesson before. That's how that happened.

LK: Who was the student?

RV: It wasn't a student. It was a visiting scientist. Her name was Mei Hua, M-e-i- H-u-a. She was here. She was a professor in China. She came here. She worked with me. There's her picture. I just saw her here two days ago, on Sunday.

LK: Is she here...?

RV: She's retired now. She worked on this. It was funny because we made these for AIDS. She made the compounds. I tried to send them to the NIH. They wouldn't accept them.

LK: Hmmm.

RV: They could only test so many compounds at that time. They only had one laboratory that was able to test them. They would select what they thought might be the best candidates. Well, the laboratory that they had selected was Bill Shannon, the guy that was my friend by that time. He's the one that tested our cyclaradine at the Southern Research Institute. It took us almost a year before the NIH would even accept our compounds.

The only reason they did was because they had hired a person whose name was Bob Schultz. I don't know if you'd want people to know this but I happened to know him. I knew his former boss. I didn't know him personally. So I called Bob. Bob's job was to get compounds from various companies and organize them and send them down to Bill Shannon for testing. So I told him. He said, "Send them. I'll make sure they get tested." They assign these numbers to them. Then, I called Bill Shannon, and I said, "They accepted my compounds. I know they sent them to you." He said, "Well, what are the numbers?" He said, "These aren't supposed to be tested for about six months. But I'll put them at the top." Then, about two weeks later, he called me and said, "Wow. Five of your compounds are really active. If I send this data to the NIH, it will be about six months before they even realize...because they're so disorganized."

This is when they first started testing. All they were doing was getting compounds from industry and screening them.

LK: Was this specifically for AIDS?

RV: For AIDS. They were just getting the AIDS virus... They didn't have any assay procedures. They were working those out. Then, Bill would be doing the testing. They could only test a few thousand compounds a year. This was between 1984 and 1987.

Maybe I'm telling you too much.

LK: No. No, not at all.

RV: Bill said, "I'm going to call the NIH people and tell them." So he did. Then, they called me and said, "Why don't you send them to us? We'd like to test them here." So they did. That's when an NIH scientist, Robert Shoemaker, called me at home on a Saturday and said, "Wow, we just read the plates, and these are great." I have in here a picture of the plates. He said, "We want you to patent these. We're going to invite you to come here. We want you to meet with the NIH Decision Network Committee." They had this big committee that would decide which compounds that they would put all their effort into. All they had was AZT, at that time, that they discovered by... Burroughs Wellcome had it sitting on their shelf, and they sent it to NIH for screening. Our compound was the first one that was actually designed to be an AIDS drug.

LK: Oh!

RV: It was an AIDS drug. The others were just discovered from things that were made twenty-five years earlier for other purposes.

They wanted me to present our work, the NIH people did, at a national meeting. They were also really anxious for us to get our patent. They wanted to publish their new assay that they came out with and use our compound as one of the first ones they discovered. They published a paper. I still have it. It was in the *National Cancer Institute Journal*. [Doctor Vince gets the journal.] They're talking about how they developed this new procedure and everything. They say in here:

The first promising agent to emerge from the screening program is carbovir, which was synthesized in 1987, was submitted to the program for testing by Robert Vince, University of Minnesota. The University holds the patent and last year licensed to Glaxo.

Etcetera.

One of the authors on the paper was Robert Shoemaker. They had developed this assay, and they wanted to publish it and everything.

Anyway, I'm probably telling you a lot of stuff that's...

LK: No, this is great!

RV: That's how our AIDS drug was discovered. Then, Glaxo licensed it. It's funny, because Glaxo was right across the street from Burroughs Wellcome. They're in North Carolina. I went down there. Most of the people that I had to talk to had come from Burroughs Wellcome. Glaxo was stealing all of Burroughs Wellcome people. That's how I found out what happened to acyclovir. They said, "The same thing is not going to happen to you that happened with acyclovir. We're not going to do that." After about ten months, they stopped working with our compound. They bought into a company in Canada that had another compound. Canada had just changed their laws that year that allowed outside companies to buy into their companies. So Glaxo was the first one to take advantage. A Canadian group had come up with some compound and Glaxo could have that, plus a percentage of all their other compounds. So that was better deal. So they just stopped working on ours.

Then, Burroughs Wellcome started coming to us saying, "We would like to develop this thing. But we want to make sure you get everything back from Glaxo so there's no strings attached." It took us another year just to get the thing back from Glaxo. We had to have the president of the University write to them and everything.

LK: Wow.

RV: I even had to get the NIH involved, because they wouldn't give it back to us. They were holding it to see if their other compound was going to work.

So, then, Burroughs Wellcome took it and, then, Glaxo bought Burroughs Wellcome.

[chuckles]

RV: It was one thing after another. Then, when they bought Burroughs Wellcome, they fired half of the people. They gave them these big, long severance packages. But some of them stayed. It took about another year before Glaxo even realized they had our compound back. It took almost ten years from the time that we discovered it until it got on the market.

LK: Which is so incredible to me. That's ten years of patent life lost.

RV: It was 1987 when we made the compound. It was 1999 when it got on the market. In the meantime, other companies had developed drugs that got on the market, so it looked like ours came later even though we were the first ones to make one.

LK: Yes.

RV: There are people who have written the story about this. One person, his name is Jie Jack Li. He writes these books about the history of drug discovery. [Doctor Vince gets a book from the shelf.] Here's one of his books...Jie Jack Li and E.J. [Elias James] Corey. E.J. Corey won the Nobel Prize in chemistry. The one before this is the one that has the story about our drug... Oh, it's called *Laughing Gas, Viagra, and Lipitor* [: *The Human Stories behind the Drugs We Use*].

[laughter]

RV: In this book—I don't know what page—he talks about that story of how my drug got developed and how Glaxo tried to take credit, and they wouldn't give us credit for it—not Glaxo, but actually Burroughs Wellcome. We had to have a lawsuit and everything. He knows the whole story, because he talks to all these scientists. He writes all these histories of medicine and things like that.

LK: I need to get ahold of those.

RV: He's a good author. It's Jie Jack Li

[pause]

They have Carbovir listed. So we called it Carbovir. Then, later, it was called Abacavir and, then, Ziagen.

LK: When you mentioned earlier that you had to send the drug to NIH for testing. Was the NIH taking sole responsibility for testing AIDS drugs because of concerns about transmission?

RV: No. One of the co-discoverers of the AIDS drug worked for the NIH. His name was Gallo, Robert [C.] Gallo.

LK: Yes.

RV: He was at the NIH. So they had access to the virus and nobody else really did. None of the companies did. The person who, then, became in charge of that was really the head of the Cancer Institute at the NIH. They kind of put it into the Cancer Institute. His name was [Samuel] Broder. I can't remember his first name. It was Broder who made the decision of what they would accept for testing. Broder is the one who didn't want to accept our compounds. He didn't think they would be active. He even wrote a book and in one of the chapters, he wrote that those kinds of compounds wouldn't be active.

LK: Hmmm.

RV: We used that in our patent, because that wouldn't be expected.

LK: Right.

RV: Even Broder said these wouldn't be, so we used that. Dr. Li has it in here on page 123 where he starts talking about...Robert Vince, medicinal chemistry. Then, he talks about how this whole thing came about and how Ziagen... There was a settlement with Glaxo. It was really Burroughs Wellcome, but they became part of Glaxo. He talks about that in here. Yes, he's good. He's written a lot of books.

LK: I'm going to check him out.

RV: A lot of chemistry ones, too, like name reactions in organic chemistry, things like that.

LK: Something that struck me about what you said earlier was this connection between cancer and research on medicines to treat viral infections. I hadn't thought about that idea that you're trying to stop DNA replication for cancer and, then, you're working with DNA replication in viruses. Was this the idea that you could have drugs to treat viral infections that weren't going to kill the body, I suppose is a general way to say it? Is that something that was emerging around the time that you were working on these herpes drugs or prior to that?

RV: One of the main targets would be DNA polymerase. That makes our DNA. Well, the only really serious virus at the time was herpes. AIDS wasn't known. This was in the 1970s. They didn't know much about AIDS until about 1984. So the only drugs that were showing to inhibit, inhibited DNA polymerase of the virus. It's hard to design a molecule that will inhibit just the virus DNA polymerase but not the human. So all the drugs, really, that would be potential herpes drugs, it was just kind of thought they would be too toxic. They would do the same thing in normal cells. But, after acyclovir was

discovered, they found out two things. One was that the virus activated the drug so it was only active in virus infected cells, so if it killed that cell, good, because it was killing cells that were full of viruses. The other thing they found out about it was it inhibited the DNA polymerase of the virus but not the human. So there is a difference. The virus enzymes will pick up a lot of things. The human ones are more specific.

Then, when AIDS was discovered, it's a retrovirus, and it has an enzyme that we don't even have called reverse transcriptase. So that made a good target. If you inhibit that, you don't have to worry about anything in the human. It's a lot easier to make an antiviral drug than it is an antitumor. So a lot of people switched over to virus research.

LK: Oh.

RV: If you try to make it an antitumor drug, everything that the tumor has, your normal cells have. So if you inhibit something, you're going to do the same thing in the normal cells. So you always have a degree of toxicity. You look for some selective toxicity, but eventually, even though it might kill a lot of cancer cells, it's going to start working on the body. With a virus or a bacteria, it's a lot easier.

LK: Okay.

With your royalties from Ziagen... I read one of the *Pioneer Press* articles about how you had this vision for creating an intercollegiate drug design center which you've done now.

RV: Yes.

LK: What was it like to get the Center for Drug Design started?

RV: We were going through this litigation, and I thought this was going to go on forever.

LK: What was the litigation?

RV: When Burroughs Wellcome, then a part of Glaxo, finally licensed our drug. We thought they were going to develop our Carbovir. What they did was make a derivative of it, and they tried to say that the derivative was not covered by our patent.

LK: Ohhh.

RV: So when they finally got their derivative... They said, "In order to make our derivative, we have to use your patented intermediate. If we use your intermediate, we'll pay you, say, five percent royalty on all the sales. If we use one of your drugs that's covered, we'll pay you ten percent." When it got approved by the FDA, they came here. We thought they were going to make the argument about just paying us five percent. But they said, "We're not paying you anything. We don't feel as though we owe you anything." Even though they had been paying us licensing fees, about \$4 million in

licensing all the time this was being developed, as soon as it got on the market, they said, “Well, our drug doesn’t come under your patent. This intermediate that you have, we don’t even make it in the United States or anything. We make it someplace else. We don’t feel as if we have to pay.”

So the same day that they left here, we filed a lawsuit.

LK: Wow!

RV: We didn’t want them to file one. We were told, “Whatever they say,”—we thought they were going to go for filing—“keep your mouth shut. If we say, ‘We disagree,’ they can go back and file a lawsuit.” So before they got a chance to do that... We didn’t say, “We disagree.” We didn’t say anything. We filed. So, then, that started the whole thing. This kept going on and on and getting bigger and bigger. They felt as though they could outspend us, that the University wasn’t going to spend millions of dollars, but they were wrong. Our president at the time was Mark Yudof, and he’s a lawyer. He said, “Look, we’re going to go after them.” He said, “I’m behind you.”

So, anyway, it was Mark Yudof then. When we did have the settlement, he suggested to me about the Center for Drug Design. He said, “You should have your own center.” The way it was set up is that twenty-five percent of the royalties was supposed to go back to the inventor’s research. I knew the University wasn’t going to let me keep all that money, especially the College of Pharmacy. They were ready to pounce on it. But Yudof was behind me.

The next day after the settlement, I met with Frank Cerra and Christine Mazier. Chris was the vice president for research at the time. I have a picture of her here someplace. They came to me and said, “What are you going to do with this money?” I said, “Well, I want to start the Center for Drug Design.” They said, “What is that?” I told them. They said, “Oh, that’s a good idea.” I said, “The president is behind it.” He even came to my office and talked to me. So they approved this thing.

But I didn’t have any place to set it up. I didn’t have any space. I went to Frank Cerra, and I said, “I want the Center to be outside of the College of Pharmacy. I want to answer directly to you,” etcetera, etcetera. So they approved all of that. It was approved by Frank and Chris Mazier and the president and the deans. They had a deans’ council. They approved it.

But, even after that, I always had this problem of having our own identity, because the College of Pharmacy kept identifying with the Center, which they still do. The reason for me wanting to go directly to Frank was that if I went through a department and, then, a dean, they’re going to be controlling everything. I wouldn’t be able to do what I wanted to do.

So I set up the Center. We used the royalties. We have about sixty people working in the Center, and we have various groups. We work on all kinds of things. Each group applies

for grants. They get grant money, but the Center also supports some of this. I have been able to build up an endowment of close to \$100 million.

LK: Wow.

RV: So that when the royalties stop coming in, the interest will support everything that our grants don't support. This has allowed me, because I take a certain amount for my research... I gave my salary back to the College of Pharmacy. I said, "You can hire somebody else, and I'll direct the Center." So I do that. Then, I use that money. I was able to get into areas that I couldn't get into before because I was restricted by what my grant was for.

LK: Ohhh.

RV: If you have a grant to do herpes research, you can't use that money to do Alzheimer's research. So we've done other things. Now, we have patents on an Alzheimer's drug. We have a new technique for detecting Alzheimer's in its early stage. We made some new cosmetics that prevent skin cancer and they, also, repair DNA damage. They prevent aging of the skin. We have three major companies that are interested.

LK: Are these local companies or international?

RV: International. We just developed a new method of detecting Alzheimer's in the very early stages before anybody else can detect it. We do this by looking at the retina of the eye. We did this in mice. At the time we were doing it, we didn't have the instrument so we could look directly into the eye, so we had to remove the retinas and look at them under a microscope that had this spectra that we wanted to use. Now, we've built a camera, and we now tested it on the mice. We can look right into the eye of a mouse and get the same readings we did by taking the retinas out.

LK: Oh, wow.

RV: We've used this and when we treat the mice that get Alzheimer's, we can follow the progress of our drug just by looking at the spectra in the retina. We can predict whether the drug is working or not, whether these mice are going to be able to remember a maze at the end. We can tell. We have patents on that now.

Then, the cosmetics are kind of interesting, because they do things that other cosmetics don't. We have a sunscreen that works by a method that's different from all the other sunscreens. Also, it's nontoxic like other sunscreens are. Some sunscreens actually cause cancer.

LK: Wow!

RV: Oh, yes, yes. The way conventional sunscreens work is they absorb UV [ultraviolet] light in their aromatic molecules. When something absorbs light, light is energy. The energy has to be converted to something. The sunscreen molecules become much more reactive; they go to what we call excited state. Then, that molecule can do two things. One is it can lose that energy by giving out heat, so it heats up the skin and causes aging of the skin, or it can react with molecules of the skin like DNA and cause tumors itself. Our molecules don't work that way. They actually mimic the DNA molecules. They're like decoy DNAs. The UV goes into them instead of to the DNA in your skin. Then, the skin thinks its DNA has been destroyed, which it hasn't but our decoys make it look like that, and so the cells start producing enzymes that repair DNA. So the DNA gets repaired a lot faster. So it slows down aging.

LK: Wow!

RV: We have patents on all of this.

LK: That's really exciting. [chuckles]

RV: We have a lot of companies interested in this. We just got our paper accepted in the *Journal of Dermatological Research*. So we're into dermatology, which I never did before. We're into Alzheimer's. Then, we do the AIDS research. We do anti-cancer research. We're working with an analgesic. This is just my group. I'm not talking about the rest of the Center. What else do we have? We have an antidote for Tylenol poisoning.

LK: Hmmm.

RV: If a kid takes a bottle of Tylenol [acetaminophen], it will kill them. There's only one antidote. Acetaminophen is a very toxic material, toxic to the liver. The antidote that they have, you have to go in the hospital. You have to get intravenous injection of about a liter of it. Our stuff is much more active than this, and it's orally active. You don't have to give it intravenously. You can if you want to. You can give it intramuscularly. We've patented that and, now, we're ready to publish some papers on it.

The University is working on all these licensing things that we've done. So we've been able to get into a lot of areas that we haven't done before. We have Parkinson's. We developed a molecule that will transport drugs into the brain and, then, release them for Parkinson's. The transporter, after it releases the drug, actually protects the drug from being destroyed in the brain. We've been able to work on a lot of things.

LK: Right.

Are you mostly bringing in researchers who already have Ph.D.s or are you bringing in students, post docs?

RV: What I do is kind of like a department. I'm the director. That would be like chair of a department.

LK: I guess I can look at...

RV: If you look at our organization diagram... This is not the most up-to-date one. I hire people who have Ph.D.s. They have research experience, and they are PIs, principle investigators. Then, I give them start-up money. We appoint them as assistant professors, that type of thing. Then, I ask them within three years, I would like you to be putting at least half of your salary on grants. With their start-up money, they can start hiring some people. Like they get some post docs. Then, they apply for grants. Usually, they've been very successful in getting grants. Then, as their grants come in, they hire more people. So, they each have a group. So this person has this group. She has her group. That's the way we work.

LK: Okay.

RV: Then, I have an executive person who is the... We call them, right now, associate directors. I have a person who does all the administrative work, Elizabeth [Wolfson]. Then, Elizabeth has two people that work for her. One [Phillip Luttmers] does all the bookkeeping. The other person does ordering, scheduling, etc. [Michelle Witt]... We do a lot of ordering. We don't have a lot of space, for some reason, even though I brought in \$600 million to the University, and we pay for everything in our Center. We even pay for the space that we use. Because we're in the Academic Health Center, we seem to not... Well, I don't want to say it. If you're not part of the Medical School you wait until everybody else gets their space and, then, we get ours, that type of thing.

LK: Ohhh. Right.

RV: A lot of the decision makers are part of the Medical School.

One of the things the Academic Health Center, to me, it's the Academic Health Center of the Medical School, because even though I brought in all this money and paid for everything and even supported some of the other programs that are in the Academic Health Center and part of our money goes to the Academic Health Center, we seem to be at the end of the list when it comes to getting space. So we have not been able to expand for ten years. Just recently, I've gotten some space over in a new building but...

LK: The one that's being built?

RV: Hasselmo Hall.

LK: Okay.

RV: But in order to get it, I have to give up the space I have here in the College.

LK: Ohhh.

RV: I gave my salary back to the College. They came back to me and said, “Well, we want you to get out of your space and your office. We’re kicking you out.” I said, “For what?” They said, “We need the space for the people we hire on your salary that you gave back to us. Also, you don’t bring in any money.” I said, “What do you mean? I bring in \$50 million a year of which the College gets \$4 million.” It’s eight percent. “I pay for everything, etcetera.” They said, “Yes, but that doesn’t count. That’s not NIH money. You have to get out of your lab.” The only way that I could stay here was I have to pay for the space here that I have. So, since I have to pay for the space and that’s why I don’t want to be identified with the College of Pharmacy or when somebody writes something to make it look like I’m part of the College, because I’m not.

[pause]

LK: Do you do any teaching through the Center for Drug Design?

RV: We just gave this workshop that the National Science Foundation [NSF] asked us to do last year. It was so successful, and everybody liked it. People come from other parts of the country from industry or other universities. They liked it so much, they asked us if we would do it this year. Now, they want us to do it every year.

LK: Oh, wow.

RV: That goes for a whole week and people come here and we all give lectures. I gave one. We teach certain things. A lot of the people in the Center give lectures in other departments. We do have some graduate students that are assigned to people in the Center. We have some undergraduates that work in the Center. We’re starting to teach some courses now. We want to teach some courses, but we’re having a hard time because in order to teach a course, you need what’s called a designator number and we don’t have a designator number because we’re not a department.

LK: Ohhh.

RV: We’re not funded by the University. We don’t get a budget from them. We pay everything ourselves. So we don’t have a designator number, for some reason. The AHC has one, but they won’t let us use it.

LK: Hmm.

RV: They want us to use the College of Pharmacy and I don’t believe that we should do that. We’re part of the AHC. We contribute to the AHC. They have this designator number, and we’ve asked to use it so we can start teaching courses, and they said, “No. You can’t use it.”

LK: Are there courses taught through this umbrella AHC?

RV: I think there are some. There's, what is it, the Center for Spirituality [and Healing] and some of those that teach courses.

LK: Oh.

RV: I don't know where they get their designator number. There's a lot of centers, and they do teaching. In fact, Spirituality, I think most of what they do is teaching.

When we were set up, we were set up to do... When Yudof was here, we talked about that I would take this money that we'd get from our royalty and put it back into research and, hopefully, we would use it to come up with more drugs. That's what we wanted to do. In order to do it, I felt the Center...we could do it. If we went through a department of a college, I knew most of the money would get wasted. Administrators are really good at spending all the money they get. I felt by having it where we weren't in a situation like that... I was able to put money away every year and build up this endowment that we have now. I doubt if we would have it if we were in some department or college.

LK: Do you feel like there's some kind of contention or like discrimination against industry funding versus NIH funding?

RV: Uhhh...

LK: In academia?

RV: I don't like industry funding, because when a company gives you money, it's more like a contract. They rarely give you money and say, "Go ahead and do whatever you want." It's more like a contract where they say, "We want you to work on this. If you design anything or develop anything, we get first rights of refusal." The University has some agreements like that with companies, so that if they do give money, the company would get a certain amount of royalties or money. It's hard to get industry money. I think it's more prestigious for people to get a grant from the NIH.

LK: Okay.

RV: When somebody becomes an assistant professor, they get a lot of pressure on them to get grants, usually from the NIH. Well, NIH... I mean if you're in physics, then you get it from the National Science Foundation. It's the same thing, you know.

LK: Right.

RV: The NSF or whatever, it's prestigious. Then, you get a lot of pressure on you to get this money, to bring it in. That's one of the things you're going to be evaluated on, that you brought in a grant. That shows that you've been recognized for your work, and it's part of being promoted and getting tenure. I don't know if there's any discrimination

against money from industry as opposed to NIH money. You can probably get a lot more if you get an NIH or an NSF grant than you would from a company.

LK: Okay. You're kind of in this third category where you're bringing in the royalty money. You said that you were told that you weren't bringing in money, but you have...

RV: I was told by the College of Pharmacy. They were using that as an excuse to kick me out.

LK: Okay.

RV: You're not bringing any money. What do you mean I'm not? I never thought of it that way. I thought, hey, I'm bringing in money. The way it was set up is I was in the College of Pharmacy. If you get royalties, eight percent of it goes to the dean of whatever college you happen to be in. So anybody in the College of Pharmacy, if they get royalties, the dean gets eight percent. In our case, it was like \$4 million a year.

LK: When you say the dean gets eight percent, that's part of their salary?

RV: No. No. To do whatever they want to with it. Deans are pretty good at spending money, so it doesn't stay around that long. They have a lot of programs they try to fund and start and everything. I didn't want that to happen to this other part of the money that would be the twenty-five percent. That was my way of protecting it, but it cost me. Some people didn't like that and felt as though they were entitled to it, not me, etcetera. If it wasn't for Yudof being here at the time, I probably wouldn't have been able to do that.

LK: Create the Center?

RV: Well, yes. I needed somebody that would allow me to do it so that certain other administrators weren't able to take that money away from me. Of course then, he left shortly after that, so I was kind of on my own. Frank Cerra did protect the Center. I have to say that if it wasn't for Frank, I probably wouldn't have been able to develop the Center. He made sure that I was protected—at least that's the way I felt. He didn't say that to me or anything. If something goofy like when they tried to kick me out of my...Frank would work out some reasonable thing that helped us to keep going.

LK: I want to move the conversation out a little bit and ask you about working with Larry Weaver when he was dean of the College of Pharmacy. I know he was dean when you came in. He had just become dean. What was his leadership style like and any comments on your relationship with him?

RV: I was actually the first person that he hired.

LK: Oh, that's cool.

[chuckles]

RV: He used to tell me that all the time. “You were the first person I hired.” When I came here, most of my association was with the chairman of the department. We didn’t have a very big department. Larry was really into developing the PharmD program. We didn’t have a PharmD program. We were over in Appleby Hall. We weren’t part of the Academic Health Center. So it was his vision to become part of the Academic Health Center and, also, to have this PharmD program. So that was his main thing. He wasn’t really involved a lot in things that we do. We were part of the College, and we used to have meetings all the time, and we would all vote for things. Everybody had something to say. We voted. We didn’t have all these little committees that now make all the decisions and the faculty don’t really get to say anything—kind of like *Animal Farm*.

LK: [chuckles]

RV: I don’t know if you’ve ever read that.

LK: I actually haven’t but...

RV: The animals get together and then things broke down from there.

I really liked Larry. I didn’t agree with all the things he wanted to do, because I was more interested in the research. That wasn’t a big thing in Pharmacy. Pharmacy started going when I came here from what I said was a lot of chemistry and the emphasis was on the drug and how the drug worked, and it was switching over to the patient instead of the drug.

LK: So clinical.

RV: The PharmD and the clinical. That was his really big thing, and I wasn’t really into that. Even though I had a degree in pharmacy, I was more interested in research. So I didn’t have a lot in common with what Larry was interested in. But, as a person, I liked Larry. He’d do anything for you. He used to invite the whole faculty out to his house. He and his wife Dee, they were just nice people. He knew what he wanted to do. He got this building approved. At first, it was supposed to be just the College of Pharmacy. Then, it became Nursing and Pharmacy, and we became part of the health sciences.

LK: Did the building, when you moved from Appleby, have a lot of good research facilities laid out for you all?

RV: Uhhh... It was okay. It was adequate when we moved over here. We started meeting with the architects, and we told them what we had to have, but, then, after a while, they didn’t meet with us anymore. Since this was over in the Academic Health Center, they had never had anything like chemistry labs, so they really didn’t design our labs the way we wanted. When we moved in, there were only about two hoods in each lab where we required more.

LK: Right.

RV: The floors on the eighth floor were all cement. There was nothing...because they had to start cutting back on things. They would just start doing that without asking us. But it was okay for what we had to do. We built up the labs even more, because as years went on, there were more requirements. You had to do everything in a hood, so we had to add hoods. It was okay. I liked it over in Appleby better for myself. It was more like being on campus. You'd walk out and see everybody. You're out there, and you see things going on. We were right across from Chemistry and there was a lot of interaction. Here, it's more like being in a company. Unless you make an effort, you don't have to go out on the campus and in the big mall there. Where at Appleby, I was always walking over to lunch. You'd see all these things. You felt like you were part of the University. So one disadvantage of it here is you don't feel like you're as much a part of the University as being over in Appleby.

LK: Do you feel more connected to the other health sciences? That idea of the umbrella was to bring all these health sciences together. Do you feel like there was more collaboration within the health sciences after that?

RV: I don't think it is because of being over here. I think that's just the way that research has evolved in the last several years. Before, we did a lot of work that nobody was really interested in. We'd do something on an antibiotic, but nobody was going to use that. So you'd just publish it and go on to the next thing, get your NIH grant renewed, etcetera. As things evolved and people became more interested in what you were developing and they might use it, and the companies were interested, then people started working together more. This is just my own opinion: I don't really think it's because of being closer; it's just because of the way research has evolved.

LK: Hmmm. Okay.

RV: I'm sure if we were over in Appleby, we'd still be collaborating with the same people.

LK: Do you feel like you've maintained those relationships with people in the basic science departments, in Chemistry and maybe Biology?

RV: Yes, we do. In my case, most of the people that I knew in Chemistry are either retired or dead.

LK: Oh.

RV: There are a lot of younger people there that I haven't really had a lot of contact with. There are some over there that I've known for years. Wayland [E.] Noland. He's been there ever since I was here. George Barany, Tom [Thomas R.] Hoye. There are several, but a lot of the ones that were here when I came are gone now.

There's collaboration, but most of our collaboration is really not with the Chemistry Department. It's with people in other departments here...Mayo [University of Minnesota-Mayo in Rochester]. I'd say the major of our collaborations are outside the University. They're in other countries or...

LK: Oh, wow!

RV: ...other universities. We have a lot of collaborations throughout the world.

LK: The Center of Drug Design or...?

RV: The Center of Drug Design, people in the Center. I do. The other PIs. We have all over France, Russia, Poland, China, Japan, Italy. We have collaborations everywhere.

LK: Do you get a lot of visiting scholars in?

RV: Yes, we do. We get people who come in here.

I had a guy come here from a Japanese company once. He approached me, wanted to come visit me. I didn't even know who he was. Why would he want to visit me, you know. Finally, he came here, and I said, "Why do you want to see me?" I didn't say it in those words. He said, "I wanted to meet you and thank you." One of these materials we made once, they started making it in ton quantities and selling it. They make so much money on it, and he wanted to come here and thank me personally.

LK: Oh, wow.

RV: It was called vince lactam. We didn't name it that.

LK: Oh, yes.

RV: There are about 200 companies in the world that make that now and sell it. Boy, I wish we had a patent on that.

LK: I saw that it was sort of the precursor for a lot of different drugs.

RV: Yes. Yes. There are these companies that make it, and they were one of them, and he came here and told me. I thought that was really nice.

LK: Yes.

RV: I'm sure he didn't come here just to see me. He was coming to this country, but he did make a special effort to come here.

LK: That's awesome. [chuckles]

This was under Larry Weaver's deanship. There was some talk about a move within the College of Pharmacy to encourage more teaching evaluations and improve teaching skills. I don't know if you remember much about that or if you have any comments on that.

RV: When Larry was there, they started teaching evaluations. Is that what you mean?

LK: Yes. I have it as 1974.

RV: The students, usually at the end of the year, would evaluate the professors, fill out these forms. It was just for the professors, at the time. You'd get all these comments and some were kind of goofy, you know.

LK: [chuckles]

RV: They'd say all kinds of things, like, "You look like Bob Newhart."

LK: [laughter]

RV: I don't look like Bob Newhart. Maybe I did at one time. I had more hair.

It was just for our benefit, I guess. But, then, it evolved into more where they started publishing. Then, they started using it to evaluate professors. That became more of a University thing. Then, they even had where somebody else would come in and sit in on your lecture, another professor, that type of thing.

They used to have these teaching awards. This one guy used to get this award every year, and he used to give everybody an A. One year, he didn't give everybody an A and he didn't get the award.

LK: Oh, wow.

RV: I felt, you know, if you really want to get good evaluations and everything, you kind of have to lower your standards and be a nice guy and give everybody A's, etc. I always felt that maybe these evaluations really... I'm not sure I agree with them.

There was one professor when we were over in Appleby who didn't do any research. He taught. His office was in the basement, and I was on the third floor. I did research, but I taught, too. I had this one student working with me [Connie Sanford]. She was the top student in the class. She did a research project with me and won a national award for it. She was the head of several of these student groups. They would meet in the basement, like for Rho Chi [Society]. One day I asked her, "How come so and so gets the teaching award all the time?" She says, "You know we meet downstairs and the students see him coming in at night, and they see you coming in at night. They know that you came in to do research, and he came in to work on his lectures and everything."

LK: Oh.

RV: “They feel he’s more interested in the student than somebody like you,” even though I felt doing research kept me up on things so that I was a better teacher—not than him but a better teacher than I would be if I wasn’t doing that. Students will evaluate you according to what you did and how much research and if you were doing research, you couldn’t be a good professor.

LK: I remember hearing that kind of stuff in college, too. So it’s still around.

Another thing that I had read about in the 1970s was a growing concern surrounding the increasing number of drugs on the market...

RV: Yes.

LK: ...and ensuring that physicians were educated in all of these different drugs and how they work for prescription usage. I didn’t know if you have any comments on that or if you were involved at all... I don’t know if the school did any physician education, at that time, continuing education.

RV: The college did continuing, but not for physicians. The whole idea was that the PharmD was supposed to be kind of like consultants to the physicians to tell the more about what drugs to use and interactions between drugs. When I first came here—it would probably be hard for anybody to believe but it’s true; it was so long ago—they didn’t even consider drug interactions, at that time. Physicians would give all these drugs. They didn’t know how they worked or interacted. Of course, they thought that they knew all about drugs.

I remember once that Dean Weaver was trying to get me involved with some of the research people in the Medical School. They had come up with this new method of taking cells from a cancer patient and determining which would be the best drug for them. I said, “Well, what do you do?” They said, “We take these cells from the tumor, and we grow them inside a capillary tube. Then, we take a solution of the drug, and we pass it through the tube. If it causes these cells to slough off, then we know that it’s a good drug for that particular tumor.” I said, “What drugs are you using?” They started rattling off the drugs. I said, “How come you don’t use cyclophosphamide?” They said, “Well, it doesn’t work.” I said, “Do you know why it doesn’t work?” They didn’t know. I said, “Cyclophosphamide has to be activated in the liver. It doesn’t work on cells.”

LK: Ohhh.

RV: If you test cyclophosphamide in a cell culture, you won’t see very much activity. In the body, it gets converted to the active form. Well, they didn’t even know stuff like that back then.

I used to use this question in my course. It was just a made up question that I had about a drug. I said, “You know, if somebody had gout and they were taking allopurinol and, then, they got leukemia or something and they started taking 6-mercaptopurine”— which is a drug—“as a pharmacist what would you have to do?” The thing is you’d have to decrease the drug down to about a third. The one drug makes the other one much more active. So if you were taking allopurinol, it’s blocking the enzyme that degrades the other drug. So, now, it’s not being broken down and you get a higher concentration. They had to know that. About five years later, I was reading in *Reader’s Digest*, and I found out that all these patients had been killed in hospitals because they were giving 6-mercaptopurine to people who were getting allopurinol. They didn’t know that there was...that’s how they discovered it. I was just using this as a test question to emphasize drug interactions.

So there wasn’t a lot of that kind of stuff until the PharmDs started getting involved. One of their big things was drug interactions. That’s when a lot of that started. Now, all people giving medications know about all these interactions; there’s been so much. But this was back in the early 1970s.

LK: Right.

RV: If you’re in medical school, you learn certain drugs, like anticancer drugs or something. You don’t learn the mechanism of how it works, how it gets activated, why it does this. That’s the kind of thing that a medicinal chemist has to know, because that’s what we base our design on: how the drug works, how it gets activated, how it gets broken down. You kind of try to design around all these things, so you know that stuff. But that wasn’t something that was really known until things started happening and, then, people started learning more about that, the PharmD people, for example. Then, they started working in hospitals and that was one of their main responsibilities.

LK: Okay.

RV: I’ve kind of lost track now with how the PharmDs are doing now.

LK: That makes a lot of sense.

RV: They weren’t all getting the PharmD degree. Just a certain fraction of the people were getting it.

LK: I’m not sure if this year is right. I have that the University ended the B.S. [Bachelor of Science] in pharmacy in 1978 to make the PharmD the basic degree.

RV: I don’t remember what year it was.

LK: If it was 1978 that would make sense as kind of a response to this concern.

RV: I know that when I got my degree in pharmacy, I was the last of the four-year program.

LK: At Buffalo?

RV: I mean in the country.

LK: Ohhh.

RV: Then they went to more like a five-year program. It wasn't PharmD. It was just a longer program. There were certain people who, then, would get a PharmD. They'd be here longer. California, for example, gave all PharmDs. That was something that Larry really wanted and fought for is getting the all PharmD, but I'm not sure when it was.

LK: Okay.

RV: I'm sure other people in the College would know.

LK: Right. In my interview yesterday, he thought it was 1998. So I was kind of surprised I was twenty years off.

RV: It could have been, but 1978 sounds kind of early to me, but I don't know.

LK: I don't know what committee work or administrative work you did within the College of Pharmacy before moving into the Center for Drug Design. There was a lot of talk in the 1970s regarding placing pharmacy students in rural communities, trying to get more pharmacy students out there. Were you involved in all of that or do you have any comments on that?

RV: I wasn't involved in it. I taught biochemistry, and I taught what was called medicinal chemistry, really the application of drugs, biological. I wasn't a practicing pharmacist. We had a lot of people who were, and they were the ones that designed a lot of these programs.

LK: Okay.

When Larry Weaver stepped down as dean, they brought in Gilbert Banker.

RV: Yes.

LK: Were you at all involved in his appointment as dean or do you have any comments on his leadership?

RV: No, I was just one of the faculty who had to vote, probably. We voted and, then, you vote for tenure, so nobody is going to come here as a dean without that. That was about my extent. I wasn't part of the search committee.

He came in. I liked him. He was good. He was a real tall guy. I remember we had a Christmas party once, when people still had Christmas parties, and he was Santa Claus. He looked so funny. And Larry was short. Larry, because he was short, had his desk cut down a little bit. Then, when Banker came in, I went in Banker's office one day, and he was sitting at the desk, and he had it up on about three phone books underneath each leg.

[laughter]

RV: It was funny. He was so tall.

LK: I had read that he provided a lot of support for Medicinal Chemistry and hiring new faculty.

RV: Yes, he was good. I liked him. He was good. He took an interest in everything that was going on. He was easy to talk to. He wasn't here that long.

LK: About six, seven years.

RV: It was that long? Okay.

LK: That's what my timeline says. Then, Robert Cipolle stepped in for four years.

RV: Oh, yes.

LK: Did Banker retire or did he...?

RV: No. He actually left here. I don't remember what circumstances. There was something that he wanted and he didn't get it. He kind of left. Maybe it had something to do with some program that he was having a hard time getting it approved and everything. I think he finally got frustrated. Don't quote me on that.

LK: Okay.

RV: He actually left here for some reason.

LK: Do you know if the College of Pharmacy was experiencing a lot of retrenchment in this period? That's a theme that I've seen within the other schools in the Academic Health Center.

RV: I don't ever remember any time when we were experiencing any retrenchment. It seems like they'd keep increasing and adding more and more people. There may have been a short period some time. I know when the new dean, [Marilyn] Speedie, came in, a lot of people left. Maybe they were replaced with other people. But it wasn't kind of retrenchment.

LK: Okay.

RV: She just had, maybe, some different ideas about programs, so some people figured, well, okay. All I've ever seen is the thing growing. I'm surprised at how many people keep getting hired when they talk about not hiring people.

LK: Right.

RV: I don't know where they're getting the money from.

LK: Did you do any work on the Admissions Committee for the College, at all?

RV: No.

LK: Did you work at all with Lyle French when he was senior vice president of Health Sciences?

RV: I was here. Just the dean kind of had contact with him. You probably had to be a dean to talk to him. We didn't have any direct exposure to him, except through our dean.

LK: Okay.

Any of the other vice presidents...?

RV: I knew Cherie Perlmutter. She was kind of an interim. I knew her probably before that, so it was more like I didn't think of her as somebody I couldn't talk to. Anytime anything came up that I thought was important, I would talk to her about it. She was good. I liked her.

LK: Did you do any work at all with the State Legislature?

RV: No, just writing letters when we were asked to about various things.

[laughter]

RV: Most of that stuff was about the practice of pharmacy and the profession itself. I was not part of that. I was more of a professor in Medicinal Chemistry. I didn't know enough about those things to talk to legislators.

LK: That kind of rounds out my questions. I didn't know if you had any final comments on the Academic Health Center or is there anything that I didn't ask you about your own work that you want to talk about?

RV: No. Whatever you're interested in... The Academic Health Center is... I like the idea of it, you know. It has all these different deans and schools and everything. We're unique within the Academic Health Center because we're a center that isn't part of

another college. So a lot of people aren't used to that. So they try to keep putting me back in the College. There are a lot of rules that were all set up for departments and deans and department heads that when we go to do something, there's no precedent for it, like this teaching thing. We'd love to teach. We think we can really teach some good courses and even have people come here from other...like industry. We know how to design drugs and that's what they want to know. Yet, when we ask the Academic Health Center if we can use the designator [number] and they say, "No, you can't use it because you're not part of the College." I feel, because we're unique, there are still people who don't know how to deal with us, I guess.

LK: I know there are tons of centers and institutes within the various colleges within the Academic Health Center. Do you think this idea of the independent center is pretty novel?

RV: Yes.

LK: It is here, but...

RV: It is here. I don't know about other places. The only reason we can do it is because we don't ask anybody for any money. All the other centers go through some department or whatever, and they have to get their funding through that department.

LK: Right.

RV: So they try to get a budget. They're always asking for money, etcetera. We don't ask anybody for anything. So that does make us unique.

LK: Yes.

RV: The only thing that we ask for is some space. We're willing to pay for it. They do charge for square footage, and we pay for that, you know. It is somewhat unique. But everybody isn't completely aware of what we do. They just assume we're part of something else.

LK: Do you know of any other centers similar to your own at other universities?

RV: Oh, there are a lot of drug design and discovery centers. There's one at Harvard [University] and Yale [University]. They just recently have put together what we call a consortium of all these centers, and they've asked us to join that, which we did.

LK: Oh.

RV: Now, they're having a symposium someplace coming up. There are centers around. There are things called drug design centers or discovery. Yes, there are. There are several of them around the country. There are some in England.

In fact, when we started trying to design something to teach, we went and looked up all these other centers to see what they do, even in England. A lot of them do some teaching, so we thought this would be great. We want to do this, too. We patterned some of our stuff and, then, we run into this roadblock about getting a designator number. If we have to go then and ask the College, then we're really teaching through the College, and we're not really teaching through the Center anymore. We think that we can do a good job because we have some real experts in drug design.

LK: Right. It seems like an interesting opportunity to bring together students from different schools within the Academic Health Center, kind of playing on that idea of collaboration.

RV: Yes. We have people in different departments who collaborate with us. Our people teach in their courses. We've talked to Chemistry, and we've talked to Pharmacology about having a course and maybe we can go through them. They love the idea. Maybe if you do talk to Frank, he knows more about our Center probably than anybody else. You might want to ask him about that.

LK: Yes. I'll make a note of that.

RV: He can answer any of your questions about our Center, the way it's designed, and why it is the way it is, and how unique it might be. But our uniqueness has been somewhat of a barrier to certain things, because if you go to do something, they might not know how to handle it. For example, if we go to the vice president's office or whoever is in charge of teaching, the provost, they don't know. They say, "Aren't you part of the College of Pharmacy?" "No." They've never dealt with that before. I used to rely on Frank to kind of pave the way for us. He's not there anymore. We've got a new person, but he's on his way out, Aaron Friedman. They're looking for a new person to replace him.

LK: Right.

RV: Then, Frank was the vice president for Academic Health Center. Period.

LK: Yes.

RV: But, then, they combined that later. When he decided he was going to retire from that, they decided to change it to vice president plus dean of the College of Medicine. A lot of people feel there's a conflict there.

LK: Yes, I can understand that.

RV: When we're going to get space, for example, we're asking the dean of the Medical School, of course, they're going to take care of the Medical School people first. So if anybody in the Medical School wants something, they get it before we get it. Then, the other people like the vice president for research in the Academic Health Center, is in the

Medical School. What we need is where everybody isn't in the Medical School if this is going to really be an Academic Health Center.

LK: Right.

RV: In my opinion, it's too much weighted toward the Medical School.

LK: I have one final question that I wanted to ask you that's not related to this. When did you meet [President] George W. Bush? I saw your picture...

[laughter]

LK: Did you go to the White House?

RV: No. He came here. He was a friend of Mark Yudof.

LK: Oh, okay.

RV: He came from Texas. Yudof had been in Texas before he came here.

LK: Where was he in Texas?

RV: I think he was at one of the universities in Texas [University of Texas, Austin]. Of course, since he was the president of the university there, and Bush was the governor at the time, they probably knew each other.

So Bush went—this was just after he got elected [president] the first time—around to all these places. [Former President George W. Bush visited the University of Minnesota Academic Health Center on July 11, 2002. He and then University President Mark Yudof were took part in a roundtable discussion on advances in research, new drug therapies, and ways to improve care.] He wanted to develop a new program, something to do with healthcare. He wanted to talk to all aspects of healthcare, some patients, some nurses, some doctors, some researchers. Before he came here, they wanted two researchers and the University chose me and Karen Ash to speak. He came. There was this big room and there were about twenty people in there all sitting around. One of the things that impressed me about him was that he came in, and he sat down, and we each had about a minute and a half to tell him what we did.

LK: Oh, wow.

RV: I told him what I did and as did the other people. There were even some patients there. After we got through, we got in this motorcade and went downtown. He gave a speech down there. They let us all sit in this one section, the people who had been talking to him. After his speech, he came over to our section, and he shook hands with each one of us, and he mentioned our name. He remembered our names and what we did.

LK: Oh, wow.

RV: When he came to me, he said, “Bob, go make more drugs.”

LK: [chuckles]

RV: People used to say, “Oh, Bush, he’s so stupid.” I was really impressed.

One of the guys that was there that I met and who came... They were all from Minnesota except this one guy that was there who sat next to me. He was from the State of Washington. He is a grandson of what’s his name? The guy that flew across the Atlantic [Ocean] the first time. [Charles A.] Lindbergh. He was Lindbergh’s grandson, Erick Lindbergh. He was really interesting, a nice guy. I said, “How come you’re here?” He said, “Bush invited me. I did this commercial...” I said, “Hey, I saw that commercial.” He was in a wheelchair, this grandson. He couldn’t walk; he had arthritis so bad. He took some drug that they were advertising and, then, they showed later that he got so well that he actually repeated the flight that his grandfather had done.

LK: Wow!

RV: Bush had seen that. He was so impressed that he wanted him to be here for this, because these were all different aspects of medicine. It was very interesting. Anyway, that’s when I met him. I can’t remember the year, but it was after the first time he was elected.

LK: Well, great.

RV: So it was fun.

LK: Yes. Any final thoughts?

RV: No. I hope I didn’t bore you going on and on about things that probably had nothing to do with the Academic Health Center.

LK: No, no. This was great. Thank you so much.

RV: Thank you.

[End of the Interview]

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